# Agricultural Biotechnology

Title: SBIR Phase II: Disease Block - Genetically Engineered Plants with Disease Resistance

Award Number: 0111331
Program Manager: Om Sahai

Start Date: September 1, 2001
Expires: August 31, 2004
Total Amount: $500,000
Investigator: Chandrika Ramadugu, ramadugu@ipgenetics.com
Company: Integrated Plant Genetics
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Phone: (386)462-0880

Abstract:

This Small Business Innovation Research (SBIR) Phase II project is to produce transgenic citrus and rice plants carrying novel gene fusions for the purpose of controlling citrus canker and rice blight disease. The fusions consist mainly of peptide aptamers and single chain variable region fragments from monoclonal antibodies (SCFVs) that bind to and interfere with bacterial pathogenicity (Pth) proteins that must be injected by the pathogens into host cells to cause disease. Fusions will be selected that show improved binding at physiologically appropriate pH and temperature ranges by BIAcore analyses. Binding affinities of aptamer SCFV fusions over a range of pH and temperatures will be determined.

The Phase II project will lead to a new, cost-effective genetic method to control a variety of important plant diseases caused by bacterial plant pathogens. Commercial potential would be to the agricultural and forest industries.

Title: SBIR Phase II: Device for In-ovo Targeting and Delivery to the Early Chicken Embryo

Award Number: 0522040
Program Manager: George B. Vermont

Start Date: September 1, 2005
Expires: August 31, 2007
Total Amount: $494,265
Investigator: Phillip Rybarczyk, prybarczyk@embrex.com
Company: EMBREX, INC.
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Phone: (919)941-5185

Abstract:

This Small Business Innovation Research (SBIR) Phase II project integrates the imaging system developed in Phase I with a smart-sensor injection system that can inject or sample from the cavity underlying the early chicken embryo with high levels of accuracy accompanied with improved hatch when compared to manual methods. The Phase I work showed that it was possible to image and detect the blastoderm in the presence of a biological membrane with high levels of accuracy (94%). The Phase II project will focus on the technology required to build an injection system using smart sensors that can detect and then move to the fluid cavity to inject (or to sample). The system will thus provide a totally automated solution to early embryo detection and manipulation, with movement in all three dimensions, while still sustaining hatchability of the developing chicken. This research would advance the state of the art for the production of chimeric chickens with superior traits or for producing transgenic chickens for the avian pharmaceutical industry.

The commercial application of this technology is in two large, important industries. In the commercial poultry industry, chimeric chickens could be created in a high-throughput system that possess desired traits like disease resistance (for example, to diseases such as Marek's, Newcastle and Coccidiosis), increased tolerance to stress, and the ability to digest certain feed compounds such as phosphates. Secondly, in the avian pharmaceutical industry, therapeutic proteins used for manufacturing drugs could be created much more cheaply by using a transgenic chicken that can produce transgenic proteins in its eggs. Many therapeutics for diseases like cancer and leukemia are manufactured in mammalian or bacterial systems that face bottlenecks in supply and are extremely expensive to produce. The proposed device advances the state-of-the-art in early embryo injection beyond the limits of the manual method so as to allow a faster, more accurate way of producing transgenic chickens and proteins

Title: SBIR Phase II: Quantitative Detection of Bacterial Pathogens in Seeds by Use of a Novel Enrichment Technique Coupled with Automated Real-Time PCR

Award Number: 0450649
Program Manager: George B. Vermont

Start Date: May 1, 2005
Expires: April 30, 2007
Total Amount: $500,000
Investigator: Parm Randhawa, randhawa@calspl.com
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Elverta CA, 95626
Phone: (916)655-1581

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims to develop a highly sensitive PCR-based diagnostic kit for the detection of pathogens in crop seeds. Seed health testing is important in order to identify infected lots that should be excluded from seed sales. Because only a few seeds in a seed lot are usually infected, highly sensitive test methods are needed. The standard method consists of extracting the pathogen into a buffer followed by plating on selective media to isolate the pathogen or identification by PCR. A major limitation of this method is that only a small sample (0.1 ml) can be tested on an agar plate, which gives a maximum sensitivity of only 10 cells per ml. In this project, a novel device called Ampli-disk, has been developed, that allows testing of a 4 ml sample. Further, this Ampli-disk can be stored and used, as needed, unlike agar plates that require fresh preparation for each use. Prior Phase I research has shown that pathogens from seed extracts can be successfully detected and quantified by using Ampli-disk coupled with real-time PCR. In the Phase II project, the objective is to develop Ampli-disks and real-time PCR primers and probes into diagnostic kits for ten most important bacterial pathogens of vegetable crops.

The commercial application of this project will be in agriculture. The proposed technology will be useful to the seed industry and in other bacterial disease diagnostics

Title: SBIR Phase II: Developing Crop Plants with Wide-Spectrum Disease Resistance

Award Number: 0450162
Program Manager: George B. Vermont

Start Date: September 1, 2005
Expires: August 31, 2007
Total Amount: $462,138
Investigator: Karen Century, kcentury@MendelBio.COM
Company: Mendel Biotechnology Incorporated
21375 Cabot Boulevard
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Phone: (510)264-0280

Abstract:

This Small Business Innovation Research (SBIR) Phase II project focuses on developing genetically engineered, broad -spectrum disease resistance in plants. An Aribdopsis transcription factor, TDR1, has been identified that causes resistance to three pathogens when overexpressed in transgenic plants. However, constitutive expression of TDR1 or any of three related genes causes growth retardation. Phase I research demonstrated that using tissue specific or inducible promoters to drive the TDR1 genes confers resistance with reduced side-effects. The research objectives of the Phase II project are to test the limits of TDR technology by assaying a broad range of pathogens, optimize the TDR phenotype by mutagenesis, demonstrate TDR function in a crop plant (tomato), and use microarray analysis to correlate gene expression patterns with specific pathogen resistance spectra in Arabidopsis. The results will establish the commercial utility of TDR technology.

The commercial application of this research will be to engineer wide-spectrum disease resistance in crops such as soybean and maize. Chemically based disease management is expensive, harmful to people and the environment, and not always effective. Breeding has long been used for developing resistant cultivars, but the gene pool is limited by reproductive barriers, the technique is slow, and the resistance is generally narrow in scope and often not durable. There clearly is a market for genetically-engineered, durable disease resistance. The main societal benefit of this project is expected to be a decrease in the use of toxic fungicides, which will positively impact the environment and human health.

Title: SBIR Phase II: Implementation of Sex Pheromone-Based Systems to Suppress Populations of Soybean Aphids

Award Number: 0450032
Program Manager: Michael R. Ambrose

Start Date: January 15, 2005
Expires: December 31, 2006
Total Amount: $499,223
Investigator: Junwei Zhu, jwzhu@iastate.edu
Company: MSTRS Technologies Inc.
2501 North Loop Drive
Ames IA, 50010
Phone: (515)294-5930

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop sex pheromone-based techniques for monitoring, mass trapping, and mating disruption of the soybean aphid. Since its first appearance in North America, infestations of the newly invasive soybean aphid, Aphis glycines Matsumura, have continued to cause a significant soybean yield loss due to either direct feeding damage or the vectoring of plant viruses by the aphid. In 2003, the total acreage with soybean aphid infestation was estimated at over 8 million, with yield loss ranging from 32% - 45% in the three biggest soybean growing states in the U.S. (Illinois, Iowa and Minnesota). This project will investigate novel suppression strategies to reduce populations of this pest, thereby reducing the size of the subsequent populations feeding on soybeans.

The commercial application of this project will be to manage aphids in the soybean crop. The research aims to increase knowledge of the chemical ecology of aphids, as well as provide a new understanding of how to use these novel aphid sex pheromone-based control strategies most effectively. This will help growers in the U.S., the world's largest soybean exporting country, to improve crop quality and yield at a minimal cost for soybean aphid management, thereby increasing their competitiveness in the world market.

Title: SBIR Phase II: Microbial Enhancement of Soybeans for Salmonid Diets

Award Number: 0449453
Program Manager: Michael R. Ambrose

Start Date: February 15, 2005
Expires: January 31, 2007
Total Amount: $499,400
Investigator: Clifford Bradley, cbradley@montana.com
Company: Montana Microbial Products
1830 Ronald Ave
Missoula MT, 59801
Phone: (406)544-1176

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims to develop a process for enhancing the nutritional value of soybeans to replace fishmeal as the primary ingredient in farmed trout and salmon feed. Fishmeal creates environmental and economic constraints for the aquaculture industry. Plant-derived proteins are a good alternate feed source, but do not meet the nutritional requirements of many farmed fish species including trout and salmon. Prior Phase I work demonstrated that a combination of a selected fungal strain with innovations in solid substrate culture (SSC) would increase the protein content, eliminate the non-digestible carbohydrates and reduce anti-nutritional factors in soybeans. This Phase II project will test pilot-scale SSC technology to determine engineering design and economics for a commercial process to manufacture the bio-enhanced soy protein, and to demonstrate the feed value of this protein in trout feeding trials.

The commercial application of this project will be in the aquaculture industry. The use of fishmeal creates economic, market and water pollution issues for fish farmers, and consumer concerns regarding environmental impacts (for example, there are reports of PCBs, dioxins, and other pesticides detected at higher levels in farmed salmon that have been fed fishmeal based diets). Replacing fishmeal with plant based proteins will promote health through increased fish consumption and will alleviate environmental and economic constraints facing the aquaculture industry.

Title: SBIR Phase II: A Gene Targeting System for Plants

Award Number: 0422159
Program Manager: Om P. Sahai

Start Date: August 1, 2004
Expires: July 31, 2006
Total Amount: $499,999
Investigator: David Wright, wright@phytodyne-inc.com
Company: Phytodyne, Inc.
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Ames, IA 50010
Phone: (515) 296-5513

Abstract

This Small Business Innovation Research Phase II project will develop a non-transgenic approach for genetic improvement of crops by using a zinc-finger nuclease strategy for homologous recombination in plants and a strategy for selection of non-selectable phenotypes. The commercial application of this project will be to enable the production of new crop varieties, including those that better withstand pests, have enhanced food value, and produce compounds of industrial importance.

The proposed approach is expected to produce genetically modified (GM) plants requiring less regulatory oversight than existing technologies for plant genetic engineering, facilitating faster and less expensive marketing of GM plants.

Title: SBIR Phase II: Nematode Intestinal Proteins as Anthelmintic Targets

Award Number: 0349756
Program Manager: Om P. Sahai

Start Date: February 1, 2004
Expires: January 31, 2006
Total Amount: $461,021
Investigator: Michelle Hresko, hresko@divergence.com
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St. Louis, MO 63141
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Abstract

This Small Business Innovation Research Phase II project proposes to develop transgenic roots that are resistant to nematode infection, through expression of small proteins, protein domains or peptides which when ingested by the nematode interfere with the function of essential proteins of the nematode intestine. The longer term goal of the project is to develop transgenic crops (soybeans, corn and cotton), that are resistant to parasitic nematodes. In Phase I research, essential proteins exposed in the nematode intestinal lumen were identified as outstanding targets for anti-nematode agents produced by plants. These proteins are accessible to the environment since the lumenal membrane of the intestine is the surface through which nutrients are absorbed by the nematode. This Phase II project is expected to show that transgenic expression of nematode intestine-toxic peptides at the site of infection would create inhospital host plants for plant parasitic nematodes and would result in resistant crops which do not require application of toxic chemicals for nematode control.

The commercial impact of this project will be on nematode control in major crops. Plant parasitic nematodes are reported to cause $80 billion in crop yield damage annually. The current chemical solutions are limited, environmentally damaging, and toxic to the applicators. Transgenic resistance to nematodes will provide an economically competitive and environmentally safe alternative.

Title: SBIR Phase II: Engineering Broad-Spectrum Disease Resistance in Crop Plants

Award Number: 0349577
Program Manager: Om P. Sahai

Start Date: January 1, 2004
Expires: December 31, 2005
Total Amount: $498,460
Investigator: Teresa Reuber, lreuber@mendelbio.com
Company: Mendel Biotechnology Incorporated
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Hayward, CA 94545
Phone: (510)264-0280

Abstract

This Small Business Innovation Research (SBIR)Phase II project proposes to further optimize the techniques for engineering broad-spectrum disease resistance in crop plants. Protection of crops against pathogens is one of the most significant unmet needs in agriculture. Despite billions of dollars spent on fungicides and other crop protection chemicals, significant economic losses continue to occur every year. Prior Phase I work has established that overexpression of the transcription factor AtERF1 confers resistance against several fungal pathogens in Arabidopsis thaliana. The objectives of the Phase II project are to characterize AtERF1 crop homologs, to demonstrate AtERF1 function in the tomato crop, to optimize the technology by targeting expression to different tissues, to broaden the spectrum of resistance through combinatorial expression with other transcription factors, to optimize AtERF1 function by creating derivatives with enhanced activity, and to improve understanding of AtERF1 function by characterization of targets in Arabidopsis and tomato.

The commercial impact of this project will be significant as there is clearly a market need for conferring broad spectrum disease resistance in economically important crop plants.

Title: SBIR Phase II: Increased Freezing Tolerance in Plants

Award Number: 9983311
Program Manager: Om P. Sahai

Start Date: June 1, 2000
Expires: May 31, 2004
Total Amount: $752,000
Investigator: James Zhang, jzhang@mendelbio.com
Company: Mendel Biotechnology Incorporated
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Abstract

This Small Business Innovation Research Phase II project will establish the feasibility of improving the freezing tolerance of canola and wheat plants. Phase I research has demonstrated that Arabidopsis plants show dramatic improvements in freezing tolerance when expressing the CBF gene. However, constitutive expression of the CBF gene was found to be detrimental to plant growth. This Phase II research will determine whether inducible promoters provide freezing tolerance with normal plant growth. Our Phase I and other published work has indicated this approach is very promising. The project goal is to produce enhanced freezing tolerant canola plants, with commercially efficacious growth levels, and provide the molecular biology tools to similarly engineer wheat plants. Canola with improved winter hardiness would be a new high value crop for the US with a value of at least $300 M, as this amount of canola oil is imported annually, and provide a new winter crop rotation system. The project results will also lead to improved winter hardiness in wheat that would improve wheat yields by $940 M. Applications in additional crops such as corn (1995 frost losses of more than $1 Billion), barley, soy, strawberries, and eucalyptus will likely follow once demonstrated in canola. Mendel has targeted canola and winter wheat for the initial applications of the WeatherGard TM enhanced freezing tolerance technology. Spring canola with increased winter hardiness will be a new winter crop suitable for the southern US. Existing spring canola varieties don't survive the winters well enough. WeatherGard TM winter canola will have increased winter hardiness that will allow it to be grown in the midwest. Existing winter canola varieties don't survive midwestern winters very well. One estimate of the value of the trait is that up to 50% of the winter wheat acres or 24 M acres would switch to canola due to its higher profitability and the advantages of crop rotation. Currently wheat is the only widely grown winter crop, so farmers would rotate it with winter canola. The higher oil and protein content of canola creates a higher per bushel value than wheat, translating to a $30/acre increase in value when growing canola. On 24 M acres this higher value crop would create $720 M of new value for farmers. Additional value will be derived from the increased productivity from better crop rotations and the double cropping potential of canola harvested in May. These latter values are hard to estimate in advance but clearly are very large. At a minimum valuation, the US imports $300 M of canola oil annually, so the US canola crop should create at least that much value. Additionally canola is an important crop worldwide (rapeseed) so export opportunities exist as well.

The expected economic benefits of winter wheat are to be in excess of $940 M dollars of extra yield for the US farm economy annually. This assumes that the northern portion of the midwest, particularly North Dakota and South Dakota, that currently can only grow spring wheat, could grow the new variety as a winter wheat with an known 25% yield advantage which represents $500 M dollars of added value. The remaining 80% of the US wheat market should also benefit from increased winter hardiness as sudden frosts after warm spells, very cold freezing temperatures and winter desiccation (essentially drought) are all common problems experienced to various amounts every winter. Improved winter hardiness is estimated to improve winter wheat yields by 10% for an increase in value of $440 M. Thus the combined canola and wheat projects could add over $1.2 to $1.6 billion annually to the US farm economy.

Title: SBIR Phase II: Multispecies Ecological Valuation and Landscape Management

Award Number: 9983279
Program Manager: Om P. Sahai

Start Date: April 1, 2000
Expires: March 31, 2002
Total Amount: $400,000
Investigator: Karen Root, kvroot@bgnet.bgsu.edu
Company: Applied Biomathematics Inc
100 North Country Road
Setauket, NY 11733
Phone: (631)751-4350

Abstract

This Small Business Innovation Research (SBIR) Phase II project will refine, validate, and extend new methods developed in Phase I to compute the community-level risk of extinction or demographic threat for individual sites or landscapes and assign a multispecies conservation value. The objective of such methods is to provide a statistically valid approach to ecological valuation and landscape management. This research will provide an independent measure of the value of a particular site based on its ecological components, i.e., species, and the threats facing it. The new methods will estimate a multispecies conservation value as a spatially explicit weighting of species-specific habitat suitability maps by their respective species-specific extinction risks. This research will also develop a multivariate generalization of recently described exact methods for computing risk of extinction for species of which little is known.

Two potential areas of commercial applications of this project include software sales and case studies. The final product of the proposed research will be part of RAMAS Library of Ecological Software, and will be made available to potential users in overnmental agencies and industrial companies.

Title: SBIR Phase II: Expression Pattern Screening for Agriculture Genomics

Award Number: 0110472
Program Manager: Om Sahai

Start Date: August 1, 2001
Expires: July 31, 2003
Total Amount: $500,000
Investigator: Richard M. Kris, richardkris@earthlink.net
Company: NeoGen, LLC
PO Box 64326
Tucson, AZ 85718
Phone: (520)906-2002

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will use a novel high throughput platform comprising of many, small gene arrays, contained within the wells of microliter plates. This platform, termed Multi-Array Plate Screening (MAPS), allows simultaneous testing of the expression of a specific group of genes of interest and appropriate controls using RNA derived from 96 separate samples, within each well of a 96-well plate. MAPS provides the endpoint assay for a high throughput screen, in which investigators can evaluate how different chemical compounds, applied to cells, tissues, or organisms in vivo, affect the expression pattern for the genes of interest.

This technology will address an unmet need of the agricultural industry to make efficient use of novel genomics information in a manner that does not require distribution of genetically modified organisms (GMOs) in the form of transgenic plants. The plants are grown in each well of a 96 well plate to facilitate high-throughput screening. The platform allows facile and efficient testing of gene targets including newly identified genes, and also provides important information about selectivity and specificity. The commercial potential from this project is in the agricultural market.

Title: SBIR Phase II: Atlantic Cod Nodavirus Vaccine

Award Number: 0724041
Program Manager: F.C. Thomas Allnutt

Start Date: July 15, 2007
Expires: June 30, 2009
Total Amount: $499,393
Investigator: Eric Anderson, mainebiotek@hotmail.com
Company: Maine BioTek
259 Main Street
Winterport, ME 04496
Phone: (207)223-4662

Abstract:

This Small Business Innovation Research (SBIR) Phase II project of develops a recombinant vaccine for the prevention of nodavirus disease of cultured Atlantic cod, fisheries of growing importanct to New England and Atlantic Canada. The recombinant technology used to build the vaccine is economical, safe and results in a potent and efficacious product that improves cod health. The research addresses recombinant antigen synthesis, formulation, safety, potency and efficacy. After translational development, manufacturing and regulatory approval, the vaccine will be available to cod producers for the prevention of nodavirus disease.

The broader impacts of this research will be to enable more facile development of the nascent cod aquaculture industry in respect to methods of viral disease control through vaccination. This is in concert with the desire of the nation to increase aquacultural production significantly by 2020 without impacting the ocean environment negatively.

# Biochips/Biosensors

Title: SBIR Phase II: Microfabricated Silicon Devices for Low Cost Microarray

Award Number: 0321601
Program Manager: Om Sahai

Start Date: August 1, 2003
Expires: July 31, 2005
Total Amount: $498,714
Investigator: Robert C. Haushalter, bob@parallel-synthesis.com
Company: Parallel Synthesis Technologies, Inc
333 Ravenswood Ave.
Menlo Park, CA 94025
Phone: (650)859-2112

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop a new, commercially viable micromachined silicon technology platform for the printing of DNA microarrays that offer significant advantages over current steel pin technology in cost and in quality. The Phase I effort demonstrated very clearly that a silicon pin reliably imbibed DNA printing solution and deposited spots with a size variance better than that of commercial steel printing pins. Phase II work will focus on the development of a new micromachining protocol based on a combination of wet and dry etching that will allow sculpting of the print tip in all three dimensions. This, in turn, will permit the size, shape and fluid delivery characteristics of the tip to be finely tuned. Printing tip sizes (range: 125 microns x 125 microns to 25 microns x 25 microns) and uptake volumes (range: 0 to 100nL) will allow the pins to precisely take up and deliver any volume or spot size/shape desired. Combined with a much denser packing of pins into a newly designed, all-silicon holder, these attributes will allow DNA microarrays to be fabricated at a cost, speed and quality previously unobtainable.

The commercial application of this project is in the area of DNA microarrays. Due to the weaknesses in the current manually machined steel pins used for printing DNA microarrays (such as extremely high manufacturing costs and low yield, poor pin-to- pin uniformity, the limited range of spot sizes deposited, waste of valuable DNA in uptake and delivery dead volumes, and deposit variability with time due to rapid tip wear), there is an urgent need for an improved printing technology. The new micromachined silicon-printing product to be developed in this project will largely eliminate these drawbacks, and they will be well positioned for market entry as a replacement for existing products by virtue of its lower cost, superior accuracy and speed.

Title: SBIR Phase II: Sensor for Real-Time pH Measurements in Gases

Award Number: 0522325
Program Manager: Michael R. Ambrose

Start Date: August 1, 2005
Expires: July 31, 2007
Total Amount: $500,000
Investigator: Jeffery Schipper, jeff@sierramedical.com
Company: Sierra Medical Technology Inc.
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Poway CA, 92064
Phone: (858)679-2300

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims to develop and market the trademarked Dx-1 pH Measurement System. This medical device integrates the breath pH sensor studied in the Phase I research with an ambulatory, telemetry based data recorder, and data analysis software to provide a non-invasive pH diagnostic tool required by physicians. This pH sensor actively condenses a moisture film on the sensor surface, creating a conduction path across its sensing electrodes. During Phase II, the company plans to complete all technical and regulatory activities in order to gain FDA clearance for product introduction.

The commercial application of this project is in the area of medical devices. The proposed sensor technology will offer a new tool for clinicians to more effectively diagnose and treat respiratory diseases, particularly for children and infants who cannot readily undergo alternative diagnostic procedures.

Title: SBIR Phase II: Ultra-High Sensitivity Surface Plasmon Resonance (SPR) Sensor for Real-Time Botulinum Detection

Award Number: 0522014
Program Manager: George B. Vermont

Start Date: August 15, 2005
Expires: July 31, 2007
Total Amount: $499,800
Investigator: Paul Melman, melmanp@newtonphotonics.com
Company: Newton Photonics
104 Manet Rd
Chestnut Hill MA, 02467
Phone: (617)928-1221

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop a prototype botulinum toxin detector based on a novel ultra-sensitive Surface Plasmon Resonance (SPR) technology. The botulinum toxin will be detected by means of the specific cleavage of a peptide substrate attached to the sensor surface. The system will provide results in a fraction of the time and at a much lower cost compared to currently available methods. The feasibility of this technology was successfully demonstrated in Phase I. The research in Phase II will include assay optimization for detection of botulinum types A and B, development of a toxin extraction protocol from complex solutions, and construction of an instrument for multiplexed detection of botulinum toxins. The developed instrument will have the capability for ultrasensitive detection of Botulinum A and B (comparable to the sensitivity of the mouse LD50 assay) on a single chip.

The principal commercial application of this project will be in the detection of biothreat agents. The proposed work, though initially aimed at rapid detection of botulism in individuals and in foods, will be extendable to other biothreat agents such as anthrax and mycotoxins. Additional applications are expected in drug discovery and biomedical research, and for potency testing of botulinum products in medical and cosmetic applications.

Title: SBIR Phase II: ELISA Biosensor for Rapid Bioterrorism Related Agent Diagnosis

Award Number: 0450635
Program Manager: Michael R. Ambrose

Start Date: January 1, 2005
Expires: December 31, 2006
Total Amount: $468,453
Investigator: Winston Ho, winstonho@maxwellsensors.com
Company: Maxwell Sensors Inc.
10020 Pioneer Blvd., Suite 103
Santa Fe Springs CA, 90670
Phone: (562)801-2088

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop a self-contained enzyme-linked immunosorbent assay (ELISA) biochip for rapid and confirmatory clinical diagnosis of multiple bio-threat pathogens such as antigens, antibodies, toxins, and viruses. The ELISA chip utilizes microfluidic technology to automate and simplify the assay process on a small chip platform. The plastic chip (reagent pre-loaded) will be affordable and ready for use, and will eliminate the need for a network of tubing connected to bulky external reservoirs and pump systems used in current large clinical laboratory systems. Prior Phase I work successfully developed the microfluidic chip platform and the reader system, and performed assays with anthrax toxin protective antigen (PA) and Francisella tularensis. The Phase II project will focus on system optimization, integration and panel tests, and will result in a prototype to be refined into a commercial product in Phase III.

The commercial application of this project will be in the area of homeland security, for detecting biological warfare agents (BWA) and in managing BWA suspected patients. The ELISA based biochip has the potential to be used as a rapid testing standard to quickly yield preliminary data in advance of microbiology tests. The system, with its extreme sensitivity and specificity, also offers commercial opportunities in the field of clinical diagnostics

Title: SBIR Phase II: Novel Bioaerosol Concentrator/Sampler for Enhanced Biosensor Performance

Award Number: 0450612
Program Manager: George B. Vermont

Start Date: March 1, 2005
Expires: February 28, 2007
Total Amount: $469,973
Investigator: Steve Wright, wright@novafilter.com
Company: Innovatech Inc
6320 Angus Dr Suite C
Raleigh NC, 27617
Phone: (919)881-2197

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop a robust, generic, front-end, bio-sampler that when combined with either a wet or dry biological detector, will result in more accurate and rapid detection of hazardous airborne biological agents. While most current systems require samples to be delivered in a fluid for analysis, emerging dry detection technologies facilitate near-real time detection, reduce sampling errors and allow for unattended operation. The prototype bio-sampler developed in Phase I demonstrated very high efficiency in the dry collection mode. This Phase II project has the following objectives: (a) to optimize sampling performance for particles at the low end of the range (<2 micron), (b) to maintain high bio-viability of collected organisms, (c) to function efficiently in the wet or the dry mode, (d) to demonstrate self-cleaning / decontamination features, (e) to evaluate scalability to larger air volumes and, finally, (f) to demonstrate enhanced overall performance in an integrated biological detection system.

The commercial application of this project will be in the area of homeland security and public safety. The proposed technology will enhance the performance of both the detection systems that are presently deployed and that of the advanced biological detectors that are currently under development. Additional applications will be in the monitoring of the environment and of industrial air quality.

Title: SBIR Phase II: X-ray Microscope for In-Vivo Biological Imaging

Award Number: 0450518
Program Manager: George B. Vermont

Start Date: February 1, 2007
Expires: January 31, 2007
Total Amount: $494,620
Investigator: Charles Gary, cgary@adelphitech.com
Company: Adelphi Technology, Inc
981B Industrial Rd
San Carlos CA, 94070
Phone: (650)598-9800

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims to develop a sub-micron x-ray tomography scanner capable of providing in-vivo and high resolution images of specimens from mice to bacteria. In this era of molecular medicine, where disease and developmental disorders are being re-defined by their peculiar molecular, genetic or cellular profiles, there exists a significant disparity between the type of information gleaned from histological methods and that obtained from conventional non-invasive imaging modalities. With a resolution that is better than these imaging modalities and more than ten times higher than that of current x-ray imaging systems, the proposed device will generate images of development and disease not possible by current methods. The Phase II research will concentrate on the development of the x-ray optical system, including beam conditioning, tomographic imaging capability, and the imaging x-ray lens, and will result in a table-top commercial prototype computerized tomographic imager with 400 nm resolution.

The commercial application of this project will be in the area of medical research. When compared to existing in-vivo imaging technologies, the higher resolution of the proposed x-ray imager will translate to improved sensitivity and specificity of morphologic changes associated with growth and disease. Researchers will be able to use this tool for investigations of a number of medical conditions, including tumor angiogenesis, atherosclerosis, osteoporosis and arthritis

Title: SBIR Phase II: Electronic DNA Biosensor

Award Number: 0450472
Program Manager: Michael R. Ambrose

Start Date: February 1, 2007
Expires: January 31, 2007
Total Amount: $499,715
Investigator: Richard Murante, rmurante@integratednano.com
Company: Integrated Nano-Technologies LLC
999 Lehigh Station Rd
Henrietta NY, 14467
Phone: (585)334-0170

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop a portable, rapid, fully - automated, non-Polymerase Chain Reaction (PCR) based, electronic DNA identification device for field use that is capable of accurately detecting low concentrations of biological agents in a broad range of samples. Prior Phase I work demonstrated the feasibility of using palladium-catalyzed nickel to form conductive DNA wires for use in constructing this device. The Phase II project will further advance the DNA detection technology by refining the metallization protocol and integrating the technology into an automated, easy to use format.

The commercial application of this project will be for use by the military and / or for homeland security. The proposed biosensor system is expected to be readily incorporated into existing nuclear, biological and chemical (NBC) detection and reporting systems, enhancing total force protection by enabling the rapid identification, containment and neutralization of biological agents

Title: SBIR Phase II: Kits for the Detection of Bioterror Pathogens

Award Number: 0450469
Program Manager: George B. Vermont

Start Date: April 1, 2005
Expires: March 31, 2007
Total Amount: $499,257
Investigator: Brenda Spangler, brenda.spangler@sensopath.com
Company: Sensopatch Technolgoies, Inc.
2100 Fairview Drive
Bozeman MT, 59715
Phone: (406)585-8192

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop field deployable kits for the detection of bio-terror pathogens. These kits would consist of fluorescent-labeled antibodies directed against protein toxins expressed by bio-terror pathogens, relying for detection on strong antibody-antigen interactions and fast chromatographic discrimination using simple chromatography strips supplied with inexpensive pre-measured reagents. In Phase I project, new water soluble blue-emitting reporter fluorophores were synthesized that were extremely photo-stable and could be easily visualized under any type of light conditions. These fluorophores were conjugated to an antibody against Bacillus anthracis as the initial proof-of-concept, and methodology was developed to attach these reporter fluorophores to monoclonal, polyclonal or recombinant antibodies. The objectives of Phase II project are to optimize reagents and chromatography, to synthesize new fluorophores for multiplexed pathogen detection, to design and assemble prototype kits, and to test and validate the kits.

The commercial application of this project will be in the area of homeland security. The proposed kits are expected to be inexpensive, versatile, and easy to use by relatively untrained first responders (such as police, firefighters, paramedics, hazmat personnel, other emergency response teams).

Title: SBIR Phase II: Rapid Detection of Bacterial Contaminants Using Micro-Fluidic Biochips

Award Number: 0422150
Program Manager: Michael R. Ambrose

Start Date: November 1, 2004
Expires: October 31, 2006
Total Amount: $417,574
Investigator: Laila Razouk, laila.razouk@biovitesse.com
Company: Biovitesse, Inc.
1608 Crow Court
Sunnyvale CA, 94087
Phone: (408)738-4655

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will develop a microfluidic based system for the detection of viable pathogens using dielectric concentration of bacteria as an intermediate step. This system would use a first-stage concentrator, followed by dielectrophoretic concentration, and finally by culturing in media with integrated impedance measurements to detect culture growth.

The commercial application of this project will be on the detection of waterborne microorganisms in biopharmaceutical manufacturing operations. The proposed method would electronically detect the viability of microorganisms in water samples in less than 3 hours, unlike the current technology that takes 2-7 days to yield results.

Title: SBIR Phase II: Nanoelectronic Capnography Sensors

Award Number: 0421966
Program Manager: Om P. Sahai

Start Date: August 15, 2004
Expires: July 31, 2006
Total Amount: $498,969
Investigator: Alexander Star, astar@nano.com
Company: Nanomix, Inc.
5980 Horton St.
Emeryville, CA 94608
Phone: (510)428-5302

Abstract

This Small Business Innovation Research (SBIR) Phase II project will develop a carbon dioxide sensor, using polymer modified carbon nanotudes, for patients receiving anesthesia. The sensor technology relies on two important areas of expertise : the nanotube transducer platform and gas analyte recognition layers. The Phase II project objectives will include optimizing the platform and recognition chemistries that were developed in Phase I. Once a technically suitable recipe is known, sensor chips will be fabricated at the wafer level for large scale testing. The capnography sensors will be packaged and embedded in disposable adapters that fits directly into the patient airway. Hardware and software systems will be designed and integrated with the adapter to deliver sensor information to the end user. At the culmination of Phase II, the capnography sensor system will be validated in a clinical environment and positioned for FDA approval and subsequent market introduction.

The commercial application of this project will be in the area of healthcare. The proposed sensor will have the attributes of low power, small size and low cost.

Title: SBIR Phase II: A Biochip for DNA Detection

Award Number: 0422246
Program Manager: Om P. Sahai

Start Date: September 15, 2004
Expires: August 31, 2006
Total Amount: $499,989
Investigator: Kristian Scaboo, kscaboo@genorx.com
Company: GenoRx, Inc
3916 Trust Way
Hayward, CA 94545
Phone: (510)732-9100

Abstract

This Small Business Innovation Research Phase II project proposes to develop an inexpensive, automated, highly sensitive biosensor chip that would detect small quantities of nucleic acids directly without the need for either a reporter molecule reaction or a PCR expansion reaction. It is expected that the proposed molecular detection platform will provide unparalleled specificity and sensitivity while decreasing sample preparation time by a factor of twenty five, capital costs by a factor of twenty, and the cost of disposables, including the chip, by a factor of five.

The commercial application of this project will be in a number of markets, including biological and biomedical research, diagnostics and forensics.

Title: STTR Phase II: Novel Lipid Deposition for Biosensor Surfaces

Award Number: 0422010
Program Manager: Om P. Sahai

Start Date: September 1, 2004
Expires: August 31, 2006
Total Amount: $460,789
Investigator: Roger Van Tassell, vantassellr@lunainnovations.com
Company: Luna Innovations, Incorporated
PO Box 11704
Blacksburg, VA 24062
Phone: (540)552-5128

Abstract

This Small Business Technology Transfer Research (STTR) Phase II project will use the LPG (Long Period Grating) technology to interrogate the interactions between drugs and G-Protein coupled receptors (GPCRs). To effectively study these interactions, one has to stabilize the GPCRs by immobilizing them to lipid layers. This Phase II project will focus on optimizing the lipid selection, composition, and attachment to the GPRCs and to the surface of the sensor. The development of stabilized lipid based GPCR coating for the LPG biosensor will provide a valuable tool in the area of drug discovery.

The commercial application of this project will be in the area of new high throughput proteomics instrumentation to aid in the development of new therapeutic products.

Title: SBIR Phase II: Portable BioDetection Platform for Rapid Identification of Multiple Biological Agents

Award Number: 0422085
Program Manager: Om P. Sahai

Start Date: August 1, 2004
Expires: July 31, 2006
Total Amount: $499,911
Investigator: Ihab Abdel-Hamid, iabdel-hamid@mesosystems.com
Company: MesoSystems Technology, Inc.
1001 Menaul Blvd.
Albuquerque, NM 87107
Phone: (509)222-2000

Abstract

This Small Business Innovation Research Phase II project will develop a portable automated biosensor for detection of proteins, viruses and/or pathogens in liquid and air samples. This technology is based on the integration of highly-specific immunodiagnostics with ultra-sensitive electrochemical sensors in a multiplexed microfluidic format that allows the measurement of up to three proteins, two viruses and two bacteria simultaneously. The biosensor is expected to have low detection limits (that is, of less than 0.5 ng/ml for proteins, 1000 PFU/ml for viruses and 700 CFU/ml for bacteria), with an overall assay time of less than 30 minutes. This system will be tested for detection of potential biological threat agents such as Staphylococcal Enterotoxin B (protein/toxin), Influenza (virus) and Bacillus anthracis (bacteria).

The commercial application of this project will be in the areas of homeland security, clinical diagnostics, food quality control and general environmental monitoring.

Title: SBIR Phase II: A Microfluidic-Based Biosensor for Food Pathogen Detection

Award Number: 0422088
Program Manager: Om P. Sahai

Start Date: August 1, 2004
Expires: July 31, 2006
Total Amount: $488,054
Investigator: Xiao-Li Su, xsu@virtual-incubation.com
Company: BioDetection Instruments, Inc.
21 West Mountain
Fayetteville, AR 72701
Phone: (479)571-2592

Abstract

This Small Business Innovation Research (SBIR) Phase II project will develop a portable, rapid and specific capillary channel based immuno-sensing system for food pathogens. The tests will be able to detect concentrations of <10 cfu/ml of various microorganisms (Salmonella, Listeria, Escherichia Coli) in less than 1 hour in contrast to current methods that typically require 24 to 48 hours for preliminary data to become available and typically 3-7 days for definitive results. The capability of the proposed instrument to achieve this significant leap forward in performance was demonstrated by the Phase I results. The Phase II objective is to further refine the instrument with the high performance, ease of use, and low per sample cost needed by the food processing industry.

The commercial application of this project will be in the areas of food safety and bio-defense. Microbial contamination of food products by pathogenic bacteria is a major concern of our society. Contaminated food is estimated to cause 76 million illnesses, 325,000 serious illnesses resulting in hospitalization, and 5,000 deaths in the United States each year. The economic impact of food-borne illnesses has been estimated as high as $10 billion annually. Recent events have also made it clear that the threat from pathogens intentionally introduced into the nation's food supply can be real, with significant economic implications.

Title: SBIR Phase II: Continuously Operating Sensor for Detection of Nerve Agent Contamination in Aqueous Solutions

Award Number: 0422090
Program Manager: Om P. Sahai

Start Date: August 1, 2004
Expires: July 31, 2006
Total Amount: $487,768
Investigator: Markus Erbeldinger, markus@agentase.com
Company: Agentase LLC
3636 Blvd of the Allies
Pittsburgh, PA 15213
Phone: (412)209-7298

Abstract

This Small Business Innovation Research (SBIR) Phase II project is to develop a continuously operating water monitoring device for the detection of chemical warfare agents and hazardous chemicals. Prior Phase I work demonstrated the feasibility of this method and resulted in the construction of a bench-top model that could respond rapidly to contamination, that was resistant to environmental and chemical interference, and that could operate for extended periods of time without user intervention. In Phase II, this model will be modified into a small, self-contained, inexpensive prototype. Several optimized prototypes will be constructed for field trials under operational conditions.

The commercial application of this project will be in the area of bioterrorism.

Title: SBIR Phase II: Anthrax Detector for Mail Sorting Systems

Award Number: 0349687
Program Manager: Om P. Sahai

Start Date: January 15, 2004
Expires: December 31, 2005
Total Amount: $505,985
Investigator: Stuart Farquharson, stu@rta.biz
Company: Real-Time Analyzers
87 Church Street
East Hartford, CT 06108
Phone: (860)528-9806

Abstract

This Small Business Innovation Research Phase II project will develop two prototype anthrax detector systems designed to screen mail entering a postal facility and/or to identify and to stop distribution of anthrax containing mail as it passes through a sorter. These systems will be able to detect 2 micrograms of spores captured from a letter containing as little as 100 micrograms, as well as similar concentrations on contaminated surfaces. The Phase I project demonstrated feasibility by successfully developing a vacuum/filter collection system that captured Bacillus cereus spores from an envelope passing through a mail sorter, which were detected by Raman spectroscopy. Some 23 micrograms of B. cereus spores were measured in 9 seconds using 1064 nm excitation, with an estimated limit of detection of 10 micrograms or 1 million spores in 10 seconds.

The Phase II project will complete the design of the anthrax detector system, with improved sensitivity nd selectivity. The broader impact of this project will be on the safety and security of mail handling and delivery across the United States.

Title: SBIR Phase II: Nanostructured Optical Fiber Breathing Sensors

Award Number: 0349441
Program Manager: Om P. Sahai

Start Date: March 1, 2004
Expires: February 28, 2006
Total Amount: $500,000
Investigator: Jeffrey Mecham, jmecham@nanosonic.com
Company: Nanosonic Incorporated
P.O. Box 618
Christiansburg, VA 24068
Phone: (540)953-1785

Abstract

This Small Business Innovation Research Phase II project will develop and commercialize optical fiber sensors for the quantitative measurement of humidity and air flow for breathing diagnostics. Prior Phase I work has demonstrated that these physically small and mechanically robust sensors respond over a wide range of relative humidities with a response time of microseconds, and are orders of magnitude faster than commercially available devices. The Phase II project will develop sensor thin film chemistries with improved response time, design and fabricate an optical fiber sensor optoelectronic support instrumentation system, and beta-test the sensors and systems with clinicians and physicians. The primary commercial impact of this project will be on home health care and clinical research. Additional applications will be in the industrial gas flow, automotive and transportation areas.

Title: SBIR Phase II: DNA Binding Proteins as Biosensors

Award Number: 0321520
Program Manager: Om P. Sahai

Start Date: December 1, 2003
Expires: November 30, 2005
Total Amount: $498,375
Investigator: Ewa Heyduk, heyduke@slu.edu
Company: Mediomics, LLC
815 Wenneker Drive
Saint Louis, MO 63124
Phone: (314)997-5918

Abstract

This Small Business Innovation Research (SBIR) Phase II project will complete the development of biosensors for detection of heavy metals and acyl-CoA using sequence-specific DNA binding proteins. The presence of the target molecule will be reported by the biosensor as a change in fluorescence signal that could be read using a hand-held battery-operated reader.

The commercial application of this project is in the area of biosensors for markets that include basic and applied research, clinical diagnosis, environmental monitoring, drug screening, and process control in manufacturing operations.

Title: SBIR Phase II: Urea Sensing Biocatalytic Polymers

Award Number: 0321504
Program Manager: Om P. Sahai

Start Date: December 1, 2003
Expires: November 30, 2005
Total Amount: $505,952
Investigator: Markus Erbeldinger, markus@agentase.com
Company: Agentase LLC
3636 Blvd of the Allies
Pittsburgh, PA 15213
Phone: (412)209-7298

Abstract

This Small Business Innovation Research Phase II project proposes to develop prototype urine-detecting products based on enzyme-polymerization and chemical sensing technologies for use in nursing homes, daycare establishments and healthcare facilities. These products will include hand-held sensors, sponge wipes, and bedding fabric pads that change color upon exposure to urine. The strict specificity of the enzymes used in sensor formulation will provide the sensing devices with rapid response times and great precision, thus limiting false positive and negative signals. Having shown the proof of concept in Phase I , the sensor optimization work in this Phase II project will focus on signal enhancement, the development of multi-component sensors for quantitative analysis, and improvements in the usability and the operational shelf life of the proposed sensing products.

The commercial application of this project will be for a broad range of public facilities, including hospitals, nursing homes, daycare centers and food / hospitality establishments.

Title: SBIR Phase II: Biosensor for Label-Free, Real-Time Monitoring of Environmental Pathogens

Award Number: 0321646
Program Manager: Om P. Sahai

Start Date: November 15, 2003
Expires: October 31, 2005
Total Amount: $510,295
Investigator: Salvador Fernandez, fernandez@ciencia.com
Company: Ciencia Inc
111 Roberts Street, Suite K
East Hartford, CT 06108
Phone: (860)528-9737

Abstract

This Small Business Innovation Research Phase II project will develop a portable system for real-time, simultaneous detection and identification of multiple environmental microbes and toxins from aqueous or aerosol samples, on site, with high sensitivity and specificity and with minimal false positives or negative events. The system consists of a disposable biosensor chip and an optical reader device. The detection is based on a proprietary optical transduction technology known as grating-coupled surface plasmon resonance imaging (GCSPRI). Prior Phase I work has demonstrated the feasibility of the GCSPR microarray technology for multiplexed detection with high sensitivity. The goal of the Phase II project is to develop a laboratory prototype of a detection/identification sensor and a prototype chip for multiplexed detection of a model set of three analytes including a bacterium, a virus and a toxin. Non-pathogenic organisms will be used as model systems. Multi-epitope detection methods will be explored for reducing the probability of false alarms. The end result of the Phase II effort will be a demonstration with the laboratory prototype using manual sample introduction. This will provide the logical and critical milestone to transition into commercial development of a portable detection system interfaced to an aerosol collector for field testing and evaluation. The commercial application of this project is in the detection of biological agents for Homeland Defense. The capability for near real-time, multiplexed measurements with a low false alarm rate will be valuable whenever rapid assessment of a contaminated environment is needed.

The potential applications would include hospitals, where nosocomial infections may arise; large buildings, where accidental contamination with mold spores, Legionella and other pathogens may create health hazards; recreational water and drinking water supplies, where waterborne pathogens are a great concern; and the food industry, where there is a need for sensitive methods for on-line and real-time detection of pathogens.

Title: STTR Phase II: Early Detection and Identification of Individual Pathogenic Microorganisms in Food with a Flow Cytometer

Award Number: 0080956
Program Manager: Om P. Sahai

Start Date: June 15, 2000
Expires: June 30, 2003
Total Amount: $449,988
Investigator(s): Richard Shorthill, shorth@me.utah.edu
Company: SoftRay Incorporated
519 South Fifth Street
Laramie, WY 82070
Phone: (307)766-6267

Abstract

This Small Business Technology Transfer Phase II Project will demonstrate the real-time detection of single foodborne pathogenic bacteria in a real-world operating environment. SoftRay demonstrated an innovative technique to detect pathogenic microorganisms in Phase I, based on laser-induced fluorescence coupled with flow cytometry. The Phase I research showed conclusively that this approach is feasible, and that the technique has key advantages over current alternatives including it is: (1) capable of detecting single microorganisms (techniques other than immunofluorescent flow cytometry or immunofluorescent microscopic imaging require in excess of 104 microorganisms; (2) able to completely examine a large volume of food or water in real time; (3) intrinsically automatic; and, (4) sensitive only to the selected bacteria or viruses. In Phase II, SoftRay will demonstrate a lost-cost, self-contained prototype system for the detection of pathogenic microorganisms in food or water, including E. coli O157:H7 on beef. This innovative technique is based on laser-induced fluorescence in which a stream of solution containing the microorganisms is labeled with fluorescent probes and is then illuminated with a laser diode (commonly called flow cytometry). The resulting fluorescence is detected with a CCD imager using a novel time-integration scheme. The proposed device will use a simple optical configuration and a laser diode to provide a low-cost, rugged, small, lightweight package that can be used to detect specific, individual bacteria in real time. Key technology objective is to develop a pathogenic bacteria detection technique that can analyze 1 ml of fluid for selected pathogens in less than 1 minute, to a sensitivity of less than 10 pathogenic microorganisms per ml.

The results of the Phase I and II project will be the demonstration of a prototype sensor capable of individual microorganism detection of unprecedented sensitivity, selectivity, and speed. This will enable rapid detection of individual specific pathogenic microorganisms in a wide array of applications, including: food processing inspection, clinical applications (such as detection of tuberculosis in sputum), biological warfare defense, and many other situations where single microorganism detection is required. The technique can also be used to detect small numbers of molecules, including explosives and groundwater contaminates.

Title: STTR Phase II: Cell-Mimic Optical Waveguide Sensor for Real-Time In-Line Biological Pathogen Detection

Award Number: 0080598
Program Manager: Om P. Sahai

Start Date: August 15, 2000
Expires: January 31, 2003
Total Amount: $449,998
Investigator: Allan Wang, awong@intopsys.com
Company: Intelligent Optical Systems Inc
2520 W. 237th Street
Torrance, CA 90505
Phone: (310)530-7130

Abstract

This Small Business Technology Transfer Research (STTR) Phase II project will develop a cell-mimic optical-based biosensor for the real-time detection of foodborne biological pathogen. Five million analytical tests are performed on food annually in the U.S.; unfortunately, current microbiological test methods are time consuming and labor intensive. Intelligent Optical Systems, in collaboration with the Scripps Research Institute, proposes to develop an optical biosensor that mimics a cell membrane that has undergone biological pathogen attack. The response of the cell-mimic biochromatic membrane to the foodborne toxins is sensitive, specific, and instantaneous. During Phase I, the team developed "highly stable" cell-mimic membranes and demonstrated them in two laboratory systems: (1) a cell-mimic optical waveguide sensor (COWS) for "in-line" monitoring, and (2) a cell-mimic optical bead sensor (COBS) for "on-site point detection". These laboratory systems were used to detect foodborne toxins (E. coli-enterotoxin and cholera toxin) with excellent speed (< 1 minute), sensitivity (500 - 1 ng/ml), specificity (molecular receptor), and simplicity (one step).

Phase II will focus on optimizing the cell-mimic biochromatic polymers, engineering and field-testing a portable COBS prototype, and extending the tests to other foodborne toxins.

Title: STTR Phase II: A Microsensor for Rapid Detection of Airborne Endotoxin

Award Number: 0080569
Program Manager: Om P. Sahai

Start Date: December 1, 2000
Expires: November 30, 2002
Total Amount: $449,929
Investigator: Russell Mileham, rmileham@midwestmicro-tek.com
Company: Microconversion Technologies Co
1322 4th St
Brookings, SD 57006
Phone: (605)688-4618

Abstract

This Small Business Technology Transfer (STTR) Phase II project is expected to result in a biosensor based instrument that can reliably and economically capture and measure airborne endotoxin in-situ with better specificity than existing assay methods. Airborne endotoxin has been identified as a major health hazard to both humans and animals in many agricultural and industrial settings. Endotoxins in the environment primarily enter the body through the lung and are difficult to clear. This contributes to the development of respiratory disorders. Regulation of human endotoxin exposure has not been possible to this point since no quick, reliable system exists to measure airborne endotoxin in the field. Current methods of measuring airborne endotoxin involve collecting dust samples in a sterile filter and sending them to a laboratory for analysis. The results of the analysis take weeks to receive and have poor specificity to endotoxin. The proposed instrument is expected to provide a more accurate, specific, rapid, and reliable alternative to existing assays for detecting airborne endotoxin in the range of 0.01 mg/m 3 to 20 mg/m 3. Measuring endotoxin levels and subsequent modification of airflow will minimize human endotoxin exposure, and lead to improvement in the respiratory health of workers.

A biosensor to detect airborne endotoxin will have commercial applications to protect human health in areas such as livestock confinement and processing facilities, produce storage and processing facilities, cotton processing facilities, waste management facilities, and air quality monitoring of office buildings. Since endotoxin also represents a threat to the health of livestock, particularly swine and poultry, the animal/veterinary sciences market is also expected to be significant.

Title: STTR Phase II: Optic Fiber Sensors for the Detection of Pathogenic Microorganisms

Award Number: 0080372
Program Manager: Winslow L. Sargeant

Start Date: August 15, 2000
Expires: July 31, 2002
Total Amount: $449,464
Investigator(s) Roger Van Tassell, vantassellr@lunainnovations.com
Company: Luna Innovations, Incorporated
PO Box 11704
Blacksburg, VA 24062
Phone: (540)552-5128

Abstract

This Small Business Technology Transfer Research (STTR) Phase II project addresses the need for rapid, reliable instrumentation for the detection of pathogenic microorganisms in food and environmental screening. The proposed system is based on MEMS-based, optical fiber, extrinsic Fabry-Perot (EFPI) biosensors. During Phase I, Luna Innovations (formerly F&S, Inc.) optimized the EFPI sensing platform for refractive index measurements, applied affinity films to measure kinetic binding with specific antibodies and non-hazardous proteins, and integrated the sensors with an inexpensive signal conditioning system for a complete detection combination. The newly developed system is capable of cost effective, robust, operationally simple detection. It is easily adapted to incorporate microfluidics or other sampling system interfaces thereby offering improvements in refractive index measurements, as well as biosensing capabilities. During Phase II, this sensing system will be incorporated with microfluidic sampling systems and used to demonstrate simple detection of proteinacious targets of Escherichi coli and Vibrio cholerae, and will later be expanded for other high priority pathogens found in raw and processed food products, contaminated water and soil, and biological warfare agents.

The prototype system has already generated tremendous interest from many companies involved in refractive index measurements for process control, target screening within the food industry, and other biological research applications. The EFPI as a refractometer has found applications within the beverage industry for milk processing, and the petroleum and chemical industry for distillation processes and concentration monitoring. As a biosensor, the EFPI will find widespread application in multibillion dollar annual markets in food, environmental, medical, and industrial applications.

Title: SBIR Phase II: Fish Freshness Quality Sensor

Award Number: 9983412
Program Manager: Winslow L. Sargeant

Start Date: July 1, 2000
Expires: June 30, 2002
Total Amount: $393,796
Investigator: Dean Smith, dsmith@srdcorp.com
Company: Sensor Research and Development Corp
17 Godfrey Drive
Orono, ME 04473
Phone: (207)866-0100

Abstract

This Small Business Innovation Research (SBIR) Phase II project will further the design, development, construction, and evaluation of a prototype fish freshness sensor based on the successful Phase I feasibility demonstration of using an array of semiconducting metal oxide chemiresistive sensors for quantitative fish freshness quality determination. The advantages of this approach to fish freshness monitoring is that the array data will provide information about the complex gases emitted by fish during degradation and will provide a basis for signal processing techniques to quantify the fish freshness.

The Phase II research is directed towards extending the Phase I demonstration of determining the freshness of Atlantic salmon to other species of fish and to a wider variety of fish handling procedures. The fish freshness sensor data will be compared with results from a gas chromatograph mass spectrometer and a sensory evaluation panel of trained individuals. A field-deployable prototype will be tested on location at fish processing plants to non-destructively determine the degree of degradation of fresh marine fin fish.

Title: SBIR Phase II: Continuous On-Line Monitor to Detect and Quantify Inorganic Contaminants in Water

Award Number: 9983370
Program Manager: Om P. Sahai

Start Date: July 1, 2000
Expires: June 30, 2002
Total Amount: $356,400
Investigator: Rex M. Harper, brimsness@ceemaine.org
Company: BRIMS NESS Corporation
3 Adams Street
South Portland, ME 04106
Phone: (207)767-4302

Abstract

This Small Business Innovation Research (SBIR) Phase II project will advance the resin/quartz crystal microbalance sensor technology demonstrated in Phase I. The device revolutionizes current water monitoring methods by allowing continuous monitoring where only periodic sampling can now be performed. In the Phase II project, ultra-pure water (UPW) monitors will be fabricated and analyzed at a university test facility as well as at a nuclear power plant and semiconductor facility. The monitor will be calibrated and a computerized model characterizing the device's performance in a UPW environment will be developed. The technology consists of applying ion exchange resins to a quartz crystal microbalance sensor device. Once manufacturing repeatability is achieved, the suite of detected contaminants will be broadened to include a wide range of toxic substances of interest to the federal government.

Ultimately we expect to increase the monitor's capability to include all heavy metals set forth in the Clean Water and the Safe Drinking Water Acts. Applications include the development of industrial process control monitors for ultra pure water applications such as semiconductor manufacturing, fail-safe devices to insure the continued effectiveness of drinking water filters, and continuous monitors to detect contaminants in EPA-regulated monitoring sites such as municipal water utilities and wastewater treatment plants.

Title: SBIR Phase II: Rubbed Protein Substrates for Low Cost Biochips Based on Liquid Crystals

Award Number: 0239240
Program Manager: Om Sahai

Start Date: February 15, 2003
Expires: January 31, 2005
Total Amount: $500,000
Investigator: Barbara Israel, bisrael@platypustech.com
Company: Platypus Technologies llc
505 South Rosa Road
Madison, WI 53719-1257
Phone: (608)441-2789

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop an entirely new class of biochips, with a particular focus on biochips designed to track the expression, activation and post-translational modification of proteins involved in cell signaling processes. The technology is based on the use of liquid crystals to image biomolecular interactions at structured surfaces. The goal of this Phase II Project is to demonstrate the substrates for liquid crystal-based biochips that detect activated states of proteins and that can be prepared from mechanically rubbed films of protein (that are) covalently attached to glass substrates. Important issues of non-specific binding, binding of activated states of specific target proteins, sample delivery, sensitivity and quantization will be addressed. These results, when combined with the results of the Phase I research, will make possible the determination of the extent to which cell signaling proteins are activated within biological samples (e.g. in cell lysates).

The commercial applications of this project will be in the areas of proteomics and in vitro diagnostics. The development of the proposed technology will allow for rapid, inexpensive, multi-target, high-throughput analysis of proteins and their modification states.

Title: SBIR Phase II: Biosensor for Rapid Whole Blood Assays using Magnetic Labels and Giant Magnetoresistive Sensors

Award Number: 0548638
Program Manager: Errol Arkilic

Start Date: January 23, 2006
Expires: January 31, 2008
Total Amount: $466,710
Investigator: Curt Bilby, curt.bilby@seahawkbio.com
Company: Seahawk Biosystems
3000 Bryker Drive
Austin, TX 78703
Phone: (512)459-7063

Abstract:

This Small Business Innovation Research (SBIR) Phase II project advances the general state of diagnostics research in the veterinary and security/defense markets using whole-blood assays. This Phase II project will develop (1) an automated Open Assay Development Platform for rapid assay prototyping; (2) whole blood assays for canine immunity assessment and canine thyroid test (T4); and, (3) multiplexed, canine whole blood assays. The approach uses magnetic beads to label biomolecules captured onto a receptor-patterned microchip that contains an embedded array of magnetic microsensors. The magnetic microsensors are wire-like structures that display giant magnetoresistance (GMR). When coupled with controlled fluidic force discrimination - an innovation that greatly reduces unwanted background signal - rapid identification of biomolecules with high sensitivity and specificity is achieved. A prototype system has been developed for both immunoassays and nucleic acid assays, with immunoassays (1 ng/mL) saturating in less than 10 minutes and unmodified DNA detected at 10fm in less than 20 minutes.
Seahawk is responding to the clinical and financial challenges veterinarians face by developing a multi-use, multiplexed instrument and associated disposable cartridges.

This technology platform offers veterinarians superior performance (faster, more accurate, easier to use) and greater profitability than existing products. Initially, the platform will include cartridges for two applications: (1) individualized immunity assessment and (2) disease diagnostics, both specifically for dogs and cats. The system provides an in-clinic, quick turnaround, cost-effective and accurate test of an animal's immune system to determine what, if any, vaccine boosters need to be administered at that time. This provides the veterinarians with three key benefits: (1) improving the quality of care - providing revaccinations only when needed and tailored to each animal; (2) generating additional or replacement revenue due to changes in revaccination protocols; and, (3) replacing annual revaccinations as the impetus for customer compliance with scheduling office visits for physical exams.

Title: SBIR Phase II: Toxic Mold Sniffer

Award Number: 0548727
Program Manager: Ali Andalibi

Start Date: September 21, 2006
Expires: September 30, 2008
Total Amount: $471,421
Investigator: Debra Mlsna, dmlsna@seacoastscience.com
Company: Seacoast
2151 Las Palmas Drive
Carlsbad, CA 92009
Phone: (760)268-0083

Abstract:

The Small Business Innovation Research (SBIR) Phase II project will develop a small, battery-powered sensor for the detection of toxic chemicals produced by molds responsible for "sick building syndrome," and for the detection of such toxic molds in infested buildings. The company's MEMS chemicapacitor technology utilizes an array of surface-micromachined capacitors coated with chemo-selective materials. The proposed device will detect toxic compounds produced by indoor molds, as well as associated volatile organic compounds.

The detection and isolation of suspect molds is a major indoor environmental concern. The sensor technology proposed for use in the company's sensor system can be packaged for single-use home detection kits, or can be incorporated into reusable detection units for surveillance by commercial interests.

Title: SBIR Phase II: Microchip Assay for Glycosylated Hemoglobin

Award Number: 0548744
Program Manager: F.C. Thomas Allnutt

Start Date: March 1, 2006
Expires: February 29, 2008
Total Amount: $480,024
Investigator: Dale Willard, dale.willard@colostate.edu
Company: Advanced MicroLabs LLC
527 Matthew St
Fort Collins, CO 80524
Phone: (970)491-4064

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims at developing the next generation of diabetic monitoring devices that will allow the measurement of multiple markers of disease regulation and progression using an innovative lab-on-a-chip technology. The project will develop the first integrated microchip CE device for measurement of an important maker of diabetes.

This technology will impact patient monitoring for disease progression and therapeutic efficacy by following biomarker more efficiently as well as being used at the point of care. This eliminates the time and cost currently required to perform follow up laboratory tests. The technology approaches the chemistry of biomarkers from a non-traditional sensor mechanism and shows great promise for the detection and use of biomarkers for specific diseases.

Title: STTR Phase II: Microfluidic CD Biochips for Enzyme-Linked Immunosorbent Assays

Award Number: 0548716
Program Manager: Ali Andalibi

Start Date: December 15, 2006
Expires: November 30, 2008
Total Amount: $500,000
Investigator: Wei-Cho Huang, wchuang@bioloc.net
Company: BioLOC LLC
1381 Kinnear Road #100
Columbus, OH 43212
Phone: (614)481-9135

Abstract:

The Small Business Technology Transfer (STTR) Phase II project will develop a low-cost and mass-producible lab-on-a-chip platform for molecular and biological analyses. The platform is a microfluidic CD for Enzyme-Linked Immunosorbent Assays (ELISA) that reduces cost, accelerates results, and improves reliability of analyses for food borne contaminants, cancer diagnoses and environmental contamination.

The CD-ELISA technology platform merges two scientific areas - polymer microfabrication and biotechnology - and can substantially reduce manufacturing costs, improve device performance, and enable the production of low-cost and high-efficiency devices. Moreover, as such a device would be more affordable it will enable point-of-use results for a broader spectrum of molecular and biological testing.

Title: SBIR Phase II: Immunological Tools for Trimetasphere Fullerenes

Award Number: 0724380
Program Manager: F.C. Thomas Allnutt

Start Date: September 1, 2007
Expires: August 31, 2009
Total Amount: $499,955
Investigator: Roger VanTassell, vantassellr@lunainnovations.com
Company: Luna Innovations, Inc.
1703 South Jefferson Street, SW
Roanoke, VA 24016
Phone: (540)769-8400

Abstract:

This Small Business Innovation Research (SBIR) Phase II research develops antibodies and immunoassays for studying therapeutics based on carbon-based nanomaterials. This research will expand the immunological tools developed in Phase I to focus on detailed characterization of anti-fullerene antibodies and validate and down-select immunoassays and reagents for validated commercial formats. Commercial formats will include enzyme-linked, immunosorbant assays (ELISAs) for medical and environmental applications, neutralization schemes for mitigating potential toxicity of fullerene/nanotubes and biosensors platform for long-term monitoring systems. Biosensor platforms based on fullerene antibodies as affinity ligands will include the quartz crystal microbalance and surface acoustic waveguide.

The broader impacts will be to provide a full spectrum of immunological tools for studying the medically-related nanomaterials and monitoring nanowaste by-products during manufacturing processes. These will be new to the marketplace and enable monitoring of the use of products based on these nanomaterials to asssure their safe application.

# Bioinformatics

Title: SBIR Phase II: Development of Integrated Fluid/Solid/Bio-Kinetic Simulation Software for the Characterization of Microsphere-based Bio-analytic Systems

Award Number: 0216507
Program Manager: Om Sahai

Start Date: October 1, 2002
Expires: September 30, 2004
Total Amt: $499,948
Investigator: Shivshankar Sundaram, jls@cfdrc.com
Company: CFD Research Corporation
215 Wynn Drive, 5th Floor
Huntsville, AL 35805
Phone: (256)726-4800

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will develop and customize advanced simulation software for the design and optimization of microsphere and cell-based assays. Current assay design by trial and error is slow, unreliable, expensive, and a bottleneck for multiplexed, high-throughput analysis. Prior Phase I research has successfully established a first-ever, truly integrated (buffer flow, resolved microsphere motion and surface biochemistry) assay design and analysis tool. The objective of the Phase II effort is to further develop the initial models demonstrated in the Phase I effort into a comprehensive, generalized design environment. A suite of bead-surface biochemistry models (enzyme kinetics, multi-step reactions) and including user specifiable surface reaction mechanisms will be developed and fully integrated. In seeking to expand the application to cell-based assays, models for the motion and capture of deformable cells will be created, and detailed flow visualization experiments tracking bead and cell motion as well as assay endpoints in microfluidic channels will be conducted to guide and validate these models. The value of the developed simulation tool will be demonstrated in the proof-of-concept design of a novel microfluidic, cell-based H-filter assay for red-blood cell based aminothiols.

The commercial applications of this project will be in the biotechnology and bioassay design markets. Miniaturized, multiplexed, high-throughput, fast, efficient and sensitive assays are a pre-requisite to translating the wealth of data from the human genome and combinatorial libraries into effective therapeutics. The developed software product will enable rational, computer-based design of these bioassays.

Title: SBIR Phase II: Bioinformatic Data Mining for AIDS Resistance Genes

Award Number: 0450627
Program Manager: George B. Vermont

Start Date: September 15, 2005
Expires: August 31, 2007
Total Amount: $499,961
Investigator: Walter Messier, wmessier@evolgen.com
Company: Evolutionary Genomics, LLC
6840 N. Broadway
Denver CO, 80221
Phone: (303)429-5800

Abstract:

This Small Business Innovation Research (SBIR) Phase II project focuses on the use of novel evolution-based data mining software to discover targets for the development of human therapeutics for currently intractable diseases. Phase I demonstrated that the evolution-based data-mining software was useful for dramatically narrowing the search for proteins that make chimpanzees resistant to the progression of AIDS after infection by HIV-1. In Phase II, the impact on in-vitro HIV-1 infectivity of a human cell line transfected with the gene encoding one of the adapted chimpanzee proteins will be assessed. Screening of other chimpanzee homologs of genes differentially regulated in human cells upon HIV-1 infection will continue to ensure that all potential AIDS resistance proteins have been identified. The adapted chimpanzee genes/proteins will be compared to those from humans in which HIV-1 infection has not progressed to AIDS for at least 10 years to see if there are any commonalities.

The commercial application of this technology is in the battle against AIDS disease. The identification of proteins that have undergone adaptive evolution should lead to drugs to mediate the progression of HIV-1 infection. This same approach may have broader impact against several other intractable diseases for which non-human primates are less susceptible than humans. This includes hepatitis-C, sepsis, type-1 diabetes, and certain cancers

Title: SBIR Phase II: A Bioinformatics System for GCxGC-MS (Comprehensive Two-Dimensional Gas Chromography)

Award Number: 0450540
Program Manager: George B. Vermont

Start Date: February 1, 2007
Expires: January 31, 2007
Total Amount: $493,692
Investigator: Qingping Tao, qtao@cse.unl.edu
Company: GC Imaging
216 N 11th St, Ste 302
Lincoln NE, 68508
Phone: (402)310-4503

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to use bioinformatics to transform complex data produced by comprehensive two-dimensional gas chromatography with mass spectrometry (GCxGC-MS) to usable chemical information. GCxGC-MS is an emerging technology for chemical separations that provides an order-of-magnitude increase in separation capacity over traditional GC. Results from Phase I demonstrated the feasibility of using bioinformatics to automatically identify chemical components in complex matrices analyzed by GCxGC-MS. Phase II will carry out further theoretical and experimental research to develop solutions that will enable broader use of GCxGC-MS system. The key project objectives include (a) developing a hybrid method that combines three approaches for chemical identification from GCxGC-MS data, (b) establishing the mathematical foundation and practical algorithms for co-elution analysis in GCxGC-MS, and (3) developing new XML technologies for shared and distributed GCxGC-MS data, metadata, and information.

The commercial impact of this project will be to develop information technologies for a new generation of analytical instruments. GCxGC-MS system is likely to capture a significant share of the existing gas chromatography market, currently in excess of $ 1 billion per year, and to open new markets in applications requiring superior separations. These applications with important societal benefits, would include environmental monitoring of air, water, and soil; development and processing of foods, flavors, fragrances, and essential oils; processing of petroleum and industrial chemicals; health-care assays of blood, urine, milk, and breath samples; and analysis and discovery of drugs and medicinal herbs.

Title: SBIR Phase II: Comprehensive Database Resource on Protein Localization

Award Number: 0239206
Program Manager: Om Sahai

Start Date: February 1, 2003
Expires: January 31, 2005
Total Amount: $499,407
Investigator: Christopher N. Larsen, clarsen@cognia.com
Company: Cognia
117 East 55th Street
New York, NY 10022-3502
Phone: (212)331-7841

Abstract:

This Small Business Innovation Research (SBIR) Phase II Project proposes to develop the database and associated software to enable analysis of protein trafficking and localization. The system will be designed to enable drug discovery researchers to identify, elucidate, eliminate and design leads and targets, while facilitating the general training of researchers. During the Phase I work, proteins involved in trafficking and diseases related to mislocalization were identified, and a relational database to house information on protein trafficking was constructed. Curation interface applications were created to allow remote data entry, and graphical user interfaces designed to maximize the utility of the information. The objective of this Phase II Project is to exhaustively populate the database from the primary journal literature. Selection of proteins involved in protein trafficking will be guided by relevant human diseases and corresponding drug discovery efforts.

The commercial application of this project is in the area of biological informatics. The potential users of the biological database to be developed in this project would include pharmaceutical and drug discovery companies.

Title: SBIR Phase II: Hypertension Treatment Responder Prediction

Award Number: 0220661
Program Manager: Om Sahai

Start Date: September 15, 2002
Expires: August 31, 2004
Total Amount: $500,000
Investigator: Albert K. Man, aman@burnham.org
Company: Predict
4540 Georgia St.
San Diego, CA 92116-2636
Phone: (619)255-8730

Abstract:

This Small Business Innovation Research Phase II project will develop a clinical predictive algorithm for hypertension medication response based upon patient genetic and medical information. The development of effective treatment for hypertension is critical to controlling costs of this disease, which has the largest negative impact on the U.S. economy in loss of productive years. Anti-hypertensive drugs have a large window of therapeutic options, including significant variation in dosages, medications, and combinations of therapies used. The objective of the Phase II project is to continue development of the software platform, GeneRx, which incorporates pharmacogenetics and nonlinear adaptive algorithms toward optimizing anti-hypertension therapy on a patient specific basis. Genetic data for each patient will be acquired by genotyping DNA from the blood samples, and scored as single nucleotide polymorphisms (SNPs) present or absent in key hypertension-related genes. GeneRx will take a patient's individual genetic, demographic, and environmental variables and predict likely efficacy of a hypertension medication. In Phase I, the basic feasibility of a predictive algorithm for predicting patient response for the ACE inhibitor class of hypertension drugs was established. The Phase II project will use patient information and blood samples from both archival and ongoing hypertension studies to predict the effectiveness of other classes of hypertension medications, including calcium channel blockers, diuretics, and beta-blockers.

The commercial application of this project is in the area of hypertension therapy.

Title: SBIR Phase II: Physiologic High Throughput Screening of Bioengineered Tissues

Award Number: 0724445
Program Manager: F.C. Thomas Allnutt

Start Date: August 15, 2007
Expires: July 31, 2009
Total Amount: $499,956
Investigator: Herman Vandenburgh, hvandenburgh@myomics.com
Company: Myomics
4 Richmond Square, STE 500
Providence, RI 2906
Phone: (401)861-9770

Abstract:

This Small Business Innovation Research (SBIR) Phase II research develops an innovative high-throughput/high content drug screening platform that utilizes three-dimensional human skeletal muscle tissue constructs that mimic in vivo skeletal muscle to quantify muscle force generation. Significant demands exist for new drugs to treat contractility disorders involving skeletal muscle. Myomics' proposed drug testing platform will contribute to significant reductions in time and costs associated with bringing new drugs to market by discovering drug candidates and eliminating ineffective compounds earlier than currently possible. Unlike existing systems, this approach incorporates biomechanics into drug discovery using mechanical sensors to detect contraction of multiple identical tissue samples over extended time periods. Significant socioeconomic and quality-of-life impacts will result for patients with contractility disorders (sarcopenia, atrophy, or Duchennes muscular dystrophy). While most drug screening protocols test one protein pathway at a time, this platform provides a unique physiological screening system and protocol which quantifies contraction as the result of multiple protein pathways interacting over time.

The broader impacts of this research will be to enhance muscle contractility disorder/disease research and provide new tools to the pharmaceutical and biotechnology industries for drug discovery. Upon successful development, the sensing mechanism will potentially be used to develop treatments for several contractile tissues relevant to a range of important human contractile disorders and diseases contributing to improved outcomes for these diseases.

# Biomaterials

Title: SBIR Phase II: Suction Retention Smart Variable Geometry Sockets (SVGS) for Transtibial Prostheses

Award Number: 0091513
Program Manager: Om Sahai

Start Date: June 1, 2001
Expires: May 31, 2004
Total Amount: $499,992
Investigator: Richard M. Greenwald, rgreenwald@simbex.com
Company: SIMBEX
Lebanon, NH 03766
Phone: (634)482-367

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will complete development of a production Smart Variable Geometry Socket (SVGS) for transtibial amputees (TTAs) and will test it with a clinical study. This non-electrical system is a simple means for ensuring and maintaining a good socket fit, with security and stability increased over the state of the art. Poorly fitting sockets, which cause pain and skin lesions, are responsible for a significant portion of TTAs rejecting prosthesis. The SVGS/TT utilizes suction retention, which provides an important benefit, particularly to diabetics, by increasing blood circulation in the residual limb.

The unique SVGS system consists of multiple, liquid-filled bladders placed by the prosthetist during socket fitting and a control for maintaining appropriate pressures on the residual limb at selected locations, all contained within the dimensions of a conventional prosthesis. The SVGS can be applied by the prosthetist with existing equipment and conventional art, thereby minimizing implementation cost. This attribute will enhance market acceptance. Phase I demonstrated feasibility; Phase II will measure efficacy and acceptance by TTAs. Phase II results will be the catalyst for successful commercialization.

Title: SBIR Phase II: All Natural Biobased High Performance Composites for Industrial Applications

Award Number: 0518940
Program Manager: George B. Vermont

Start Date: September 1, 2005
Expires: August 31, 2007
Total Amount: $450,117
Investigator: N Hecht, bhecht@acrtucson.com
Company: Advanced Ceramics Research, Inc
3292 E Hemisphere Loop
Tucson AZ, 85706
Phone: (520)573-6300

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to optimize and commercialize the manufacturing of all natural biobased composites from renewable resources. Phase I research demonstrated the technical feasibility of fabricating soybean oil based composites using a selected fiber/resin polymer composite combination. The Phase II project will focus on optimization and scale-up of the fabrication approach and process to improve the performance of the biobased composites. Further, with the help of commercial partners, Phase II work will develop a number of full scale prototype products with the following features: (1) the products contain 80% or more natural fibers and resins; (2) the products rely on economical and environmentally friendly tooling and manufacturing processing; and (3) the products comply with performance, safety, durability, and cost requirements set by end-users.

The commercial applications of this project will be in a number of areas, including low cost building materials for industrial and household furniture, packaging materials, piping for remote areas and aquaculture systems. The proposed biobased composites are expected to have higher value-in-use industrial applications than their petroleum counter-parts (that is, to be available at a lower cost while offering the same functionality).

Title: SBIR Phase II: Advanced Controlled-Impedance Transfemoral Knee/Ankle Prosthesis

Award Number: 0450632
Program Manager: Michael R. Ambrose

Start Date: January 15, 2005
Expires: December 31, 2006
Total Amount: $500,000
Investigator: Edwin Iversen, ed@utaharm.com
Company: Motion Control, Inc.
2401 S 1070 W # B
Salt Lake City UT, 84119
Phone: (801)978-2622

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims to develop a transfemoral prosthesis which will allow wearers to walk and run more smoothly, with greater stability and less effort. Typically, transfemoral amputees have difficulty achieving a natural gait, thus causing discomfort and greater energy expenditure. It is expected that the development of this advanced prosthesis will greatly enhance the function and comfort of amputees and bring new technology to the prosthetic industry. In Phase I research, a unique engineering model of the knee and the ankle was developed, implementing the pneumatic compliance (spring) and electrically-controlled hydraulic damping. In Phase II, complete prototypes of the microprocessor-controlled knee/ankle prosthesis will be developed, with the following features: (a) compliant (elastic, rather than stiff) knee flexion during stance phase, which will return energy to the wearer and improve comfort, (b) co-ordination of knee and ankle impedance to match desired walking cadence, and minimal energy expenditure by tuning the spring rate to the natural frequency; and (c) myoelectric control of knee impedance. In addition, high-performance features will be integrated into the prosthetic device, including adaptive swing phase knee impedance, and automatic control of stance phase impedance.

The commercial application of this project will be in the area of prosthetic devices for use by people with knee and foot (transfemoral) amputation. The proposed product will allow the amputees to wear their prosthesis for a longer time period, with less effort and more safety, and to walk on more rugged and uneven terrain. Estimates of revenues resulting from this project show gross sales starting at $750,000 per year, growing rapidly after 5 years to over $8,000,000

Title: SBIR Phase II: Tissue Engineered Cartilage for Drug Discovery

Award Number: 0422194
Program Manager: Om P. Sahai

Start Date: August 1, 2004
Expires: July 31, 2006
Total Amount: $498,843
Investigator: Brian Pfister, bpfister@articular.com
Company: Articular Engineering, LLC
1818 Skokie Blvd. Suite 158
Northbrook, IL 60062
Phone: (847)498-9634

Abstract

This Small Business Innovation Research Phase II project is to develop scale-up production technology to produce engineered cartilage for drug discovery using a proprietary Alginate Recovered Chondrocyte (ARC) method. This method stimulates adult human cartilage cells to form a cartilaginous tissue with proper compositional and functional properties. ARC cartilage tissue is expected to offer a cost-effective alternative to current culture systems and expensive animal studies while utilizing human tissue.

The commercial application of this project will be in the area of drug discovery for cartilage-related problems such as rheumatoid arthritis.

Title: SBIR Phase II: Scalable Synthesis and Processing of Nanocrystalline Hydroxyapatite

Award Number: 0349884
Program Manager: Om P. Sahai

Start Date: February 15, 2004
Expires: January 31, 2006
Total Amount: $499,999
Investigator: Edward Ahn, eahn@angstrommedica.com
Company: Angstrom Medica, Incorporated
150 California Street
Newton, MA 02458
Phone: (617)454-3620

Abstract

This Small Business Innovation Research Phase II Project proposes to use a newly developed synthetic nanocrystalline hydroxyapatite (HAP) bone material to produce high-strength, resorbable synthetic bone implants for anterior cruciate ligament surgeries. This material solves the problem of current orthopedic implants (made of polymer and/or metal) which either permanently reside as foreign material in the body or quickly degrade into a formless mass of non-ossified, non-load bearing tissue. The objectives of the Phase II work are to concurrently scale up manufacturing processes for HAP to near-commercial levels while developing an anterior cruciate ligament (ACL) prototype product for testing in vivo.

The commercial impact of this project will be in the area of orthopedics. The proposed technology will help decrease the time of healing in surgeries requiring implants (fractiures, ACL) and will minimize the need for second surgeries to remove the screws and/or to correct for morbidities.

Title: SBIR Phase II: A New Vibration Mixer for Bone Cement

Award Number: 0079484
Program Manager: Om P. Sahai

Start Date: September 15, 2000
Expires: August 31, 2002
Total Amount: $399,892
Investigator: Pamela Saha, pssaha@prodigy.net
Company: Clinical and Industrial Technology Co
1570 Woodbury Road
Seneca, SC 29672
Phone: (864)653-6472

Abstract

This SBIR Phase II project is aimed at developing a novel vibration mixer for the mixing of surgical grade bone cement. Self-curing polymethylmethacrylate (PMMA) or acrylic bone cement is used extensively in total joint replacements, in the repair of bony defects and in the fixation of pathological fractures. For surgical use, the methylmethacrylate polymer and the liquid monomer are hand mixed. This hand-mixing entraps air bubbles making the cement porous. Presence of these bubbles adversely affects the mechanical properties of bone cement, making it much weaker under load and may contribute to early failure of cemented artificial joints. Results of the Phase I study indicate that ultrasonic vibration during cement mixing significantly reduced its porosity and increased the fatigue life and mechanical strength of bone cement, compared to hand-mixed cement. Recently, it was shown that combining sonication and vacuum mixing reduced the porosity and further improved the fatigue life, compared to either mixing methods alone. During the Phase II study, the frequency and amplitude of sonication and the vacuum pressure to obtain the best mechanical properties of the cement will be optimized. Subsequently, a new cement mixer will be designed and built incorporating these mixing features.

It is expected that the improved mechanical properties of vibrated bone cement will reduce the incidence of cement fracture and this will improve the success rate of total joint replacements. Considering that cement mixers are used in several thousand hospitals in the United States alone, we expect this new cement mixer to be adopted by a large number of Orthopaedic surgeons in these hospitals.

Title: STTR Phase II: Cold Gas Dynamic Spray Processing of Bioactive Nano-hydroxyapatite/Titanium Nanocomposite Coatings

Award Number: 0110323
Program Manager: Cheryl F. Albus

Start Date: September 1, 2001
Expires: February 29, 2004
Total Amountt: $500,000
Investigator: Larry E. McCandlish, mccandlish@ceramare.com
Company: Ceramare Corporation
12-D Jules Lane
New Brunswick, NJ 08901
Phone: (732)937-8260

Abstract:

This Small Business Technology Transfer (STTR) Phase II Project will develop a fully integrated process for applying a well-bonded, bioactive coating to the stem of an orthopedic hip implant by a novel Cold Gas Dynamic Spray (CGDS), or Hyperkinetic Deposition process. The new process is a potential major advance in the state-of-the-art for surface modification of medical implants. The medical community hitherto has relied primarily on plasma spraying to activate implant surfaces. Plasma spraying is a cost-effective means of applying the coating material but is far from ideal. In particular, the high temperatures experienced by the hydroxyapatite feed powder during plasma spraying can seriously degrade its compositional integrity and thus its bioactive properties. The cold spray process eliminates this problem, and enables, for the first time, high-surface-area nanostructured hydroxyapatite powder to be incorporated into the implant surface without sacrificing its intrinsic bioactivity. As an added benefit the implant surface is left in a state of compression, which should extend the service life of the implant by eliminating the possibility of surface cracking caused by low-cycle fatigue.

The commercial applications for this project will be to improve the life of implants.

Title: STTR Phase II: Variable Diameter Fiber Reinforced Biopolymers for Minimally Invasive Orthopedic Implants

Award Number: 0548663
Program Manager: Rathindra Dasgupta

Start Date: September 20, 2006
Expires: September 30, 2008
Total Amount: $499,849
Investigator: James Mason, grangeng@comcast.net
Company: Granger Eng
PO Box 845
Granger, IN 46530
Phone: (574)272-0552

Abstract:

The Small Business Technology Transfer Research (STTR) Phase II project will develop a new ceramic fiber technology for reinforcing injectable bioplastics used in orthopaedic applications. The main goal of this research project is to achieve a significant increase in strength and stability of the proposed product over current injectable polymer based biomaterials through a combination of variable diameter fibers and new cements.

The proposed product would result in the enablement of new surgical techniques. In addition, the research might be applicable to injection molding of mass produced plastics which could significantly strengthen many products.

Title: SBIR Phase II: Novel Titanium Tantalum Materials for Improved Biomedical Implants and Medical Devices

Award Number: 0724433
Program Manager: Cheryl F. Albus

Start Date: August 1, 2007
Expires: July 31, 2009
Total Amount: $500,000
Investigator: Harvey Fisher, hfisher@dynamettechnology.com
Company: Dynamet Technology, Inc
Eight A St
Burlington, MA 01803
Phone: (617)272-5967

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will use Titanium-Tantalum (Ti-TA) alloys, with the objective that these materials will become commercial alloys used in orthopaedic and stinting devices. Ti-30Ta has potential as a highly biocompatible implant alloy with a modulus closer to that of bone (thus mitigating bone shielding), and is potentially less notch-sensitive than standard titanium implant alloys. This project will also demonstrate that advanced powder metallurgy can produce novel titanium alloys that are extremely difficult and prohibitively expensive to produce by other means. Critical material property data of these alloys will be generated that will lead medical device manufacturers to incorporate these alloys into specific devices and to conduct the necessary testing and clinical trials for commercial product release.

The broader impacts from the use of Ti-Ta alloys will enable the development of improved medical devices that will last longer; are less invasive, promote faster patient recovery times and minimize the risk of adverse reactions. Advances in orthopedic and cardiovascular products will also significantly reduce short-term and long-term health care costs associated with such medical conditions and surgical procedures. Ti-Ta materials will also offer advantages for non-biomedical applications, in regard to mechanical properties as well as to shape memory and superelastic properties. For example, such materials can be expected to also offer improved properties such as resistance to corrosion, oxidation and high temperatures. Thus, availability of these alloys will be applicable to a wide variety of industrial, consumer and aerospace products in addition to biomedical applications, resulting in significant commercial potential.

# Biomedical Devices and Instrumentation

Title: SBIR Phase II: Three-Dimensional Atom Probe Imaging for Nano-Biotechnology

Award Number: 0216620
Program Manager: Om Sahai

Start Date: October 1, 2002
Expires: September 30, 2004
Total Amount: $499,850
Investigator: Steven L. Goodman, sgoodman@imagoscientific.com
Company: Imago
6300 Enterprise Lane
Madison, WI 53719-1193
Phone: (608)274-6880

Abstract:

This Small Business Innovation Research Phase II project will develop the Local Electrode Atom Probe (LEAP) to rapidly provide three-dimensional atomic-scale imaging and elemental identification of nano-biotechnology devices. Structural characterization of nano-biotechnology devices is currently problematic because available microscopy and analytical techniques have substantial limitations in quantitative imaging at the atomic-scale. Moreover, current microscopy techniques cannot adequately resolve three-dimensional biomacromolecules, which are intrinsic to nano-biotechnology devices. Until better analytical instrumentation is developed, researchers will "fly blind" as they develop more complex nano-biotechnology devices. The overall goal of this Phase II project is to rapidly analyze the three-dimensional atomic-scale structure and elemental composition of biological and organic molecules on nano-biotechnology devices. The focus will be on developing technologies to analyze commercial specimens using LEAP technology, and to initiate commercialization and marketing of this technology to academic and industrial researchers. The commercial application of this project will be in the area of bioanalytical instrumentation and nano-biotechnology devices.

Title: SBIR Phase II: Novel Nanosized Magnets for Highly Sensitive Multiplexing Bio-Molecular Detection

Award Number: 0450641
Program Manager: George B. Vermont

Start Date: February 1, 2007
Expires: January 31, 2007
Total Amount: $497,185
Investigator: Ted Sun, ted@ls-tek.com
Company: LS Technologies
44160 Old Warm Springs Blvd
Fremont CA, 94538
Phone: (510)651-1329

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop and validate highly sensitive contrasting agents in-vivo, for magnetic resonance imaging (MRI) diagnosis, based on a series of novel nano-sized ferromagnets. Prior Phase I work used combinatorial chemistry to synthesize magnetic nanoparticles with significantly enhanced magnetic resonance signal and sensitivity than currently available paramagnetic contrasting agents. The specific objectives of Phase II research are to further optimize the nano-magnet cores with combinatorial chemistry , to functionalize their surfaces for in-vitro imaging of cells, to validate the newly developed contrasting agents in comparative animal MRI studies against products in use, and to evaluate their toxicity effects.

The commercial application of this project will be in the area of whole-body imaging techniques. The proposed technology will enable superior medical images to be taken at significantly higher throughput and sensitivity, and at a lower cost. Further, it may allow for new medical diagnosis-imaging applications using magnetic resonance (for example, in the early detection and prevention of cardiovascular disease).

Title: SBIR Phase II: Hybrid Inorganic/Organic Ion Exchange Material for the 227Ac/223Ra Generator

Award Number: 0450581
Program Manager: George B. Vermont

Start Date: April 15, 2005
Expires: March 31, 2007
Total Amount: $452,553
Investigator: Hariprasad Gali, hari.gali@lynntech.com
Company: Lynntech, Inc
7607 Eeastmark Dr Ste 102
College Station TX, 77840
Phone: (979)693-0017

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims to develop a generator to produce pure radium-223 for use in cancer therapy. The alpha-emitter Ra-223 has a longer half-life than the other alpha-emitting radioisotopes (213 Bi, 212Bi and 211At) that are currently being evaluated for use in radio-immunotherapy (RIT), and has been shown to have higher bone uptake than the commercially available beta-active bone seekers. This makes it very attractive for Ra-223 to be developed further for radiopharmaceutical applications and for use as a pain palliation agent. However, the research and clinical application of this isotope are hindered by the limited availability of pure Ra-223. A simple technique to produce the isotope is a generator where a suitable parent, in this case Ac-227, is immobilized on an ion exchanger column and Ra-223 is eluted when required. Current separation methods frequently use organic resins, which tend to degrade under ionizing radiation and thus the product may contain impurities. Prior Phase I work developed new hybrid inorganic/organic ion exchange materials with high affinity for actinium, but low affinity for radium and good resistance against radiation. The Phase II project will optimize the exchanger performance and fabricate a prototype of the Ra-223 generator.

The commercial application of this project will be in the area of cancer therapy. It is expected that the easy - to - use generator, which poses a smaller radiation hazard to personnel, will be used at medical research centers, radio - pharmacies and hospitals to produce pure radium - 223 to treat patients with bone metastases and other small solid tumors.

Title: SBIR Phase II: Detection and Identification Instrument for Single Molecule Analysis

Award Number: 0450539
Program Manager: George B. Vermont

Start Date: March 1, 2005
Expires: February 28, 2007
Total Amount: $500,000
Investigator: Arieh Karger, AKarger@RMDInc.com
Company: Radiation Monitoring Devices Inc
44 Hunt Street
Watertown MA, 2472
Phone: (617)668-6801

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop a novel, low cost laboratory instrument for genetic analysis and single molecule studies. The technology is suitable for the detection and identification of DNA and RNA through fluorescent hybridization probes without the need for Polymerase Chain Reaction (PCR) amplification, or for proteins and small molecules through fluorescence immunoassays. The general scheme is based on single molecule detection (SMD) and utilizes the two-color cross-correlation spectroscopy (TC-FCCS) technique with coincident detection analysis scheme to simultaneously probe ten focal regions of a microfluidic assay. High efficiency single photon detectivity Geiger mode microavalanche photodiode (uAPD) arrays will function as detection elements.

The commercial application of this project will be on biological and medical research, and on the drug development process. Examples of potential applications range from the study of conformational dynamics and interactions of macromolecules to biochemical kinetics of single molecules.

Title: SBIR Phase II: Catheters with Anticoagulation and Fibrinolytic Properties

Award Number: 0422181
Program Manager: Michael R. Ambrose

Start Date: November 1, 2004
Expires: October 31, 2006
Total Amount: $510,774
Investigator: Jun Du, Ydu@spirecorp.com
Company: Spire Corporation
1 Patriots Park
Bedford MA, 01730
Phone: (781)275-6000

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will develop blood-compatible biomaterials for end-stage renal dialysis (ESRD) catheters through an integrated biological coating (IBC) that combines protein passivation, anticoagulation, and fibrinolytic mechanisms on the surface. Phase II work will build on the Phase I demonstration that internal and external surfaces of BaSO4-loaded polyurethane catheters were activated by an electron cyclotron resonance (ECR) process that promoted uniform deposition of an IBC coating. In the Phase II project, the coating process will be optimized and deposition equipment will be upgraded to enhance reliability and repeatability. Finished catheters will be produced and evaluated for blood compatibility through in vitro human blood testing and ex vivo sheep shunt model experiments. Finished IBC catheters will also undergo rigorous mechanical, biocompatibility, and toxicity testing to show compliance with FDA standards.

The principal commercial application of this project will be on the catheter industry. The proposed technology will also find applications in coatings for other blood-contacting devices such as grafts, polymeric stents , valves and by-pass systems

Title: SBIR Phase II:  Robotic Scrub Technician

Award Number: 0422114
Program Manager: George B. Vermont

Start Date: November 1, 2004
Expires: October 31, 2006
Total Amount: $491,500
Investigator: Michael Treat, mt23@columbia.edu
Company: Robotic Surgical Tech, Inc.
5141 Broadway
New York NY, 10034
Phone: (212)932-4520

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will develop a robotic scrub technician that anticipates a surgeon's request for an instrument during surgery using robotics technology. Phase II research will build upon the success achieved in Phase I work , and will implement cognitive architecture over the current physical  and sensory system of the robot.  To validate the cognitive architecture, the robot will assist surgeons while performing operations on a physical simulator and in experimental animals.  In this way, errors both robotic and human will come into play.  The robot's actions will be judged using criteria for speed and clinical  appropriateness, and the cognitive architecture will be modified to eliminate undesired  behaviors.  It is expected that the robot will perform in a clinically acceptable way.

The commercial impact of this project will be in the area of healthcare. The proposed work addresses the issue of critical shortage of nurse technicians, and could reduce personnel costs in hospitals. Furthermore, the use of robots for this environment may free up human technicians to do more critical tasks

Title: SBIR Phase II: Three-Dimensional (3D) Laparoscope

Award Number: 0422102
Program Manager: George B. Vermont

Start Date: March 1, 2005
Expires: February 28, 2007
Total Amount: $428,918
Investigator: Kurtis Keller, kurtis@inneroptic.com
Company: Inneroptic Technology Incorporated
106A N. Churton St.
Hillsborough NC, 27278
Phone: (919)962-1746

Abstract:

This Small Business Innovation Research (SBIR) Phase II project is to develop a fully functional prototype 3-D laparoscope, which will be superior to the 2-D laparoscopes currently used in surgeries, based on laser illuminated miniaturized projector for computer generated light patterns and two cameras for acquisition of color and depth.

The commercial application of this project will be in surgical operations. This device will have the capacity to provide depth and computer enhanced view of the surgical domain more akin to open surgery. This would allow for more precision in surgical procedures, thereby eliminating hand-eye coordination issues and reducing mistakes and accidents

Title: SBIR Phase II: MicroElectroMechanical Systems (MEMS) Wavefront Correction Device for Ophthalmic Adaptive Optics

Award Number: 0421965
Program Manager: Om P. Sahai

Start Date: August 15, 2004
Expires: July 31, 2006
Total Amount: $492,983
Investigator: Steven Rodgers, steve.rodgers@memx.com
Company: MEMX, Inc.
2620 Augustine Drive
Santa Clara, CA 95054
Phone: (408)764-0185
Abstract

This Small Business Innovation Research (SBIR) Phase II project proposes to develop a MEMS wavefront correction device for ophthalmic adaptive optics. The use of adaptive optics in ophthalmics shows great promise, but the lack of suitable cost-effective solutions has hindered the advance of research and the development of associated commercial markets. The proposed work will leverage the most sophisticated surface micromachining technology available to design and deliver, for the first time, a MEMS wavefront correction chip that addresses all of the requirements specified by the vision science community. The commercial application of this project will be in the area of ophthalmology. Ophthalmic equipment suppliers need low cost wavefront correction devices for use in next generation phoropters and autorefractors, LASIK preview systems, and high resolution fundus imaging systems.

The ophthalmic market for low cost wavefront correction devices, once such devices are available, is projected to be at least $20 million per year. Such devices may also have utility outside of ophthalmics. Optical coherence tomography, confocal microscopy, portable military imaging systems, free space optical communication systems, and semiconductor lithography are other potential application areas for wavefront correction devices.

Title: SBIR Phase II: Multipass Second Harmonic Generation

Award Number: 0421974
Program Manager: Om P. Sahai

Start Date: September 15, 2004
Expires: August 31, 2006
Total Amount: $492,690
Investigator: Guido Knippels, gknippels@picarro.com
Company: Picarro, Inc.
480 Oakmead Parkway
Sunnyvale, CA 94085
Phone: (408)962-3919
Abstract

This Small Business Innovation Research (SBIR) Phase II project is to develop low-cost, 20-50 mW blue and green lasers for bioinstrumentation applications. The Phase II program objectives are to : (1) design, assemble and test 20 mW 505 nm laser prototypes; (2) to validate laser performance in a commercial bio-instrumentation application; and, (3) to assemble, test, and validate 50 mW blue-green laser prototypes using a higher efficiency second harmonic generation (SHG) architecture.

The commercial application of this project will be the availability of inexpensive laser light sources for researchers in cellular biology and DNA sequencing.

Title: SBIR Phase II: Automated Monitoring and Alarming for Elder Care

Award Number: 0422154
Program Manager: Om P. Sahai

Start Date: September 1, 2004
Expires: August 31, 2006
Total Amount: $481,203
Investigator: Rajeev Sharma, rsharma@advancedinterfaces.com
Company: Advanced Interfaces, Inc.
403 South Allen Street
State College, PA 16801
Phone: (814)867-8977

Abstract

This Small Business Innovation Research (SBIR) Phase II project will develop an automated monitoring system for residents living in elder care facilities. This system will enable the facility staff to quickly respond to any event or behavior requiring intervention, such as an accidental fall, using computer vision for tracking and behavior analysis. Prior Phase I research demonstrated the feasibility of this approach for fall detection and behavior analysis with the help of a laboratory prototype. This work also highlighted several challenges, such as dealing with changing lighting conditions and complex behaviors. Phase II research will focus on addressing these challenges and creating twelve beta sites in actual elder care facilities to further develop and test the algorithms.

The commercial application of this project will be on institutions linked to the care of the elderly. With over 50% of the growing population of seniors staying in independent / assistive living facilities or nursing homes, injuries and deaths resulting from unattended falls represent a serious societal and economical problem. Over 1.8 million seniors fall each year, with each fall costing an average of $9,400 in hospitalization. The proposed work could lead to a solution that provides a way for quickly responding to falls, saving hospitalization costs up to 26% and more importantly, reducing the likelihood of death by as much as 82%. It would also help in generating a feeling of security for the elders and their care givers, without a substantial increase in healthcare costs.

Title: SBIR Phase II: Novel Breath Diagnostic Instrument for Detection of Disease

Award Number: 0349782
Program Manager: Om P. Sahai

Start Date: February 1, 2004
Expires: January 31, 2006
Total Amount: $490,293
Investigator: Douglas Baer, d.baer@lgrinc.com
Company: Los Gatos Research
67 East Evelyn Avenue, Suite 3
Mountain View, CA 94041
Phone: (415)965-7772

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop a carbon isotope ratio analyzer based on Off-Axis Integrated Cavity Output Spectroscopy to measure the ratio of the isotopic abundances of 13C to 12C in exhaled breath. The compact analyzer will serve as a medical diagnostic instrument and will operate in a point-of-care setting. The instrument combines robust telecommunications-grade diode lasers with Off-Axis ICOS, an innovative technology that provides extremely long optical paths (several kilometers typical) for ultrahigh sensitivity. The instrument will be inexpensive, portable and easy to use and report measurements of 13CO2/12CO2 with sufficient sensitivity and precision to replace mass spectrometry in 13C-labeled breath tests for diagnosis of several diseases. Prior Phase I work has successfully demonstrated a laboratory instrument with a precision of 0.24 per mil (0.024%) in less than 6 minutes. In Phase II, a prototype instrument capable of autonomous operation, will be developed and tested in on-going clinical trials.

The commercial impact of the project will be significant, as the proposed instrument will aid in quick diagnosis of gastrointestinal diseases at the doctor's office, thereby enhancing rates of patients' compliance with treatment regimens.

Title: SBIR Phase II: Mouthrinse Generator for Plaque and Halitosis Control

Award Number: 0349689
Program Manager: Om P. Sahai

Start Date: March 1, 2004
Expires: February 28, 2006
Total Amount: $492,100
Investigator: Charles Tennakoon, charles.tennakoon@lynntech.com
Company: Lynntech, Inc
7607 Eastmark Drive, Suite 102
College Station, TX 77840
Phone: (979)693-0017
Abstract

This Small Business Innovation Research (SBIR) Phase II will develop and commercialize electrochemically operated devices that will revolutionize the oral hygiene industry by providing an on-demand generation of mouthwash in a portable device and in an irrigator. The mouthwash generated in these devices will be effective in controlling halitosis and dental plaque and will also provide tooth whitening. In the Phase I study, all of the proposed objectives and specified criteria of success were accomplished to amply establish the proof of concept and feasibility of the project. In Phase II, further optimization of the parameters will be followed by the design and fabrication of prototypes in conjunction with a prominent company dealing with turnkey manufacturing, and the testing of 100 portable units in a clinical setting.

The commercial impact of this project will be in the area of oral hygiene products. It is broadly estimated that up to 85 million Americans have halitosis, and over 35 million suffer from periodontal disease. Thus, the cost effective devices to be developed in this project are expected to have a large market potential in the $ 4.7 billion oral care industry.

Title: SBIR Phase II: Polymer Imaging Guide For Endoscopic Applications

Award Number: 0321408
Program Manager: Om P. Sahai

Start Date: November 1, 2003
Expires: October 31, 2005
Total Amount: $511,692
Investigator: Dave Welker, welker@paradigmoptics.com
Company: Paradigm Optics Inc.
14615 NE 13th Court Ste B106
Vancouver, WA 98685
Phone: (360)573-6500

Abstract

This Small Business Innovation Research (SBIR) Phase II project aims to develop high quality, inexpensive polymer-based (plastic) optical fiber imaging guides and other new and unique endoscopic devices through the use of innovative polymer processing techniques. Polymer imaging guides have several distinct advantages over their glass counterparts, including reduced cost, smaller bend radius, and increased ruggedness. Additional benefits include the ability to dope the polymer matrix with molecules that can be used as environmental probes, scintillating material, or indicators ; the ability to tailor the guide for highly specific applications, and the ability to impart diverse functionality into a single imaging guide. The Phase II project is expected to result in a truly disposable endoscope.

The commercial application of this project is in the area of biomedical devices and instrumentation. It is expected that the polymer imaging guide developed in this project will be used as a direct replacement for glass guides in all types of fiber optic endoscopes currently manufactured. The resulting benefits would be lower costs, less patient discomfort, higher reliability, earlier detection of abnormal conditions, and an increase in the number of procedures that could be performed with endoscopes in an outpatient setting.

Title: SBIR Phase II: Advanced Optical Instruments for Monitoring Asthma

Award Number: 0321447
Program Manager: Om P. Sahai

Start Date: November 1, 2003
Expires: October 31, 2005
Total Amount: $500,000
Investigator: Khosrow Namjou, knamjou@ekipstech.com
Company: Ekips Technologies, Inc.
710 Asp Ave., Suite 500
Norman, OK 73069
Phone: (405)307-8803

Abstract

This Small Business Innovation Research Phase II project will develop a laser based breathmeter for detecting and monitoring asthma in children and adults. The Phase I work proved the feasibility of constructing a machine, based on infrared laser absorption spectroscopy, that is capable of measuring exhaled nitric oxide (eNO) and exhaled carbon dioxide (eCO2) levels to evaluate airway inflammation for indications of asthma and to monitor treatment compliance. In the Phase II project, a dedicated hardware design for electronics and data processing plus user-friendly custom written software will be integrated into a compact system that is cost effective, highly sensitive, real-time, and reliable for monitoring airway inflammation.

The commercial application of this project is in the area of biomedical devices and instrumentation.

Title: SBIR Phase II: Micromachined Ultrasonic-on-a-Chip for Medical High-Resolution Imaging

Award Number: 0321576
Program Manager: Winslow L. Sargeant

Start Date: November 1, 2003
Expires: October 31, 2005
Total Amount: $499,993
Investigator: Eli Wiener-Avnear, leeoat@worldnet.att.net
Company: LEEOAT Company
2631 Colibri Lane
Carlsbad, CA 92009
Phone: (760)438-1439

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will optimize and finalize the design and the simulation of the ultrasound-on-a-chip (UOC) probe, and itegrate it into a portable ultrasound medical imager with high spatial resolution and enhanced picture definition for noninvasive clinical diagnosis of the internal lumens. The UOC probe architecture is based on patented ultraprecision micromachining technology. The objective is to fabricate and test the UOC probe and integrate it into a portable cost-effective medical imaging prototype system for noninvasive real-time high-definition volumetric medical imaging.

The realization of the merits of the ultrasound-on-a-chip based portable medical imager will open a wide window of commercialization opportunities for medical and nonmedical applications.

Title: SBIR Phase II: Neural Inverse Control for Ventilators

Award Number: 9983474
Program Manager: Sara B. Nerlove

Start Date: July 15, 2000
Expires: September 30, 2003
Total Amount: $761,987
Investigator: Neil Euliano, neuliano@nd.com
Company: NeuroDimension Incorporated
3701 NW 40th Terr
Gainesville, FL 32606
Phone: (352)377-5144

Abstract:

This Small Business Innovation Research Phase II project from NeuroDimension Incorporated will develop new, biologically inspired solutions to the problem of ventilator control of human subjects. The problem is difficult because the patient is analogous to a time-varying, nonlinear plant. Adaptive inverse control is powerful enough to adapt to changing conditions while maintaining system stability. In Phase I, NeuroDimension developed a control architecture and development environment for neural inverse control and applied it to controlling a ventilator. This solution outperformed the state-of-art commercial ventilator. The goal is to develop a system that will optimize most of the major settings currently set by clinicians on present-day ICU ventilators. The complexity of these ventilators subject their operators to speculative and empirical interpretation of many ventilatory parameters, leading to potentially hazardous misuse. NeuroDimension proposed system will model and extract relevant physiologic conditions in the patient and use this information to either control the ventilator automatically or to advise the clinician on how to change the settings. The primary technical approach utilizes neural fuzzy hybrid systems, Kohonen self-organizing maps (SOMs)-a SOM clusters the input space and assigns a different model to each cluster--and switching multiple inverse controllers. The firm has assembled a unique team of experts in the fields of neural control and ventilation to accomplish this task.

NeuroDimension proffers technology that has application to a number of possible products including, inverse neural control application software; an ultra-intelligent respiratory monitor; and an easy to use and optimal closed-loop ventilator controller.

Title: SBIR Phase II: IBEX - Restoring Functional Mobility in the Elderly Through In-Bed Exercise

Award Number: 0078585
Program Manager: Om P. Sahai

Start Date: December 1, 2000
Expires: June 30, 2001
Total Amount: $399,659
Investigator: Robert C. Dean, RCD@Synnovations.com
Company: Synergy Innovations, Inc.
10 Water Street, Rm. 405
Lebanon, NH 03766
Phone: (603)448-5454
Abstract:

This Small Business Innovation Research Phase II project completes development of a production In-Bed Exerciser (IBEX) and tests its efficacy. This unique, active exerciser is a portable and efficient means of giving, in bed, physical therapy sufficient to maintain or restore the walking muscles of bedridden people. Geriatrics are especially vulnerable to bed confinement; they can lose ability to walk after 5-10 days. Becoming bedridden is a leading indicator of mortality for the elderly. A growing elderly population, a shortage of Physical Therapists, their inability to provide force levels and intensity of exercise needed, and pressure to constrain medical costs, demand such a machine. The Company has innovated a portable exerciser that attaches to the bed, is computer controlled, provides bilateral, reciprocal or one-leg exercise and records performance. Phase I demonstrated feasibility.

The objective of this SBIR Phase II project is to use scientifically designed clinical trials to prove efficacy. Results are the prelude to successful commercialization according to the enclosed plan. The greatest social benefit will be improved quality of life for the elderly.

Title: SBIR Phase II: Integrated Circuit Design for Biological Data Transmission

Award Number: 0238696
Program Manager: Om Sahai

Start Date: January 15, 2003
Expires: December 31, 2004
Total Amount: $499,924
Investigator: James C. Morizio, jmorizio@tbsi.biz
Company: Triange Biosystems, Inc.
5114 Huxey Glenn Court
Durham, NC 27703-9293
Phone: (919)596-8069

Abstract:

This Small Business Innovation Research (SBIR) Phase II Project proposes to develop, test, market and produce low-power wireless headstage systems for the neural prosthetic market. The wireless neural headstage devices will be able to transmit and to receive sixteen electrodes sourced from a patient. The analog signals will be encoded and transmitted wirelessly to a remote receiver where they will appear on a 16-channel connector. The wireless headstage technology will replace the tethered connections and create a more natural and productive laboratory environment for patient data acquisition. Ultimately, wireless technology will improve the quality of life for anyone using a commercial neural prosthetic device by offering extended freedom of motion, improved product safety and reliability, and less visual distractions.

The primary commercial application of this project is in the wireless neural prosthetic market. Additional applications are expected in the biomonitoring business markets, such as for electrophysiological patient testing and monitoring.

Title: SBIR Phase II: Instrument for Tumor Cell Purging

Award Number: 0091448
Program Manager: Om Sahai

Start Date: February 15, 2001
Expires: January 31, 2003
Total Amount: $499,982
Investigator: Manfred R. Koller, fkoller@oncosis.com
Company: Oncosis
6199 Cornerstone Court
San Diego, CA 92121
Phone: (619)550-1770

Abstract:

This Small Business Innovation Research (SBIR) Phase II project describes a novel laser-based technology for large-scale analysis and processing of living cells. One application of this technology is the detection and elimination of contaminating tumor cells from autologous hematopoietic stem cell (HSC) transplants for cancer patients. Published studies have shown that: contaminating tumor cells contribute to cancer relapse; (2) successful tumor purging provides a clinical benefit; and (3) current purging methods are inadequate. A technology that reliably eliminates tumor cells from transplants, while leaving HSCs undamaged, is needed. A patented innovative approach integrating fluorescence scanning cytometry, real-time image analysis, and specific laser-induced killing of individual cell targets will be used. The Phase II project will complete the clinical-scale prototype instrument, leading into clinical trials. The instrument design will then be configured for successful commercial manufacturing, and further improvements in capabilities will be pursued in order to maintain market leadership and expand into other markets.

The studies conducted in the Phase II project will lead to commercialization of a method to eliminate detectable tumor cells from an HSC transplant with a several hour automated procedure. The resulting instrumentation will also be useful in a number of other clinical and research applications that require cell analysis and purification with high purity, yield and speed.

Title: STTR Phase II: High Speed Instrumentation for Real Time Biological Imaging

Award Number: 0091549
Program Manager: Om Sahai

Start Date: March 15, 2001
Expires: February 28, 2003
Total Amount: $499,999
Investigator: Stephen C. Minne, Steve@nanodevices.com
Company: NanoDevices, Inc
516 E. Gutierrez, Suite E
Santa Barbara, CA 93103-3253
Phone: (805)884-0240

Abstract:

This Small Business Technology Transfer (STTR) Phase II project is to develop a new type of atomic force microscope that can image nanometer scale features, in real time, in the physiological environment. In all of its forms, the microscope is probably the most widely used tool in the investigation of biological structure and function. The introduction of the atomic force microscope (AFM) to biology created much excitement because the AFM fills a gap in the capabilities of the microscopes that are available to biologists. The study of living and moving biological systems, on time scales of seconds, with nanometer scale resolution, is becoming increasingly important in biological research. Self-assembled monolayers, proteins, and cellular processes all fall into this category. Existing AFMs fall short of the requirements for these applications because of speed and sensitivity limitations in fluid operation. The project is based on the AFM, for nanometer scale imaging of biological samples that is orders of magnitude faster than current AFMs. Additionally, the new system will be optimized for fluid operation in order to give researchers active control over imaging dynamics. This composite system will allow researchers to probe nanometer scale biological phenomena at speeds never before accessible.

The technology could dramatically increase biological imaging in two ways: (1) faster imaging and (2) higher resolution in fluid. The increase in speed and resolution will help facilitate projects to provide faster results to researchers.

Title: SBIR Phase II: New Elastomeric Microelectrodes for Improved Neuroprostheses

Award Number: 0216035
Program Manager: Om Sahai

Start Date: October 1, 2002
Expires: September 30, 2004
Total Amount: $499,970
Investigator: Francis L. Keohan, fkeohan@capecod.net
Company: Cape Cod Research
19 Research Road
East Falmouth, MA 02536
Phone: (508)540-4400

Abstract:

This Small Business Innovation Research Phase II project is to develop electrically conductive polymer-silicone composite materials for improving the performance of implantable neural prostheses. Prior Phase I study has demonstrated the feasibility of synthesizing electrically conductive polymer nanocomposites with mechanical properties of silicone elastomers. Polymer-based prototype electrical devices were found to be stable toward simulated physiological conditions and cyclic current pulsing. The Phase II program will extend the benefits of these systems to the fabrication of more complex devices such as multi-poled cuff electrodes for chronic peripheral nerve stimulation and recording. An expanded test plan would include development of advanced device fabrication methods and extensive testing of the prototype neural prostheses for electrical response, tissue compatibility, and durability in chronic implantation applications. The optimized elastomeric electrodes will be characterized for biocompatibility, stability and electrical properties. Methodology will be developed for fabricating prosthetic electrodes for extensive in vitro pulsing studies and acute animal testing. Finally, test protocols for the new electrode products will be established in an effort to obtain FDA approval.

The commercial applications of this project will be in the area of biomedical devices and systems that serve the needs of disabled individuals following stroke or spinal cord injury.

Title: SBIR Phase II: No Preparation, Flexible, Dry Physiological Recording Electrodes

Award Number: 0216284
Program Manager: Om Sahai

Start Date: October 1, 2002
Expires: September 30, 2004
Total Amount: $500,000
Investigator: Frederick J. Lisy, lisy@orbitalresearch.com
Company: Orbital Research Inc
673 G Alpha Drive
Cleveland, OH 44143-2140
Phone: (440)449-5785

Abstract:

This Small Business Innovation Research Phase II project is to complete the development of a low-cost, no preparation required, and flexible dry physiological recording electrode. These electrodes have the potential to significantly improve quality of care and reduce total cost of biopotential signal analysis by reducing the time and preparation required to obtain a good signal and reducing the total cost of fabricating high quality electrodes. The Phase I results showed feasibility of fabricating dry electrode structures on rigid substrates onto low-cost flexible substrates. However, further work is necessary to optimize the fabrication processes and to ensure that the lowest cost and highest performing flexible dry electrode systems and fabrication processes are chosen to establish a solid foundation for future use. The key objectives of this Phase II project include parallel development of two particularly promising fabrication techniques, selection of a single fabrication technique for further development, and testing and evaluation of the capabilities of the dry electrodes in clinical environments.

The commercial applications of this project will be in the area of physiological monitoring of patients in a clinical setting. Physiological measurements such as ECG (electrocardiogram), EMG (electromyogram), and EEG (electroencephalogram) are expected to benefit from the use of dry electrodes, in part due to the reduced time and preparation needed to apply the electrodes and in part, due to the elimination of abrasive skin prepping and electrolytic gels in the measurement procedure.

Title: STTR PHASE II: Nuclear-Magnetic Resonance (NMR) Properties of Carbon Nanomaterials for Medical Applications

Award Number: 0321630
Program Manager: T. James Rudd

Start Date: August 1, 2003
Expires: July 31, 2005
Total Amount: $499,947
Investigator: Steven A. Stevenson, stevensons@lunainnovations.com
Company: Luna Innovations, Inc.
PO Box 11704
Blacksburg, VA 24062-1704
Phone: (540)953-4267

Abstract:

This Small Business Technology Transfer (STTR) Phase II project aims to develop advanced contrast agents for magnetic resonance imaging diagnostics. In Phase I dramatically improved contrast agents based on carbon nanospheres were demonstrated. The researchers discovered this new class of molecules called Trimetaspheres, which involve three Gadolinium metal ions encapsulated in a fullerene molecule. They are more than 50 times better in terms of relaxivity than the currently available contrast agents and safer, because the metal ions cannot escape the carbon cage. In the Phase II project full-scale production of the Gadolinium Trimetaspheres will be accomplished at the kilogram level to satisfy the market demand. These Trimetaspheres will be developed into future high field contrast agents and functionalization will be pursued to make the Trimetaspheres more soluble and biocompatible for various medical applications including cell targeting. Following this, the Trimetaspheres will be characterized and evaluated for R1 MRI contrast agents for both high and low magnetic fields. Subsequently Trimetaspheres will be developed for R2 MRI agents for high magnetic s.

Commercially, Trimetaspheres have proven potential in the $1.5 billion market of MRI contrast agents. Trimetaspheres dramatically improve patient care and lower medical costs by improving existing MRI diagnostics and providing new contrast agents that allow diagnoses in cases where there is no current method. The technology developed in this project has immediate applications in current MRI measurements and satisfies requirements for future high field strength MRI instruments. Improved contrast agents increase the likelihood of accurate diagnosis, and ultimately reduce the treatment cost. There are many instances where a MRI scan is not prescribed because no contrast agent exists. For example within the brain, Trimetaspheres can pass the blood-brain barrier and are small enough to fit inside the smaller regions of blood vessels. In addition, Trimetaspheres will lead to applications in other diagnostic equipment (x-ray, PET), and have advantages as a therapeutic delivering radiation upon targeted biodistribution.

Title: SBIR Phase II: Microelectrochemical Assays for Malaria Parasites

Award Number: 0548742
Program Manager: F.C. Thomas Allnutt

Start Date: February 16, 2006
Expires: February 29, 2008
Total Amount: $518,000
Investigator: Zoraida Aguilar, zoraida.aguilar@vegrandis.com
Company: Vegrandis
535 West Research Blvd
Fayetteville, AR 72701
Phone: (479)571 2592

Abstract:

This Small Business Innovation Research (SBIR) Phase II project focuses on the development of an automated, high-throughput, sensitive and specific assay for the micorelectrochemical detection of malaria parasites. The use of microelectrochemical assay will allow for the detection of malarial parasites with a combination of attributes, such as all four species to the level of one parasite per microliter of blood without sample preparation.

This technology will impact the current blood donor screening guidelines that call for the deferral of potential donors for one year following travel to malaria endemic regions. Not only do cases of fatal transfusion-transmitted malaria occasionally occur, but also the availability of the blood supply is reduced. This technology will aid the blood banking industry by providing an inexpensive, high-throughput, low detection limit malaria test as blood donor screening tool.

Title: SBIR Phase II: POINT - Precision Optical Intra-Cellular Near-field Technology

Award Number: 0548768
Program Manager: Ali Andalibi

Start Date: September 25, 2006
Expires: August 31, 2008
Total Amount: $338,122
Investigator: Joanne Ebesu, doconnell@oceanit.com
Company: Oceanit Laboratories
1001 Bishop St Suite 2970
Honolulu, HI 96813
Phone: (808)531-3017

Abstract:
This SBIR Phase II project proposes to develop a novel high-resolution instrument capable of penetrating live cells. Currently there are no methods that allow the inside of a living cell to be imaged down to 50 nm resolution or less. Confocal microscopes, MRI and ultrasound cannot image to this resolution and the use of electron microscopes destroys the cells. The potential to develop nanosensors capable of penetrating a cell without destroying its natural environment may provide new information about the molecular makeup of a cell. The proposed Precision Optical Intra-cellular Near-field Technology (POINT) is an innovative adaptation of Near-Field optical microscopy using solid emersion lens (SIL) technology coupled with a sub-wavelength aperture probe. The goal of the Phase I project was to research the feasibility of developing a near-field probe and solid immersion lens combination that would be useful for biological research by providing nanometer scale resolution and enhanced light throughput to image inside intact cells. A small optical excitation volume is provided by a near-field probe, circumventing the diffraction limit to obtain sub-wavelength spatial resolution. This new capability offers higher sensitivity and resolving power than is presently available in microscopy, and could provide a more detailed understanding of molecular processes underlying mutations that lead to any of a number of diseases such as cancer. Solid immersion lenses were successfully fabricated in house by grinding and polishing commercially available ball lenses and validation experiments were then carried out. It was demonstrated that a tighter focused laser spot and narrower spectral width were achieved when using a SIL. This corresponds to higher light coupling to a probe placed at the bottom of the SIL. Successful probe fabrication was achieved based on optical modeling for optimum light throughput.

In phase II we will develop the platform needed to use this SIL/Probe optical tool in conjunction with a regular microscope. The use of a nanoposition stage for precise alignment and extremely small motion of the probe will be integrated as well as a feedback mechanism that signals when physical contact is achieved, such as the probe penetrating a cell's membrane. Various SIL/Probe designs will be characterized including a custom SIL with phase grating for laser wavelengths in the blue. The work in Phase II is a direct follow-on from what was achieved under the Phase I effort.

Title: SBIR Phase II: Non-Contact Optical Stethoscope for Neonatal Patients

Award Number: 0724449
Program Manager: Muralidharan S. Nair

Start Date: July 15, 2007
Expires: June 30, 2009
Total Amount: $500,000
Investigator: Andrey Vyshedskiy, andrey@stethographics.com
Company: Stethographics
21 Wayside Road
Westborough, MA 01581
Phone: (508)320-2841

Abstract:

This Small Business Innovation Research (SBIR) Phase II research project will develop a non-contact optical stethoscope for use in Neonatal Intensive Care Units (NICU). Premature babies in NICU require monitoring for signs of lung congestion and heart disease. Currently NICU medical personnel use acoustic stethoscopes. The use of acoustic stethoscope has a number of highly undesirable side effects including withdrawal response, flinching, apnea, hypoxemia, change in sleep state, and possibility of contamination. During Phase I a prototype non-contact optical stethoscope, capable of recording good quality heart and lung sounds was developed. The non-contact stethoscope is based on a standard technique of interferometry with a novel fiber optic design. The fiber optic design avoids the use of glass components - mirrors, lenses, splitters, and prisms - and yields a light, rugged and inexpensive interferometer.

The non-contact optical stethoscope based on the fiber optic interferometer could greatly improve the quality of care for neonates, burn victims, immuno-suppressed patients, and in those cases where direct contact should be avoided. A laser interferometer based on a novel fiber optic design has been developed. The interferometer based on fiber optics is light, inexpensive, and rugged as it does not require component alignment. The handheld point-and-listen microphone based on the fiber optic interferometer can be ideally positioned to enter the existing laser interferometry market and to open new markets including medical, preventive maintenance of rotating machinery, military urban and rescue operations, as well as law enforcement surveillance.

# Bioprocessing and Industrial Bioproducts

Title: SBIR Phase II: Clinical-Scale Suspension Bioreactor for Primary Hematopoietic Culture

Award Number: 0296135
Program Manager: Om Sahai

Start Date: January 1, 2002
Expires: December 31, 2003
Total Amount: $400,000
Investigator: Todd A. McAdams, lcfarrar@aol.com
Company: Montec Research
1901 South Franklin
Butte, MT 59701
Phone: (406)723-2222

Abstract:

This Small Business Innovation Research Phase II project describes the development of a disposable, highly efficient suspension bioreactor for primary hematopoietic (blood cell-forming) cell culture. The unique challenges (heterogeneous nature, donor variability, and shear-sensitivity) of these cultures render traditional flask or suspension cultures unable to economically and consistently produce large quantities of cells. In Phase I, the feasibility and characteristics of a disposable suspension bioreactor was demonstrated. In Phase II, a scaled-up prototype of a large, agitated disposable bioreactor designed for clinical use (stem cell transplantation) will be constructed, characterized, and tested for reliability and durability. Gas and mass transfer correlations established in Phase I will be verified and extended. The use of medium optical density as a surrogate measure for cell density will be investigated.

The final product will be a system that combines the simple, disposable nature of flask culture with the control and monitoring capabilities of a suspension bioreactor. The resulting system will enable the cost-effective production of large numbers of primary hematopoietic cells and will improve the effectiveness and decrease the cost of medical procedures in the fields of transplantation, immunotherapy, and gene therapy.

Title: SBIR Phase II: Designer Cellulases for Biomass Conversion

Award Number: 0522310
Program Manager: Michael R. Ambrose

Start Date: October 1, 2005
Expires: September 30, 2007
Total Amount: $500,000
Investigator: William Coleman, wcoleman@kairos-scientific.com
Company: Kairos Scientific Inc.
10225 Barnes Canyon Rd., A110
San Diego CA, 92121
Phone: (858)626-8170

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will develop new technology to improve the high-temperature performance of endoglucanase, which can be used to manufacture pulp from wood chips and other biomass. Producing pulp for papermaking via thermomechanical pulping (TMP) of biomass is a highly energy intensive process that is performed at high temperatures. Research is proposed to demonstrate the feasibility of using a directed evolution strategy and high-throughput, solid-phase enzyme library screening to engineer a new endoglucanase variant with significantly improved thermoactivity, thermostability and resistance to inhibitors. This enhanced enzyme will be sold as an additive to manufacturers who produce pulp and paper via the TMP process. Major benefits include energy savings and improvement of paper quality.

The commercial application of this project will be on the pulp and paper industry. New screening technology will be used to engineer an enhanced enzyme that will modify pulp fibers under high-temperature conditions. This enzyme additive will accelerate the pulp refining process and thereby lower production costs by reducing the amount of electricity needed to complete the conversion. Any significant reduction in the energy input will be very economically attractive to the pulp producers. If introducing an effective enzyme treatment could eliminate even a modest 10% of the current energy expenditure, the potential worldwide savings could total nearly US$500 million per year. The enhanced enzyme will be able to create a new market by offering these significant savings to the pulp producers. In addition, the information gained from this study could be applied to other similar enzymes to expand the market for thermostable biocatalysts and broaden the understanding of protein structure-function

Title: SBIR Phase II: New Approaches to Using Renewable Biomass Derived Materials in Epoxy and Vinyl Ester Resin Products to Reduce Styrene and Other Petroleum Based Raw Materials

Award Number: 0521976
Program Manager: George B. Vermont

Start Date: September 1, 2005
Expires: August 31, 2007
Total Amount: $499,993
Investigator: Earl Wagener, ewagener@bellsouth.net
Company: Tetramer Technologies, L.L.C.
657 S Mechanic Street
Pendleton SC, 29670
Phone: (864)653-4339

Abstract:

This Small Business Innovation Research (SBIR) Phase II project seeks to reduce the levels of styrene in commercial vinyl ester-styrene resin formulations and other polymers by replacing all or a portion of the high VOC (Volatile Organic Compounds) toxic monomer with a biomass-derived material. Prior results have shown that the styrene content can be reduced from 45% to 35% or lower without increase in cost or the loss of polymer physical properties. Phase II work will entail commercial development with three customers, scale-up process engineering to commercial levels and expansion of the technology into the broader thermoset market.

The commercial application for this technology is in polymer and resin markets where styrene and other petroleum based, high VOC monomers are used. These are huge markets, and the products are used in hundreds of applications. Successful introduction of these replacements will reduce our dependence on imported oil, promote the use of domestic, crop-based resources, and reduce the use of high VOC pollutants.

Title: SBIR Phase II: Low Cost, Needleless Drug Injection System

Award Number: 0450559
Program Manager: George B. Vermont

Start Date: February 15, 2005
Expires: January 31, 2007
Total Amount: $483,086
Investigator: James Scherer, jjscherer@novawavetech.com
Company: Novawave Technologies
900 Island Dr Ste 101
Redwood City CA, 94065
Phone: (650)610-0956

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop a cheap and novel needleless injector (NI) that uses a ceramic-based electrokinetic pumping mechanism together with suitable nozzle arrays. The Phase II effort will focus on building numerous prototype pump / nozzle systems and determining the ability to achieve performance adequate for subcutaneous and intramuscular injections. Models for predicting the temporal response of the pump / nozzle systems will also be refined and compared to experimental results.

The commercial application of this project will be for delivering therapeutics such as vaccines and drugs for both human and veterinary markets. The ability to precisely control the injection temporal profile with the proposed device will enable injection site pain and trauma to be significantly reduced, thereby increasing effectiveness of NI drug delivery as well as reducing the probability of cross - contamination.

Title: SBIR Phase II: Characterization of the Metabolic Competency of Centrifugal Bioreactors

Award Number: 0421962
Program Manager: Om P. Sahai

Start Date: October 1, 2004
Expires: September 30, 2006
Total Amount: $500,000
Investigator: Heath Herman, hherman@kbi-usa.com
Company: Kinetic Biosystems, Inc.
430 Tenth Street, N.W.
Atlanta, GA 30318
Phone: (404)607-7331

Abstract:

This Small Business Innovation Research Phase II project is to develop a pilot-scale Centrifugal Bioreactor (CBR) for the continuous cultivation of hybridoma cells. The commercial application of this project will be in the biopharmaceutical industry for cell culture production of therapeutic agents. It is expected that the technology will reduce the scale and capital costs of commercial animal cell culture equipment and improve the quality and consistency of the secreted protein product.

Title: SBIR Phase II: A Novel Resonant-Enhanced Crystallization (REC) Process

Award Number: 0349704
Program Manager: Om P. Sahai

Start Date: January 15, 2004
Expires: December 31, 2005
Total Amount: $512,000
Investigator: Fangxiao Yang, fxyang@resodyn.com
Company: Resodyn Corporation
1901 South Franklin
Butte, MT 59701
Phone: (406)723-2222

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop a novel Resonant-Enhanced Crystallization (REC) process for pharmaceutical and biotechnology industry applications. REC technology is expected to be superior to the conventional crystallization process that incorporate impeller stirring for crystallization, due to its enhanced mass and heat transfer, lower shear (or reduced crystal breakage), and improved crystal size distribution.

The commercial impact of the project would be on pharmaceutical and biotechnology industries. REC technology will make the crystallization process more attractive to pharmaceutical separation and purification operations.

Title: SBIR Phase II: Development of Novel Enzymatic Antibiofilm Formulations

Award Number: 0321768
Program Manager: Om P. Sahai

Start Date: November 1, 2003
Expires: October 31, 2005
Total Amount: $499,914
Investigator: Nelson Barton, nbarton@diversa.com
Company: Diversa Corporation
4955 Directors Place
San Diego, CA 92121
Phone: (858)526-5000

Abstract:

This Small Business Innovation Research Phase II project will develop a powerful enzyme / biocide formulation for industrial water treatment. The research concept targets enzyme-facilitated diffusion of biocide for maximum biofilm control efficacy and provides a resultant low cost product with lowered environmental load. Proprietary gene evolution technologies will be used to enhance enzyme efficacy and to optimize process stability to provide robust enzyme candidates for formulation with conventional biocides. Optimized enzyme / biocide formulations will be tested against multispecies biofilms grown under simulated industrial process conditions.

The commercial application of this project is in the area of industrial bioproducts. Microbial fouling is a common problem in a variety of industrial, household, personal hygiene, and medical settings. To this end, a critical need exists for improved microbial control methods that are effective, economically beneficial, non-toxic and environmentally friendly. The anti-biofilm enzyme products, such as those targeted in this project, are expected to meet these needs for a market that represents an opportunity value of $995 million.

Title: SBIR Phase II: Cell-Based Microfluidic Platform for Drug Discovery

Award Number: 0321506
Program Manager: Om P. Sahai

Start Date: November 1, 2003
Expires: October 31, 2005
Total Amount: $498,620
Investigator: Brett Schreyer, b.schreyer@bioprocessors.com
Company: BioProcessors Corporation
35C Cabot Rd.
Woburn, MA 01801
Phone: (781)935-1400

Abstract:

This Small Business Innovation Research Phase II project will complete the development of the microscale bioreactor platform as a useful tool for cell culture studies in drug discovery research and development. The Phase II work has three key objectives: (1) to expand the capabilities of the microscale bioreactor to allow for the measurement of pH, dissolved oxygen, and protein titer; (2) to construct a fully automated bioprocessing cluster tool; and (3) to demonstrate the cost and speed advantages of the high-throughput approach to bioreactor production of recombinant protein.

The commercial application of this project is in the area of cell culture bioreactors for drug discovery and development.

Title: SBIR Phase II: Biological Process to Utilize Gases from Livestock Confinement Facilities in Biomass Production

Award Number: 9983163
Program Manager: Om P. Sahai

Start Date: August 1, 2000
Expires: July 31, 2002
Total Amount: $400,000
Investigator: Bruce Schroder, bgschroder@msn.com
Company: Dairilean Inc
P O Box 88647
Sioux Falls, SD 57105
Phone: (605)743-5204

Abstract:

This Small Business Innovation Research Phase II project will build and test a 1/30 scale prototype photo bioreactor system, which converts waste gas emissions from confinement swine facilities into algae (biomass). Large confinement production facilities account for a majority of livestock production and represent a significant source of odor and greenhouse gases as well as large quantities of solid and liquid waste. Phase I research demonstrated the ability to capture waste gases from a confinement swine facility and use it to produce micro-algae using a photo bioreactor. The research demonstrated that the algae in the photo bioreactor removed more than 90 percent of the waste gases and odors. During Phase II a 1/30-scale prototype photo bioreactor system will be built and attached to an existing swine confinement facility. The system will be tested using a variety of media and algae or photo organism species during the Phase II research. If successful a full scale demonstration unit will be built and tested in Phase III with sales of the system following. The system will address a serious environmental problem while reducing operating costs for swine producers by providing a feed supplement, algae biomass, and creating the potential to extract valuable co-products from the micro-algae.

The initial market for the bioair photobioreactor will be large swine operations. Pro Edge, a large swine producer, has agree to purchase the first demonstration unit and plans to purchase an additional 100 to 300 systems if they work as anticipated. While sales of the system will generate revenue, the ultimate goal is to extract high value components from the algae for use in pharmaceuticals, pigments, carbohydrates, and other chemical products. The market for these products is estimated to be approximately $6 billion in 2000.

Title: SBIR Phase II: A Novel Integrated Bioleaching Process for Chalcopyrite: An Alternative to Smelting

Award Number: 0078471
Program Manager: Om P. Sahai

Start Date: October 1, 2000
Expires: September 30, 2002
Total Amount: $322,708
Investigator: Gregory Olson, lbl@rmi.net
Company: Little Bear Laboratories, Inc.
5906 Mcintyre Street, Bldg.#2
Golden, CO 80403
Phone: (406)446-3648

Abstract:

This Small Business Innovation Research Phase II project is developing a novel electrobiochemical leaching (EBL) approach to recover copper from chalcopyrite, providing an alternative to smelting. Chalcopyrite is the most common copper ore, yet it is difficult to process hydrometallurgically because it passivates due to formation of refractory surface layers. The EBL approach in Phase 1 was shown to prevent this passivation and to result in faster and more complete copper extraction than conventional bioleaching approaches. The Phase II research objectives are to: 1) demonstrate the versatility of the process by determining the extent of copper extraction from different sources of chalcopyrite ore; 2) determine the optimum bioreactor configurations for the EBL approach; and 3) make a large laboratory scale (50 to 100 kg) demonstration of the process for determining preliminary process economics. The research will measure the extent of copper extraction and extraction kinetics by EBL, including the determination of metallurgical balances.

The results of the Phase II research will provide the data required to establish preliminary economic feasibility of the process and to convince investors or operators (mining company) to support a pilot scale demonstration. If successful, the EBL approach will provide a new technology in mineral extractions that will open additional reserves of copper in the US and elsewhere and reduce smelting of copper

Title: SBIR Phase II: Low-Frequency Sonochemistry -- A Cutting Edge Industrial Processing Technology

Award Number: 0078350
Program Manager: Rosemarie D. Wesson

Start Date: October 1, 2000
Expires: September 30, 2002
Total Amount: $434,000
Investigator: Johan van Walsem, hjvanwalsem@aol.com
Company: Resodyn Corporation
1901 South Franklin
Butte, MT 59701
Phone: (406)723-2222

Abstract:

This Small Business Innovation Research (sbir) Phase II project will demonstrate use of the novel low-frequence sonic technology for application as an advanced fermentation process. This project objective will establish a fundamental understanding of the low-frequency sonic technology capabilities to increase the productivity and yield of various aerobic fermentation processes, e.g., bacteria, yeast and mycelial. The Phase II program includes the development, design and demonstration of a prototype processing system as an efficient and cost-effective method for advanced fermentation applications. The Phase I objectives were fully achieved and feasibility of the innovative technology was demonstrated to provide extraordinarily high rates of gas mass transport into liquids, at low energy values and at low shear rates. The quality and amount of scientific and engineering data exceeded expectations, providing a solid base for a Phase II success. Post-Phase II experimentation was undertaken, which demonstrated specific commercial applications that have market-pull for use of the innovative fermentation methods. Several potential Phase III commercial fermentation applications have been identified. A commercial partner for Phase II co-funding and Phase III funding has been obtained. The commercial partner has also agreed to purchase equipment from Montec for their newly acquired fermentation business.

Commercial applications for fermentation processes include large quantity drug production for enhancement of both human and animal health, amino acids such as lysine for animal feeds and phenylalanine for production of aspartame, food preservatives such as ascorbic acid (vitamin C), vitamins and a plethora of other commodity compounds. In general, the production of an increasing number of biologically active compounds is shifting from traditional organic synthesis to fermentation. In these areas, the development of a lower cost, higher productivity technology has strong commercial appeal both in new and retrofit situations. Fermentation is the commercial end of the genetic engineering revolution and is virtually used in all of the cutting edge therapeutics.

Title: SBIR Phase II: Clinical-Scale Suspension Bioreactor for Primary Hematopoietic Culture

Award Number: 0078716
Program Manager: George B. Vermont

Start Date: December 1, 2000
Expires: February 28, 2002
Total Amount: $400,000
Investigator: Todd McAdams, lcfarrar@aol.com
Company: Tissue Therapeutics
2143 Sheridan Road
Evanston, IL 60208
Phone: (847)467-4559

Abstract:

This Small Business Innovation Research Phase II project describes the development of a disposable, highly efficient suspension bioreactor for primary hematopoietic (blood cell-forming) cell culture. The unique challenges (heterogeneous nature, donor variability, and shear-sensitivity) of these cultures render traditional flask or suspension cultures unable to economically and consistently produce large quantities of cells. In Phase I, the feasibility and characteristics of a disposable suspension bioreactor was demonstrated. In Phase II, a scaled-up prototype of a large, agitated disposable bioreactor designed for clinical use (stem cell transplantation) will be constructed, characterized, and tested for reliability and durability. Gas and mass transfer correlations established in Phase I will be verified and extended. The use of medium optical density as a surrogate measure for cell density will be investigated.

The final product will be a system that combines the simple, disposable nature of flask culture with the control and monitoring capabilities of a suspension bioreactor. The resulting system will enable the cost-effective production of large numbers of primary hematopoietic cells and will improve the effectiveness and decrease the cost of medical procedures in the fields of transplantation, immunotherapy, and gene therapy.

Title: STTR Phase II: Engineering Geobacter for Enhanced Electricity Production

Award Number: 0548633
Program Manager: F.C. Thomas Allnutt

Start Date: September 25, 2006
Expires: September 30, 2008
Total Amount: $499,665
Investigator: Christophe Schilling, cschilling@genomatica.com
Company: Genomatica Inc.
5405 Morehouse Dr. Suite 210
San Diego, CA 92121
Phone: (858)824-1771

Abstract:

This Small Business Technology Transfer (STTR) Phase II project aims to develop commercially viable bacterial strains (Geobacter sulfurreducens) for use as biocatalysts in microbial fuel cells. The research genetically manipulates these bacteria to enable the utilization of alternative substrates and increase current generation through the expression of an energy consuming futile cycle. The rates will be increased and alternative cheaper substrates utilized during this project.

The broader impact of this research will result in development of novel microbial fuel cells that can convert renewable resources such as biomass and agricultural wastes to electrical energy in an efficient fashion with varied commercial applications.

Additionally, innovative the metabolic engineering strategy that is developed could be applied to other industrially relevant microorganisms. In addition, there are significant societal and educational components of this program. One example would be a microbial fuel cell that harnesses electricity from organic waste can be valuable in electrifying remote rural communities in developing countries by decentralizing power generation while protecting the environment.

Title: STTR Phase II: A New Hyperspectral Imaging Spectrometer

Award Number: 0620581
Program Manager: F.C. Thomas Allnutt

Start Date: August 24, 2006
Expires: October 31, 2008
Total Amount: $479,219
Investigator: Rand Swanson, swanson@resonon.com
Company: Resonon
619 North Church Ave Suite 3
Bozeman, MT 59715
Phone: (406)586 3356

Abstract:

This Small Business Technology Transfer (STTR) Phase II research project develops a macroscopic fluorescent scanner that utilizes hyperspectral imaging with enhanced capability for reading microarrays, multiwell plates, and two dimensional (2D) gels. The system utilizes novel optical design to provide more efficient light gathering and less aberration for better imaging versus conventional hyperspectral optical designs. The anticipated technical benefits include improved signal-to-noise (greater sensitivity) and the better dye multiplexing (enabling the use of multiple dyes to detect of multiple analytes simultaneously). The broader impact of this research will be to enable more rapid advancement of scientific discovery by providing enhanced tools for study of the complexity of biological signaling, metabolic and response networks using non-radioactive optical detection methods to improve safety and reduce waste problems with optical detection.

Title: SBIR Phase II: Dynamic Signal Processing and Information Extraction for E-Noses

Award Number: 0522225
Program Manager: George Vermont

Start Date: November 30, 2005
Expires: November 30, 2007
Total Amount: $506,000
Investigator: Neil Euliano, neil@conveng.com
Company: Convergent Engineering
4817 SW 34th Street, Suite 4
Gainesville, FL 32608
Phone: (352)378 4899

Abstract:

This Small Business Innovation Research SBIR) Phase II project focuses on the development of electronic nose signal processing and dynamic pattern recognition systems specifically tuned to the properties of odors. This advanced e-nose signal processing toolbox should improve current selectivity by an order of magnitude. A prototype exhaled-breath propofol (anesthetic) monitor for use in measuring depth of anesthesia in patients undergoing surgery will be built and demonstrated.
The initial commercial application of this project will be in the medical surgery area where the product should provide more accurate patient dosing during anesthesia. The technology, however, may be broadly applicable to such key areas as medical diagnostics, illicit drug detection, glucose monitoring, etc.

Title: SBIR Phase II: Continuous Spray-Capture Production System

Award Number: 0620389
Program Manager: Rosemarie Wesson

Start Date: September 21, 2006
Expires: September 30, 2008
Total Amount: $467,005
Investigator: Piechocki Piechocki, JPiechocki@ABN-Corp.com
Company: Advanced BioNutrition Corp.
7155-H Columbia Gateway Drive
Columbia, AL 21046
Phone: (410)730 8600

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will develop a technology that allows the stabilization of live probiotic bacteria for incorporation into food products outside the dairy case. ABN proposes a novel microencapsulation solution that involves pumping viscous liquids through a spray nozzle, followed by the capture of the resultant particles in a cross-linking fluid. The Phase II objectives are to complete the commercial acceptability of this novel process by modifying the system to make all processes steps compliant with current Good Manufacturing Processes and by designing and fabricating the final critical drying step for the microencapsulated probiotics. This final step will provide a product that is stable enough to be used by the food and feed industries to allow the use of probiotics in products that do not need to be refrigerated.

The manufacturing technology proposed herein is an enabling technology that will open many new commercial opportunities for a number of industries. Stabilization of the probiotics and incorporation into nutritional bars, beverages, cereals, and other food products that do not require refrigeration will greatly expand the commercial potential, and choices for consumers who will benefit from these gut-friendly bacteria. The same technology could also be used for the stabilization and delivery of enzymes, vaccines, and other small molecules whose oral delivery is limited by gastric digestion.

Title: SBIR Phase II: Development of a BioAcoustic Mixing Platform

Award Number: 0646562
Program Manager: F.C. Thomas Allnutt

Start Date: March 15, 2007
Expires: February 28, 2009
Total Amount: $500,000
Investigator: Todd McAdams, lcfarrar@resodyn.com
Company: Resodyn Corporation
130 N Main St Ste 600
Butte, MT 59701
Phone: (406)497-5252

Abstract:

This Small Business Innovation Research (SBIR) Phase II research project develops a mixer based on sound waves applicable for use in bioreactors for cell culturing and fermentors. Cell culturing and fermentation are large markets where significant growth is forecast over the next several years. This research will establish the optimal design and operating conditions for this non-invasive and non-destructive mixing technology. It is anticipated that performance for many applications can be enhanced by 50% or greater over state-of-the-art technology using this novel agitation technology.

The broader impact will be to reduce the costs of pharmaceutical production, when such production is based on biological feedstocks. Media and process development for biological production of pharmaceuticals is costly and time-intensive and performed using stirred-tank bioreactors due to the limitations of orbital shake-flask and cell culture flasks. A mixing technology that could unify laboratory-scale and pilot-scale experiments would be highly valuable in speeding the pace of process development. Low-frequency acoustic energy will dramatically enhance gas-liquid mass transport without increasing hydrodynamic shear stress. The research project will enhance the scientific understanding of low frequency acoustic mixing processes by quantifying the impact of acoustic frequency on oxygen transfer rates and cellular growth. The significance to society that the successful development is a dramatic increase in the pace of biotechnological process development. This will lead to more rapid commercialization of and lower prices for pharmaceutical products that enhance overall quality of life.

Title: SBIR Phase II: Development of Resonant Waveguide-Grating Elements for High Throughput Screening of Proteins

Award Number: 0724407
Program Manager: Muralidharan S. Nair

Start Date: July 15, 2007
Expires: June 30, 2009
Total Amount: $500,000
Investigator: Debra Wawro, wawro@resonantsensors.com
Company: Resonant Sensors Inc.
202 E. Border Street
Arlington, TX 76010
Phone: (817)300-8297

Abstract:

This Small Business Inovation Research (SBIR) Phase II research project applies a new sensor principle to develop commercial High-Throughput Screening (HTS) systems for drug-development applications. The advantages of the Guided-Mode Resonance (GMR) sensor concept for such applications reside in its inherent physical characteristics including polarization diversity, materials independence, choice of spectral regions, angular-addressing flexibility, and associated compact system configurations. These properties enable tag-free sensor technology with high sensitivity, high accuracy, and multi-parameter detection. A major objective is the development and verification of GMR-sensor HTS commercial system prototypes in standard formats. Integrated analysis software will present data on biomolecular binding events, including background density and molecular accumulation dynamics, to the user. An additional main thrust is the development of attachment chemistry and methods for sensor activation where a set of protocols and processes for example measurands will be optimized to maximize detection sensitivity. Finally, by applying transmission sensor formats with shaped input light beams and integrated detector matrices, the next-generation compact system designs for massively parallel screening of drug compounds will be provided.

This research project will stimulate progress in drug discovery. Guided-mode resonance sensors operate without chemical tags permitting observation and study of unperturbed biochemical processes, as no foreign substance is introduced. Therefore, these sensors provide enhanced understanding of chemical and biomolecular reactions and may lead to advances in chemical process development and drug discovery and design. Moreover, this class of biosensors has other potential applications including medical diagnostics, proteomics, genomics, environmental monitoring, and homeland security. Application of this technology to microfluidics, lab-on-a-chip, and wireless integrated sensors for homeland security and environmental monitoring may provide new tools for accurate and cost-effective detection of biotoxins, explosives, and hazardous materials.

Title: SBIR Phase II: An Innovative Photobioreactor for Commercial Production of Astaxanthin from Genetically Improved Haematococcus Pluvialis Strains

Award Number: 0724411
Program Manager: F.C. Thomas Allnutt

Start Date: July 1, 2007
Expires: June 30, 2009
Total Amount: $499,866
Investigator: Fan Lu, lf1230nc@yahoo.com
Company: Algaen
3488 Bramlet
Clemmons, NC 27012
Phone: (336)577-4354

Abstract:

This Small Business Innovative Research (SBIR) Phase II reserach develops an innovative biotechnology for commercial production of natural astaxanthin using genetically improved microalgal strain(s) grown in a proprietary large-scale photobioreactor, and to demonstrate the effectiveness of the new strains in improving bioavailability of astaxanthin. The proposed R&D efforts aim to overcome the major weakness inherent in the present production of astaxanthin-enriched Haematococcus: poor bioavailability of astaxanthin for humans and animals. The company will use several genetically modified Haematococcus strains with remarkably improved bioavailability of astaxanthin. The major objectives of the Phase II research are to design, construct, and evaluate an innovative large-scale photobioreactor system for sustainable mass culture of these new strains. The improved production system will increase astaxanthin productivity by 1.5- to 2-fold with at least 30% cost reduction.

The broader impacts of this technology will be to overcome two major hurdles for the Haematococcus-based astaxanthin industry. The application of this biotechnology will lead to major increases in astaxanthin sales by 2015. It will also result in job expansion in the Haematococcus-astaxanthin production and related industries (e.g., cosmetic, pharmaceutical, and nutraceutical). Reduction in the production costs will lead to decreasing prices, making astaxanthin more affordable to allow more people to take advantage of astaxanthin as a strong antioxidant for improving health and well-being.

Title: SBIR Phase II: High Performance Cement Additive from an Agricultural Byproduct

Award Number: 0724463
Program Manager: F.C. Thomas Allnutt

Start Date: September 15, 2007
Expires: August 31, 2009
Total Amount: $500,000
Investigator: Rajan Vempati, chkgroup@worldnet.att.net
Company: ChK Group, Inc.
11700 Audelia Road
Dallas, TX 75243
Phone: (972)234-6744

Abstract:

This Small Business Innovation Research Phase II project develops the manufacturing process for a cement additive from an agricultural biomass waste to be used in the production of High Performance Concrete (HPC), and blended cement. This additive imparts increased strength and durability to concrete; therefore will mostly be used in high-rise buildings, highway construction, and infrastructures built in severe environmental conditions, e.g. petrochemical plants and marine structures. This project will generate increased revenues to the US farmers by selling their byproduct at a higher price and will create jobs in rural areas. Also, potential exists to license the technology to several emerging economies, where there is an urgent need to build transportation-, energy- and building-infrastructures.

The Broader Impacts of this research will be increased and higher value use of this agricultural waste in high strength cement. Utilization of this improved product will reduce pollution caused by the current alternatives in both air and at landfill sites. This research is intended to provide a profitable alternative to farmers producing this crop and create rural jobs.

# Environmental Biotechnology

Title: SBIR Phase II: Development of a Differential Long-Path Spectrophotometer for On-line Measurements of Controlled Halogenated Organic Compounds in Potable Water

Award Number: 0109973
Program Manager: Om Sahai

Start Date: September 1, 2001
Expires: February 29, 2004
Total Amount: $498,274
Investigator: Yogesh C. Agrawal, yogi@sequoiasci.com
Company: Sequoia Scientific, Inc.
2700 Richards Road
Bellevue, WA 98005
Phone: (425)641-0944

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will develop a prototype instrument for measuring harmful bi-products of chlorination in drinking water. These disinfection bi-products are subject to EPA regulations. The Phase I project demonstrated that the concept of differential UV absorption measurement, i.e. absorption before and after chlorination, is suitable for the needed measurement. A pre-production prototype instrument will be constructed during the Phase II project. This device shall employ a multi-pass cell design using our novel dual-ratio technique that eliminates concerns about long term drifts. The overall instrument architecture design and systems design will be carried out prior to assembly of the full microprocessor-controlled recording device. Extensive laboratory and field tests will be used to review design changes before production.

The potential commercial applications of the instrument proposed may be used in the laboratory or in-line at utilities. The market for the proposed product is quite substantial, as EPA regulations will result in the installation of such devices at all utilities and drinking water facilities.

Title: SBIR Phase II: An Automated Water Pathogen Monitoring System

Award Number: 0450613
Program Manager: George B. Vermont

Start Date: March 1, 2005
Expires: February 28, 2007
Total Amount: $512,000
Investigator: Zoraida Aguilar, zoraida.aguilar@vegrandis.com
Company: Vegrandis, LLC
535 W. Research Blvd.
Fayetteville AR, 72701
Phone: (479)571-2592

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims to develop an automated instrument for rapid and specific detection of waterborne pathogens in municipal water supplies using methods combining immunoassay with electrochemistry. Although the disposable cartridges for this instrument could be specified for nearly any pathogen of interest, this project will focus primarily on the detection of Cryptosporidium parvum oocysts. C. parvum is a threat to the nation's water supply, does not respond to common antibiotics and resists water purification treatments.

The commercial application of this project will be on the monitoring of drinking water supplies for pathogens. This would include testing of water at the source, in distribution networks, and at bottling and packaging facilities. The proposed device would eventually be adapted for emergency field use, for home use by safety conscious consumers, and for medical, industrial, recreational and combat purposes.

Title: SBIR Phase II: Field Demonstration of a Novel Biotechnology for In-Situ Bioremediation of Methyl Tert-Butyl Ether (MTBE) in Groundwater

Award Number: 0450486
Program Manager: Michael R. Ambrose

Start Date: May 1, 2005
Expires: April 30, 2007
Total Amount: $499,999
Investigator: Fatemeh Shirazi, fshirazi@microvibiotech.com
Company: Microvi Biotech LLC
11966 W 119TH ST
Shawnee Mission KS, 66213
Phone: (913)696-9934

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims to develop a novel process for in-situ bioremediation of methyl tert-butyl ether (MTBE) in groundwater. The Environmental Protection Agency (EPA) considers MTBE a potential human carcinogen. Currently, MTBE's Maximum Contaminant Level (MCL) in drinking water has been set for 18 parts per billion. It is estimated that the cost of cleaning up MTBE contamination nationwide is $29 billion and growing. Bioremediation holds a great promise for destruction of MTBE in groundwater. The key problems with currently used bioremediation methods for MTBE are (1) the inability to establish high densities of MTBE- degrading bacterial, (2) the inability to maintain contact between the degrading bacteria and MTBE, and (3) the upsets and losses of key bacteria. Prior Phase I work has successfully demonstrated the effectiveness of a new technical approach called Biological Permeable Barrier (BPB) that uses encapsulated MTBE-degrading bacteria for removal of MTBE in water. The primary objective for the Phase II project is to assess the long-term performance of a BPB field pilot unit to remove MTBE at Port Hueneme Navy site, and to assess the cost and performance of the BPB / MicroBeads system for longer periods of time under field conditions. The novelties of this technical approach are four folds : (1) the proposed system will deliver high cell density of MTBE-degrading bacteria right to the zone of contamination; (2) the proposed system will create the perfect environment for bacteria with a high degree of degradation and stability; (3) the proposed system will protect the bacteria against environmental stresses; and, (4) the proposed system will prevent wash out of key bacteria. It is anticipated that the proposed BPB pilot scale unit at Port Hueneme will effectively degrade MTBE and other contaminants in groundwater to non-detectable levels.

The immediate commercial application of this project will be on the bioremediation of MTBE in groundwater. However, the proposed technology holds promise for effective, controlled and cost efficient cleanup of groundwater at sites contaminated with other toxic and polluting chemicals as well. Other potential applications include the treatment of industrial wastewater and drinking water.

Title: SBIR Phase II: The Use of Halophytic Plants and Fish for the Bioremediation of Coal Bed Methane Discharge Waters

Award Number: 0422222
Program Manager: Om P. Sahai

Start Date: September 15, 2004
Expires: August 31, 2006
Total Amount: $500,000
Investigator: John Woiwode, woiwodejon@cs.com
Company: AquaMatrix International, Inc.
270 Veronica Lane, Suite D
Jackson, WY 83001
Phone: (307)739-7185
Abstract

This Small Business Innovation Research (SBIR) Phase II project is to develop a process that uses halophytic plants and aquaculture effluent to treat highly saline coal bed methane (CBM) discharge water. Vast volumes of water are a necessary though unwanted byproduct of the gas drilling process. The saline discharge is widely viewed as an environmental liability. Discharges into streams are essentially forbidden, while indiscriminant surface discharge causes soil salination. Prior Phase I work has shown that halophytic plants may be successful in sequestering significant amounts of sodium when irrigated with CBM discharge waters. This Phase II project will confirm Phase I greenhouse data with field trials of plants irrigated with CBM water and fish effluent when compared with controls under otherwise normal farming practices. Soil impacts and tilth will also be examined in great detail.

The commercial application of this project will be to alleviate the negative impact of CBM discharges on the environment in Wyoming, and to open up huge areas of land for responsible CBM exploration and recovery.

Title: SBIR Phase II: Advanced Thermal Treatment Process For Sewage Sludge

Award Number: 9983559
Program Manager: Om P. Sahai

Start Date: April 1, 2000
Expires: March 31, 2002
Total Amount: $400,000
Investigator: Michael Klosky, enertech1@mindspring.com
Company: EnerTech Environmental Incorporated
739 Trabert Avenue, NW
Atlanta, GA 30318
Phone: (404)355-3390

Abstract:

This Small Business Innovation Research Phase II project will demonstrate the technical and economic feasibility of the Slurry Carbonization process in generating an improved fuel product from low grade Municipal Sewage Sludge (MSS). Approximately 7.8 million dry tons of MSS are generated each year in the U.S. as a byproduct of municipal waste water treatment. MSS management is a growing concern due to the increase in generated volumes of sludge, demand for lower pollutant discharges, and rise in disposal costs. Slurry Carbonization is a moderate temperature and pressure treatment, which removes oxygen functional groups from the MSS and produces a homogeneous, carbon-hydrogen enriched char product for co-combustion or reburning in suspension-fired coal boilers. The overall objective of Phase II research is to develop the scientific and engineering data necessary to design, build and operate a demonstration facility in Phase III scale-up. Phase II research will focus on bench-scale optimization using EnerTech's 2.2 gal/hr PDU and pilot-scale engineering studies using HTI's 510 lb/hr PDU. Pilot-scale combustion and reburning experiments then will be conducted in EER's 1.0 MM Btu/hr BSF.

It is anticipated that Phase II research will establish Slurry Carbonization as an economically and environmentally desirable method of MSS utilization. In addition to treatment of MSS, other applications of EnerTech's Slurry Carbonization process technology include clean coal combustion and the production of homogeneous slurry fuels from industrial sludge, pulp and paper mill wastes, Kraft mill black liquor, MSW, RDF, wood wastes and other sources of renewable biomass.

Title: STTR Phase II: Development of a Solar Air Conditioner for Small Cooling Loads

Award Number: 0110570
Program Manager: Om Sahai

Start Date: December 15, 2001
Expires: November 30, 2003
Total Amount: $500,000
Investigator: Hector M. Sanchez, acmech@prtc.net
Company: A/C & Mechanical Serv Co
Box 393
Mayaguez, PR 006810393
Phone: (787)833-8050

Abstract:

This Small Business Technology Transfer (STTR) Phase II project will develop a reliable prototype of a novel, compact and low cost solar air conditioning system for hot and humid climates. The system will consist of an air-cooled single effect absorption machine driven by an array of high performance flat plate collectors and a thermal storage tank. A microncontroller based control system will allow an optimal system operation. The capacity of the system is projected to be in the range of 3-5 cooling tons.

The marketing, manufacturing, installation, and product development of the proposed technology is envisioned as a partnership of three small businesses dedicated to: installation of A/C systems, marketing and manufacturing of solar collectors, and to research.

Title: SBIR Phase II: Ultraviolet (UV) Water Remediation with Surface Discharge UV Lamps

Award Number: 0237472
Program Manager: Om Sahai

Start Date: March 1, 2003
Expires: February 28, 2005
Total Amount: $488,279
Investigator: Raymond B. Schaefer, rschaefer@phoenixsandt.com
Company: Phoenix Science & Tech Inc
27 Industrial Avenue
Chelmsford, MA 01824
Phone: (978)367-0232

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop an Ultra-Violet (UV) water remediation process using a novel Surface Discharge Pulsed UV lamp (SD lamp) to treat organic contaminants. The objective of the Phase II research is to extend Phase I accomplishments and to develop a prototype Surface Discharge UV water treatment system for subsequent commercialization. For UV water treatment, the SD lamp offers advantages in terms of inherent UV efficiency, spectrum, high intensity and the absence of concerns linked to the use of mercury. Prior Phase I studies have shown that the effectiveness of SD lamps is greater than that of commercial mercury lamps by more than what would be expected based on UV efficiency alone. The proposed NSF Phase II Project will examine the reasons for this high effectiveness and to use this information in order to develop a Phase II prototype SD UV water remediation system. This Phase II work will be carried out in conjunction with a major UV water treatment company.

The commercial application of this project will be in the area of water treatment. The Surface Discharge UV lamp is expected to replace mercury lamps currently used in most UV water treatment systems.

Title: SBIR Phase II: Bioremediation of Chlorinated Solvents in Saturated, Low Permeability Soils

Award Number: 0239859
Program Manager: Om Sahai

Start Date: January 15, 2003
Expires: December 31, 2004
Total Amount: $499,996
Investigator: Kent S. Sorenson, ksorenson@nwindenv.com
Company: North Wind
P.O. Box 51174
Idaho Falls, ID 83405
Phone: (208)528-8718

Abstract:

This Small Business Innovation Research (SBIR) Phase II Project proposes to develop an innovative solution to the problem of chlorinated solvent contamination in variably saturated, low permeability soils. Prior Phase I work has demonstrated that: 1) chitin is an effective electron donor for stimulating biodegradation of chlorinated solvents, 2) that chitin enhances bioavailability of the solvents, 3) that chitin can be incorporated into a proprietary hydraulic fracturing process for low permeability soils, and 4) that the delivery method for chitin is effective in the field on a small scale. The objectives of the Phase II Project are to evaluate biodegradation efficiency and longevity of chitin on a large scale. Current approaches for low permeability soils are very capital-intensive and are seldom totally effective. The proposed approach, in contrast, is low-cost and passive, and applicable "in situ". The method is particularly attractive since chitin is available in abundance as a byproduct from the shellfish industry.

The commercial applications of this project are in the area of soil bioremediation.

Title: SBIR Phase II: Development of a Novel Sensing Material for Waterborne Pathogens

Award Number: 0239587
Program Manager: Om Sahai

Start Date: February 1, 2003
Expires: January 31, 2005
Total Amount: $499,748
Investigator: Mary Reppy, reppy@absbio.com
Company: ABS Inc
701-4 Cornell Business Park
Wilmington, DE 19801-5782
Phone: (302)654-4492

Abstract:

This Small Business Innovation Research (SBIR) Phase II Project proposes to develop a method to detect Cryptosporidium parvum oocyst in water using a novel sensing coating deposited on filters. C. parvum has been responsible for a number of outbreaks of cryptosporidiosis, including the outbreak in Milwaukee in 1993 that affected 400,000 people. Cryptosporidiosis is characterized by abdominal pain and severe diarrhea, and can be fatal to immune-compromised individuals. Currently, there is no easy and reliable test allowing the routine monitoring of drinking water supplies for C. parvum. The approved EPA method for this purpose is slow, expensive, and requires interpretation by highly trained personnel. The innovation inherent in the proposed pathogen detection platform resides in a unique "smart" polymer filter coating that permits pathogen concentration, detection, and signal generation in a single step. The signal is generated from interactions between the target and specific antibodies, resulting in a fluorescent signal. Prior Phase I work has already demonstrated the effectiveness of this approach. The proposed Phase II effort will focus on the optimization of the filter coating and the development of the accompanying hardware and testing protocol needed for commercialization and EPA approval of a complete water-testing product.

The commercial application of this project is in the market for detection of pathogens in drinking water supplies. The testing market for C. parvum, the specific pathogen targeted in this Phase II project, is estimated to be $75 million in the U.S. and $ 100 million worldwide. It is expected that further adaptations of the pathogen detection technology proposed in this project will have added applications in the markets for the testing of foods and beverages, and in medical diagnostics.

Title: SBIR Phase II: In Situ Remediation of Methyl Tert-Butyl Ether (MTBE) Using Bioaugmentation

Award Number: 0091432
Program Manager: Om Sahai

Start Date: February 1, 2001
Expires: June 30, 2003
Total Amount: $495,582
Investigator: Paul B. Hatzinger, hatzinger@envirogen.com
Company: Envirogen, Inc.
4100 Quakerbridge Road
Lawrenceville, NJ 08648-4702
Phone: (609)936-9300

Abstract:

This Small Business Innovation Research (SBIR) Phase II Project is designed to develop and demonstrate a new in situ treatment technology for the destruction of methyl tert-butyl ether (MTBE) in groundwater. The gasoline additive MTBE is the second most prevalent groundwater contaminant in the United States, and there are currently no economical technologies for its removal from the water supply. This technology utilizes a novel bacterium of the species Hydrogenophaga flava (ENV735) for the remediation of MTBE. This bacterium, which was recently isolated by Envirogen scientists, is one of only two bacterial strains discovered that are capable of growth on MTBE. Phase II experiments will be conducted to: (1) assess the movement and distribution of the bacterium in the subsurface; (2) develop an adhesion-deficient strain for improved aquifer distribution; and (3) optimize commercial-scale growth, shipment, and injection of the bacterium for. A field demonstration will be conducted to fully test the technology under in situ conditions.

The bioaugmentation with ENV735 has broad potential as an in situ remediation technology for MTBE-contaminated aquifers. If the results of the field trial are positive, commercialization of the bioaugmentation technology is anticipated in the short term.

Title: STTR Phase II: Development of an Automated Instrument Platform for Facilitating Submitochondrial Particle (SMP) Toxicity Assays

Award Number: 0091595
Program Manager: Om Sahai

Start Date: June 1, 2001
Expires: May 31, 2003
Total Amount: $492,166
Investigator: Karl Gustavson, kgustavson@harvardbioscience.com
Company: Harvard Bioscience, Inc.
84 October Hill Road
Holliston, MA 017461371
Phone: (608)276-9820

Abstract:

This Small Business Technology Transfer (STTR) Phase II project will develop and optimize a novel bioassay tool for routine low-cost biomonitoring of water quality. Submitochondrial particle (SMP) toxicity bioassays, based on the in vitro responses to toxicants of the integrated enzyme functions in oxidative phosphorylation, are good predictors of conventional whole organism tests, yet can be completed in minutes. Phase I research proved the concept that SMP technology could be streamlined and semi-automated, enhancing their convenience and commercial potential. In Phase II, prototypes of two dedicated instruments will be developed to accommodate both the cuvette and 96-well microplate-based formats. Accessory liquid and cuvette handling tools will be developed to increase sample throughput. Features will be added to computer software developed in Phase I for running the tests, including support for other protocols; better error detection; statistical treatments and graphical presentation of data. SMP production methods and quality control procedures will be improved and standardized. The software and instrument prototypes will be tested at four independent laboratories to establish assay variability and to gain additional information on appropriate applications of the tests.

If successful, this project will provide affordable tools that will allow for screening of water quality and wastewater discharges by industry and municipalities.

Title: SBIR Phase II: A Novel, Non-Toxic, General Purpose Oxygen Activated Disinfectant

Award Number: 0216382
Program Manager: Om Sahai

Start Date: September 1, 2002
Expires: August 31, 2004
Total Amount: $500,000
Investigator: G. Duncan Hitchens, hitchens@lynntech.com
Company: Lynntech, Inc
7610 Eastmark Drive, Suite 202
College Station, TX 77840-4024
Phone: (979)693-0017

Abstract:

This Small Business Innovation Research (SBIR) Phase II project is to develop a novel method for on-site and on-demand generation of an extremely potent and safe disinfectant. Phase I research has established the basic feasibility of this unique method to generate the disinfectant, as needed, at appropriate concentrations. The overall objective of the Phase II project is to design, demonstrate, and challenge test a fully operational bench-scale device for on-site and on-demand generation of the disinfectant. Additional work will be done to improve the yield of the disinfectant, to examine various additives, and to conduct antimicrobial experiments in accordance with EPA test requirements.

The commercial applications of this project will be in the areas of domestic/personal healthcare, food service and healthcare delivery.

Title: STTR Phase II: Plant Bioreporters for Arsenic

Award Number: 0548751
Program Manager: F.C. Thomas Allnutt

Start Date: September 25, 2006
Expires: September 30, 2008
Total Amount: $500,000
Investigator: Mark Elless, elless@edenspace.com
Company: Edenspace
15100 Entp Ct Suite 100
Chantilly, VA 20151
Phone: (703)961-8700

Abstract:

This Small Business Technology Transfer Research (STTR) Phase II project will develop plant bioreporters for arsenic which is widely dispersed in the environment. Detecting and monitoring arsenic in soil and water, particularly in large or remote areas, is often cost-prohibitive due to the expense of sample collection and analysis. This research will lead to an innovative, cost-effective, real-time system to monitor water and soil quality offering high spatial resolution, stand-off reporting, ready scaling to large treatment areas, and continuous in place reporting of bioavailable arsenic. Applications for this technology include detection and investigation of arsenic contamination and risk assessment during remedial activities at contaminated sites.

The broader impact of this technology will be to enable more extensive use of in place environmental cleanup methods such as phytoremediation, assist efforts to monitor and clean the environment, and reduce environmental health hazards posed by arsenic. Improving the ability to accurately assess arsenic contamination will improve awareness of contaminated areas and make affordable arsenic monitoring by homeowners, farmers, and industry. Of particular usefulness would be the ability of farmers and gardeners to detect the potential bioavailability of arsenic to food crops as a result of arsenic in biosolids and pesticides.

Title: SBIR Phase II: Environmental Neurotoxicity Using Zebrafish

Award Number: 0548657
Program Manager: F.C. Thomas Allnutt

Start Date: February 7, 2006
Expires: January 31, 2008
Total Amount: $512,000
Investigator: Catherine Willett, kptnkate@phylonix.com
Company: Phylonix Pharm Inc
100 Inman St Suite 300
Cambridge, MA 02139
Phone: (617)441-6700

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims at developing a large-scale quantitative assay procedure for the evaluation and detection of potential developmental neurotoxic environmental pollutants. The assay will use zebrafish as the model to investigate the presence of these potential pollutants and as such, will be a relatively simple, fast and cost effective method to evaluate and prioritize potential chemicals for subsequent testing.

The ability to detect, evaluate and determine levels of potential developmental neurotoxic compounds in ground water and other industrial sites will provide for a more comprehensive understanding of potential hazards that industrial runoff may have. To date, very few chemicals that are being tested have been assayed for their potential neurotoxic effects. This assay will provide such a method for testing and will have an impact on environmental pollution and public health.

Title: SBIR Phase II: Water Purification Technology for Removal of Chemical and Biological Contaminants

Award Number: 0620568
Program Manager: Errol Arkilic

Start Date: August 25, 2006
Expires: July 31, 2008
Total Amount: $499,997
Investigator: Lisa Farmen, farmen@yahoo.com
Company: Crystal Clear Technologies
3933 N.E. Royal Court
Portland, OR 97232
Phone: (503)544-2330

Abstract:

This Small Business Innovation Research (SBIR) Phase II research project develops a low-cost, water purification technology for removal of biological and chemical contaminants. In combination with research at the University of Oregon and technology licensed from the University of Texas, a proprietary surface-modified mineral adsorbents will sequester high concentrations of chemical contaminants, such as arsenic, lead, mercury, PCE, TCE and MTBE. The current effort will: a) optimize specific bifunctional ligands and mineral substrates capable of removing heavy metals to meet the EPA drinking water standards; b) demonstrate alternative ligand/substrate combinations capable of selective removal of contaminates from a water stream; c) demonstrate qualification to EPA and California drinking water requirements of a CCT water filter and ultra-violet lamp combination; d) field test the solution in an underdeveloped location.

Currently two-thirds of the world's population does not have access to clean water and one-third lack access to a reliable source of water. In certain parts of the world, mostly the underdeveloped world, water is already the most precious necessity. From the executive summary of the World Water Assessment Program sponsored by the United Nations under UNESCO: "In 2000, the estimated mortality rate due to water sanitation hygiene-associated ... diseases.. was 2,213,000." That equates to one person every 15 seconds. In the U.S., an 2001 EPA report estimates that over two million Americans get sick from contaminated water each year. In China, over one billion people lack acceptable water resources. At the completion of the Phase II effort, CCT will have a complete solution, using both passive and active technologies, for a low cost, sustainable water purification module.

# Genomics

Title: SBIR Phase II: Genomic Mapping of DNA by Means of GeneEngine(TM) Technology

Award Number: 0320449
Program Manager: Om Sahai

Start Date: August 1, 2003
Expires: July 31, 2005
Total Amount: $499,998
Investigator: Rudolf Gilmanshin, rgilmanshin@usgenomics.com
Company: U. S. Genomics
6 'H' Gill Street
Woburn, MA 01801-1721
Phone: (781)937-5550

Abstract:

This Small Business Innovation Research Phase II project aims to build a technology for long-range, high-resolution DNA mapping based on the proprietary GeneEngine(TM) platform. This technology will be a unique tool for genomics because of the combination of features: single- molecule sensitivity, ability to analyze very long DNA molecules, high throughput, and potential for automation. The basic feasibility of this technology was shown in Phase I. The Phase II project is aimed at creating efficient procedures for sample preparation and measurement, as well as for developing analysis algorithms and combining them into an automated software package. These procedures and software will be united to form a toolkit for DNA mapping.

The commercial application of this project will be in the area of Genomics. The product resulting from this project will comprise of instruments and consumables (e.g. reagents) for mapping of whole microbial genomes based on long-range, single-molecule DNA mapping. The ability to scan microbial genomic DNA for genetic information at a fraction of the cost and time of that needed currently will be valuable in a number of commercial applications in life science research and the healthcare industry, including the elucidation of complex genetic pathways, identification of target genes for development of novel anti-infective drugs, correlation of genomic information with unique functions and with drug response, as well as for DNA-based molecular diagnostics and prognostics. The principal market for these applications would be the bio-pharmaceutical companies and academic research laboratories, with additional longer-term markets expected in the area of clinical diagnostics.

Title: SBIR Phase II: Software for Micro RNA Detection and Analysis

Award Number: 0522270
Program Manager: George B. Vermont

Start Date: August 15, 2005
Expires: July 31, 2007
Total Amount: $405,905
Investigator: Gary Fogel, gfogel@natural-selection.com
Company: Natural Selection Inc
3333 N Torrey Pines Ct Ste 200
La Jolla CA, 92037
Phone: (858)455-6449

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will develop machine learning tools for RNA gene detection. Prior Phase I research resulted in the successful development of artificial neural networks for the discrimination of functional RNA (fRNA) coding regions from non-coding regions in four model eukaryotes. The Phase II project will focus on (1) refinement of best evolved neural networks for 10 key eukaryotes capable of discriminating fRNA coding from non-coding sequence information, (2) experimental verification of predicted fRNA coding regions in human and mouse, (3) development of machine learning algorithms capable of discriminating between eukaryotic fRNA subtypes, (4) extension of the approach to include machine learning tools capable of discriminating between fRNA subtypes and to evaluate this potential for additional functionality, and (5) development of a user-friendly graphical user interface (GUI) for the product.

The commercial application of this project will be to identify a new class of targets for drug design and discovery for the pharmaceutical industry. The educational aspects of the proposed work will be to assist in dissemination of knowledge about the importance of fRNAs to the next generation of scientists.

Title: SBIR Phase II: Development of Anticancer Drugs Using Novel Drug Delivery Systems

Award Number: 0521900
Program Manager: George B. Vermont

Start Date: September 15, 2005
Expires: August 31, 2007
Total Amount: $500,000
Investigator: C.J. Yu, yucjyu@aol.com
Company: GlyPort, Inc.
118 S. Berkeley Ave.
Pasadena CA, 91107
Phone: (626)844-7896

Abstract:

This Small Business Innovation Research (SBIR) Phase II project focuses on the enhancement of water solubility and efficacy of sparingly soluble anticancer drugs. Many of the clinically accepted anticancer drugs have side effect problems because of the dosages that must be used to overcome low solubility and bioavailability properties. A new delivery vehicle has been developed, which, when attached to known chemotherapeutic agents , increases water solubility and improves the drugs anticancer activity in in-vitro tests. The Phase II goals are to evaluate further enhancement of solubility with modified delivery segments, do in-vivo evaluations in mice with human tumor xenografts, and to do pharmacokinetic studies of the drugs in the rat model.

The commercial application of this technology is in cancer chemotherapy. Increased solubility and bioavailability should reduce the quantity and side effects of the expensive drugs that are currently used. Furthermore, certain drugs that could not be used previously because of poor cellular uptake, might now be made available using this mode of delivery.

Title: SBIR Phase II: Development and Manufacture of High-Density Plate Washer

Award Number: 0450448
Program Manager: Michael R. Ambrose

Start Date: January 15, 2005
Expires: December 31, 2006
Total Amount: $500,000
Investigator: Richard Kris, richardkris@earthlink.net
Company: NeoGen, LLC
2602 E Avenida De Posada
Tucson AZ, 85718
Phone: (520)906-2002

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims to develop a plate washer capable of washing very high-density plates, such as 1536 well plates, for ELISA and high-throughput screening assays. Currently, there are automated plate washers for 96 and 384 well plates, but there are none available for plates with ultra-high density. This is because currently available washer technology, employing a nozzle system, cannot be made reliable enough to allow dispense and aspirate nozzles to properly reach within each of the many, very small wells, and because the thin nozzles needed can get easily clogged using many standard buffers. In contrast, the proposed system uses a steady stream or sheet of solution, making the system less likely to clog.

The commercial application of this project will be to allow use of high-throughput screening assays by industrial and academic researchers involved in genomics and drug discovery research. The proposed technology will enable additional use of fluorescent chemical compounds, that typically require a wash step to remove interfering substances, for screening

Title: SBIR Phase II: Development of a Microfluidic Device for Rapid Analysis, Sorting, and Collection of Biological Particles Using Photonic Forces

Award Number: 0422059
Program Manager: Om P. Sahai

Start Date: September 1, 2004
Expires: August 31, 2006
Total Amount: $499,940
Investigator: Jonathan Diver, jdiver@genoptix.com
Company: Genoptix, Inc.
3398 Carmel Mountain Road
San Diego, CA 92121
Phone: (858)523-5003

Abstract

This Small Business Innovation Research (SBIR) Phase II project will develop a fluorescence activated cell sorter (FACS) that uses optical forces to move cells and to sort cell sub-populations. The specific Phase II objectives are : (1) to build an integrated prototype cell sorter with flexibility to configure multiple lasers and detectors, (2) to develop a self contained microfluidic cartridge that can handle 1,000-100,000 cells/sample and sort with purities greater than 95% and total recovery rates greater than 80%, (3) to develop microfluidic flow assays, and (4) to validate that the mechanical and optical stresses do not adversely affect cells.

The proposed work will result in a prototype cell sorter, self-contained microfluidic cartridges, and a panel of assays that demonstrate the broad utility of the instrument. The commercial application of this project will be in the area of cell-based assays for use in biological and biomedical research.

Title: SBIR Phase II: Novel Method for Class Switching IgM Secretors to IgG

Award Number: 0238667
Program Manager: Om Sahai

Start Date: January 1, 2003
Expires: December 31, 2004
Total Amount: $500,000
Investigator: Yevgenya Akselband, yaks@onecell.com
Company: One Cell Systems Inc
100 Inman Street, Suite 200
Cambridge, MA 02139-1206
Phone: (617)868-2399

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop a rapid IgSwitch Assay for inducing and isolating IgG class switch variants from IgM hybridomas using in-vitro culture conditions, microencapsulation technology and fluorescence activated cell sorting. The IgSwitch Assay is expected to be a significant improvement over conventional methods used to isolate class switch variants, and will be useful in cell line development and monoclonal antibody production. Prior Phase I research has already demonstrated the feasibility of the proposed method using a model IgM hybridoma. This Phase II project will develop in-vitro culture conditions that promote switching to different IgG subclasses. The Phase II research will also validate reagents for a family of isotype specific IgSwitch Assays.

The commercial application of this project will be in the area of monoclonal antibodies. Use of the targeted IgSwitch Assay in monoclonal antibody production will help to generate new IgG specific antibodies from a largely untapped source of IgM hybridomas, for potential use as research, therapeutic, diagnostic, and imaging reagents.

Title: SBIR Phase II: Thermostable Phage DNA Polymerases: Improved Tools for Genomics Research

Award Number: 0215988
Program Manager: Om Sahai

Start Date: October 1, 2002
Expires: September 30, 2004
Total Amount: $499,928
Investigator: Thomas W. Schoenfeld, tschoenfeld@lucigen.com
Company: Lucigen
2120 W. Greenview Dr.
Middleton, WI 53562-2547
Phone: (608)831-9011

Abstract:

This Small Business Innovation Research Phase II project will develop novel DNA polymerase reagents for use in current and developing DNA diagnostic procedures. The approach is to develop thermophilic phage DNA replicases in place of the currently used DNA repair enzymes. The feasibility of this approach was demonstrated during Phase I research. This follow on Phase II project will extend the methods used in Phase I to isolate additional activities, characterize them and develop them as reagents for various amplification platforms.

The commercial applications of this project will be in a number of markets that use molecular analysis of DNA. They include the areas of biomedical research, medical testing, genetic identity testing, public health and agriculture.

Title: SBIR Phase II: Development of Agents to Promote Cellular Ga-67 (Gallium-67) Uptake

Award Number: 0450618
Program Manager: George B. Vermont

Start Date: October 1, 2005
Expires: September 30, 2007
Total Amount: $499,992
Investigator: Takuji Tsukamoto, taku@chemica.com
Company: Chemica Technologies Inc
325 S.W. Cyber Dr.
Bend OR, 97702
Phone: (541)385-0355

Abstract:

This Small Business Innovation Research Phase II project focuses on the development of new pharmaceutical agents to selectively enhance tumor imaging using gallium 67. A photo-degradation product of nifedipine, nitrosipine, has been found to selectively enhance the uptake of Ga67 by tumor cells. A specific derivative of nitrosipine has an even better selective uptake of the radioactive imaging agent. This project will synthesize and test other nitrosipine derivatives and determine the efficacy of Ga67 uptake in animal models using these complexing agents.the commercial application of this technology is in the area of diagnostic imaging. The use of Ga67 in tumor imaging is currently very limited due to poor selectivity of the agent for tumor cells. Enhanced uptake in tumor cells relative to normal cells would expand the types of tumors that could be effectively imaged and possibly replace the more costly and complex PET scan imaging using radioactive fluorinated sugars

# Marine Biotechnology

Title: SBIR Phase II: Applying Transgenic Technology to Improve the Pearl Production Process

Award Number: 0239065
Program Manager: Om Sahai

Start Date: March 1, 2003
Expires: February 28, 2005
Total Amount: $499,979
Investigator: Dale J. Sarver, dalej@aloha.net
Company: Black Pearls Inc
P.O. Box 525
Holualoa, HI 96725-0525
Phone: (808)322-7108

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will develop the technology to produce faster growing oysters that yield bigger and higher quality pearls than those currently available. Prior Phase I work has already shown the production of the first-ever verifiable transgenic pearl oysters, and the successful isolation of the first nacre gene from Pinctada margaritifera. The proposed work in this Phase II project will demonstrate commercial viability by isolating other potentially important genes from Pinctada, a proven transfection methods, and evaluating nacre quality and deposition rates in transgenic phenotypes. Biosecure land-based grow-out of transgenic oysters, as mantle-tissue donors only, will increase application efficiency and overcome environmental concerns.

The commercial application of this project will be in the black pearl market that is estimated to be of the order of $ 5 billion worldwide. A U.S.-led expansion of this lucrative industry could provide economic benefits to Hawaii and to U.S.-affiliated Pacific Islands, increasing investment, employment opportunities and self-sufficiency in these remote islands, and reducing the economic burden on the U.S. Government.

Title: SBIR Phase II: Use of Inducible Antimicrobial Peptides for Rapid Diagnosis, Prevention, and Management of Disease in Finfish Aquaculture

Award Number: 0349772
Program Manager: Om P. Sahai

Start Date: February 15, 2004
Expires: January 31, 2006
Total Amount: $499,812
Investigator: James Carlberg, jcarlberg@kentseatech.com
Company: Kent SeaTech Corporation
11125 Flintkoe Avenue Suite J
San Diego, CA 92121
Phone: (858)452-5765
Abstract

This Small Business Innovation Research (SBIR)Phase II Project proposes to develop a new approach for controlling disease in the aquaculture industry. This approach is based on the use of a recently discovered natural antibiotic compound in hybrid striped bass (HSB) called bass-hepcidin. Hepcidin is an antimicrobial peptide (i.e. bactericidal molecules) that is part of the fish's innate immune system. Prior Phase I work has demonstrated that HSB (and probably many finfish) respond to disease challenges by increasing their hepcidin levels. This finding is useful because elevated hepcidin levels indicate that fish are being challenged by disease, and artificially increasing hepcidin levels (by feed additives or other means) may stimulate the fish's immune response to assist in combating disease. This Phase II project will develop an ELISA diagnostic test for hepcidin and conduct follow-on clinical studies with several important aquaculture species. If successful, this research may result in the development of two types of hepcidin-based products that will be of immense value to aquaculturists: 1) hepcidin test strips that provide an instant positive-negative indication of the presence of disease processes, analogous to pregnancy test kits, and 2) feed additives that stimulate the production of hepcidin in finfish, to be used to control disease outbreaks.

The commercial impact of this project will be significant as there is clearly a market need for products to control infectious diseases in fish that cause tremendous economic loss, of the order of $ 3 billion, each year.

Title: SBIR Phase II: Ploidy Induction with Penaeid Shrimp for Protection of Investment in Selective Breeding

Award Number: 0079315
Program Manager: Om P. Sahai

Start Date: July 15, 2000
Expires: June 30, 2002
Total Amount: $399,800
Investigator: Robert Shleser, Shleser@aloha.net
Company: Aquatic Farms
1164 Bishop Street, #124
Honolulu, HI 96813
Phone: (808)259-5042

Abstract:

This Small Business Innovation Research Phase II project focuses on mass production of triploid marine shrimp. Marine shrimp culture experienced exponential growth between 1980 and 1990, increasing from 5% to 28% of total world production. Since then, farmed shrimp production has stagnated due to disease and water quality problems. Disease problems are largely due to dependence on wild caught shrimp broodstock and post larvae, which carry many untreatable viral diseases. A solution to this problem is closed-cycle culture, which also permits genetic selection for improved production performance. To protect a breeder's investment in specific pathogen free (SPF)stock, specific pathogen resistant (SPR) stock, and genetic selection, it is highly desirable to sell only sterile post larvae. Triploidy is a possible solution since triploids of other species are typically sterile and may exhibit superior culture performance. In addition triploidy may allow for the culture of exotic species in environmentally sensitive areas where exclusion of exotics is desirable. Phase II will focus on development of tetraploid breeding stocks that will be crossed with normal diploid stocks to produce triploid progeny.

The successful outcome of our R&D effort will result in significant changes in marine shrimp culture. It will prevent competitors from propagation of shrimp stocks that have been genetically selected for aquaculture performance. It will help stimulate large-scale investment in SPF, SPR, genetic selection and closed-cycle shrimp culture. It will help create opportunities to expand use of exotic shrimp species into environmentally sensitive culture areas. Our company intends to be at the forefront of these opportunities.

Title: SBIR Phase II: Broadband Split-Beam Fish Tracker

Award Number: 0109976
Program Manager: Om Sahai

Start Date: March 15, 2002
Expires: February 29, 2004
Total Amount: $500,000
Investigator: Jae-Byung, Jung jae-byung@scifish.com
Company: Scientific Fishery Systems
PO Box 242065
Anchorage, AK 99524
Phone : (907)345-7347

Abstract:

This Small Business Innovation Research (SBIR) Phase II Project will develop a broadband split-beam fisheries sonar system for shallow water applications. As the number of fish in rivers and streams diminishes and becomes threatened, endangered or extinct, there is a need for better fish monitoring tools for such shallow water environments. Through a series of workshops, the leaders in the riverine sonar community have highlighted several deficiencies in the current monitoring systems. This Phase II Project proposes to build a fish tracking and counting system that addresses many of these deficiencies, and that has a ten-fold better range resolution and at least a 6 dB improvement in detection. The broadband sonar system, to be built in the course of this project, will include (a) a unique bizonal shaded transceiver array, (b) a full complement of functions for collection, storage, analysis and display of data, and (c) a multi-hypothesis tracker for tracking fish in low SNR and dense target environments. The sonar system will be validated first in a comprehensive set of pool tests, and then subjected to a rigorous set of evaluation experiments in the Kenai and Copper Rivers of Alaska and in the Rogue River of Oregon.

The commercial applications of this project are in a broad range of markets that require fish counting and tracking equipment. The overall market size for such equipment worldwide is estimated to be on the order of 1.8 billion dollars.

Title: STTR Phase II: Engineering of Non-leaching Antibacterial Non-woven Textiles

Award Number: 0450527
Program Manager: George Vermont

Start Date: October 21, 2005
Expires: October 31, 2007
Total Amount: $505,450
Investigator: Nina Lamba, cclbiomed@verizon.net
Company: CCL Biomedical, Inc.
224 North Washington St.
Havre de Grace, MD 21078
Phone: (410)939-9356

Abstract:

This Small Business Technology Transfer Innovation Research (STTR) Phase II project proposes the development of a unique family of biocidal polymers that have been shown to be non-leaching, and do not require regeneration or refreshment of activity. The Phase I study demonstrated the synthesis of these polymers containing potent broad-spectrum biocides. The polymers were spun into nanofiber webs using electrospinning techniques. The webs were challenged with bacteria and a 99% reduction in bacterial viability in one hour was demonstrated. The Phase II program will continue to explore the electrospinning processing of the polymers. The polymers will be optimized for activity against bacteria, viruses and molds. Microscopic and mechanical tests will be performed on materials to identify structure-property relationships.

The commercial application of this technology will be in textile products where antimicrobial protection is critical, e.g., homeland security (biodefense) garments, first responders emergency clothing, hospital garments and supplies, etc. Current systems are water leachable and use can lead to reduced protection.

Title: SBIR Phase II: Enabling High Output Metabolism in Plant Cells

Award Number: 0548640
Program Manager: F.C. Thomas Allnutt

Start Date: January 11, 2006
Expires: December 31, 2007
Total Amount: $511,937
Investigator: Michele Champagne, kasllc@hawaii.rr.com
Company: Kuehnle Agro Systems
2800 Woodlawn Dr. Suite 281
Honolulu, HI 96822
Phone: (808)753 2693

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims to develop and validate a novel chloroplast transformation vector for protein expression in chloroplasts. The research project will broaden scientific understanding of the parameters of chloroplast transformation by addressing stoichiometric expression of multiple transgenes for effective engineering of pathways such as carotenogenesis, feedback regulation and expression of multimeric proteins.

The commercial impact of this technology will provide an enabling strategy for expression of genes of interest in chloroplasts to potentially increase the production of high value nutraceutical and pharmaceutical compounds. Application of this technology for stable, high output metabolism with regulatory compliance will reduce production cost and increase the reliability for downstream processing and eventual commercialization.

Title: SBIR Phase II: Rapid and Automated Differential Gene Expression Profiling

Award Number: 0548750
Program Manager: Ali Andalibi

Start Date: September 21, 2006
Expires: September 30, 2008
Total Amount: $499,995
Investigator: Jian Tajbakhsh, jtajbakhsh@maxwellsensors.com
Company: Maxwell Sensors Inc.
10020 Pioneer Blvd Suite 103
Santa Fe Springs, CA 90670
Phone: (562)801 2088

Abstract:

The Small Business Innovation Research (SBIR) Phase II project will develop a rapid and automated microarray expression profiling chip and system for gene expression profiling. As part of this project a miniaturized automated system will be developed to integrate key steps in target synthesis, labeling and hybridization.

The use of the integrated system will enhance the reproducibility and cost of running microarray experiments.

Title: SBIR Phase II: Compact genetic assessment using the Infrarray SNAP (Simple Nucleic Acid Profiler)

Award Number: 0724423
Program Manager: Ali Andalibi

Start Date: September 15, 2007
Expires: August 31, 2009
Total Amount: $499,986
Investigator: Steve Savoy, ssavoy@nanohmics.com
Company: Nanohmics
6201 East Oltorf St.
Austin, TX 78741
Phone: (512)389-9990

Abstract:

This Small Business Innovation Research (SBIR) Phase II research project aims to further develop a microfluidic device for the detection of nucleic acids for a variety of studies where genetic analysis and identification of target sequences are required. The instrument proposed is designed to be compact and capable of reading a disposable cartridge on which sample preparation, amplification, and multiplex detection, with a modest-sized microarray, are performed. The proposed instrument is enabled by direct imaging of a PhotoGenerated Reagent (PGR) microarray, with an image sensor positioned near the face of the microarray. It is also enabled by the use of up-converting phosphors as the label, which are in turn excited by infrared radiation that passes through the silicon microarray.

The development of and inexpensive, fully integrated and automated microfluidic device for use in genetic analysis would give individuals in academic, commercial and defense settings access to affordable microarray analysis. The availability of such a versatile platform would allow the development of arrays for any nucleic acid target, as well as easy multiplexing. With such a platform, production of custom arrays and off-the-shelf ones will be achieved with great facility. Moreover, the integrated platform will reduce the cost and effort associated with microarray analysis.

Title: SBIR Phase II: Novel Labeling Method for Multicolor Fluorescence in situ Hybridization (FISH) Probes

Award Number: 0724876
Program Manager: Ali Andalibi

Start Date: September 1, 2007
Expires: August 31, 2009
Total Amount: $500,000
Investigator: Joan Aurich-Costa, joan@onecell.com
Company: One Cell Systems Inc
100 Inman St Ste 200
Cambridge, MA 02139
Phone: (617)868-2399

Abstract:

This Small Business Innovation Research (SBIR) Phase II research project aims to further develop a panel of multicolor oligonucleotide fluorescence in situ hybridization (FISH) probes for performing preimplantation genetic diagnosis (PGD) and detecting aneuploidies in eggs used for in vitro fertilization (IVF) protocols. The use of oligonucleotides offers advantages such as enhanced specificity and sensitivity, shorter hybridization times as well as a reduction in manufacturing cost when compared to currently available genomic DNA derived probes. The panel that the company plans to develop will cover 8 chromosomes known to be particularly susceptible to deletions and rearrangements and would allow simultaneous detection of any abnormalities that may be associated with them.

The development of a panel of probes for the detection of genetic abnormalities in preimplantation embryos will increase the success rate of IVF procedures and thus reduce the financial and emotional cost associated with them. Moreover, use of the proposed labeling method can be useful in a variety of areas outside of PGD, including basic research, clinical diagnostics and cytogenetic testing.

# Pharmaceutical Drug Delivery

Title: SBIR/STTR Phase II: Automated Analyzer for Drug Delivery Systems

Award Number: 0216220
Program Manager: Om Sahai

Start Date: October 1, 2002
Expires: September 30, 2004
Total Amount: $499,378
Investigator: Leah R. Williams, williams@aerodyne.com
Company: Aerodyne Research Inc
45 Manning Road
Billerica, MA 018213934
Phone: (508)663-9500

Abstract:

This Small Business Innovation Research Phase II project will develop a new analytical tool for characterizing drug delivery aerosols and powders. This instrument will be based on a previously developed aerosol mass spectrometer that provides real-time size distribution and chemical composition measurements for aerosol particles. During Phase I research, a new inlet for the aerosol mass spectrometer, allowing detection of particles in the size range relevant to inhalable drug delivery aerosols and powders (2 to 10 mm in diameter), was successfully developed. The key objectives of the Phase II project are (a) to further improve the collection efficiency for particles in the 2 to 10 mm diameter size range; (b) to design and construct a sampling apparatus that conforms to Food and Drug Administration (FDA) and U. S. Pharmacopeia Convention (USP) guidelines for sampling drug delivery aerosols from metered dose inhalers (MDIs) and dry powder inhalers (PDIs); and (c) to develop and to validate an analytical method that meets FDA standards.

The commercial applications of this project will be in the area of drug delivery.

Title: SBIR Phase II: A New Biotherapeutic Approach to Combating Unwanted Bacteria

Award Number: 0421991
Program Manager: Om P. Sahai

Start Date: July 15, 2004
Expires: June 30, 2006
Total Amount: $498,903
Investigator: Hideki Suzuki, hsuzuki@conjugon.com
Company: ConjuGon, Inc.
505 South Rosa Rd, Suite 29
Madison, WI 53719
Phone: (608)441-2890

Abstract:

This Small Business Innovation Research Phase II research project will develop a commercial biotherapeutic using a unique bacterial conjugation technology to deliver cytotoxic genes and their products to bacterial pathogens. The Phase I work successfully demonstrated proof of concept by effectively killing multi drug resistant bacteria in vitro. The Phase II project will optimize the technology further to create a treatment for nosocomial (hospital acquired) urinary tract infections.

The commercial application of this project will be in the area of anti-infective therapy. The proposed work provides a unique therapeutic approach that can compliment standard antibiotic therapies as well as reduce the dire problem of the burgeoning development of antibiotic-resistant bacteria in the clinic.

Title: SBIR Phase II: High-Throughput Specific Cell Loading by Optoinjection

Award Number: 0321740
Program Manager: Om P. Sahai

Start Date: November 1, 2003
Expires: October 31, 2005
Total Amount: $512,000
Investigator: Glenn Sasaki, gsasaki@oncosis.com
Company: Oncosis
6199 Cornerstone Court
San Diego, CA 92121
Phone: (619)550-1770

Abstract

This SBIR Phase II project proposes to develop a novel technology for laser-enabled analysis and processing (LEAP) of living cells. The ability to load cells with compounds is critical in many areas of research and medicine such as drug discovery and gene therapy. Current methods have limitations with respect to specificity, efficiency, toxicity, and/or throughput. Optoinjection is a novel and versatile procedure for cell loading that has been demonstrated in a few laboratories. Unfortunately, this is a slow, laborious procedure carried out on specialized microscopes. Oncosis has developed the LEAP platform for high-speed cell imaging and purification via lethal laser effects on unwanted cells. Phase I results demonstrated feasibility for using the LEAP platform to implement optoinjection in a high-throughput, cell-specific manner that would enable the commercialization of this novel form of cell loading. Phase II studies are proposed to optimize and implement optoinjection in biologically relevant experimental systems, resulting in data supporting this powerful new tool for the analysis and manipulation of living cells within a physiological environment. The instrument design will then be configured for successful commercial manufacturing, and further improvements in capabilities will be pursued in order to maintain market leadership and to expand into other markets.

The commercial application of this project is in the areas of cell-based life science research and drug discovery. Over $ 2.6 billion was spent during 2001 on research instrumentation in academic life science research and commercial drug discovery, and growth to $ 5.3 billion by 2005 has been forecasted. For the specific application of optoinjection, LEAP provides many advantages over current techniques including simplicity, robustness, efficiency, speed, high viability, and specificity. The commercial opportunity for this platform is therefore significant, as is the scientific enablement of experimentation that is not currently possible.

Title: SBIR Phase II: High Speed Chemical Analysis of Combinatorial Libraries

Award Number: 9983700
Program Manager: T. James Rudd

Start Date: March 1, 2000
Expires: February 28, 2003
Total Amount: $748,739
Investigator: Jack Syage, jsyage@syagen.com
Company: Syagen Technology
1411 Warner Avenue. Suite B&D
Tustin, CA 92780
Phone: (714)258-4400

Abstract:

This Small Business Innovation Research Phase II project will develop a high through-put drug screening technology based on the successful Phase I feasibility demonstration. High throughput methods in parallel and combinatorial organic synthesis are revolutionizing the field of drug discovery and biological screening. However, progress is seriously impeded by lack of reliable methods for conducting high throughput chemical analysis (HTCA) for composition and purity assessment. Current approaches rely on liquid chromatography/mass spectrometry (LC/MS). With a cycle time of about 5 min, an LC/MS instrument can analyze about 300 samples in a 24 hr period. We propose an innovative MS concept that reduces cycle time to about 10 sec, raising the potential analysis rate to >5,000 samples/day. The innovation is based on a novel ionization source that achieves (1) near-universal and efficient ionization of drug compounds, (2) minimal fragmentation molecular ion spectra for accurate analysis, (3) minimal interference from air constituents and commonly used solvents, and (4) suppression of competition-for-charge and ion suppression effects experienced by conventional methods. The proposed technology advances analytical and research capabilities to improve fundamental understanding of drug molecules and to build a knowledge base for implementing more rational approaches to lead drug optimization.

Market research indicates the potential for exponential growth on the basis of quick penetration of the chemical analysis niche of the rapidly growing field of combinatorial and parallel synthesis methods for drug discovery. The proposed high throughput chemical analysis system has the potential to dominate the market for combinatorial library analysis, which is a rapidly growing field of drug discovery. Our real-time, complex mixture analyzers will also be marketed for applications in drug testing, environmental monitoring, and on-line process monitoring.

Title: SBIR Phase II: High-Throughput Purification of Combinatorial Libraries

Award Number: 0321765
Program Manager: Rosemarie D. Wesson

Start Date: July 1, 2003
Expires: June 30, 2005
Total Amount: $499,990
Investigator: Jack Syage, jsyage@syagen.com
Company: Syagen Technology
1411 Warner Avenue. Suite B&D
Tustin, CA 92780-6461
Phone: (714)258-4400

Abstract:

This SBIR Phase II project aims to develop a prototype of a highly parallel, mass-selected purification system for large pharmaceutical drug libraries. High-throughput purification is driven by the industry recognition that combinatorial chemistry samples must still be purified even after chemical screening. This project will examine monolithic parallel preparative liquid chromatography configurations. The key enabling technology is low-pressure photoionization mass spectrometry (LPPI MS), which permits accurate molecular detection in mixtures of compounds without the problems of competition-for-charge and ion suppressions that plague conventional ionization methods. A practical purification rate of >1 sample/min (12 parallel purifications in <12 min column cycle time) corresponding to a potential 16-hr daily rate of >960 sample purifications/day is expected. This work will transition into a Phase II prototype involving strategic partners to commercialize the technology.

The proposed high throughput purification system for combinatorial libraries has the potential to dominate an important niche market for molecular analysis and screening for drug discovery. This rapidly growing market will fuel applications in many other directions of drug development. The proposed activity will have a broad and profound impact on society as a whole by providing valuable information that can lead to improved drug therapy and early detection of disease. The practical outcome is to improve health care and reduce costs. This project also has the potential for explosive commercial growth, which will stimulate economic development.

Title: STTR Phase II: Antibacterially-Active Nanoparticles

Award Number: 0620572
Program Manager: F.C. Thomas Allnutt

Start Date: August 3, 2006
Expires: July 31, 2008
Total Amount: $499,977
Investigator: Seyoung Jang, syjang77@hotmail.com
Company: Nanopharma
3802 Spectrum Blvd.
Tampa, FL 33612
Phone: (813)469-7107

Abstract:

This Phase II Small Business Technology Transfer (STTR) research project develops a novel nanoparticle delivery system for treatment of antibiotic-resistant infections. This extends previous findings using antibacterially active polyacrylate nanoparticles to animal infection models. Penicillin containing nanoparticles are the intial focus due to the clinical importance of penicillin in treating bacterial infections and the extreme sensitivity penicillin has to degradation by proteins produced by methicillin-resistant Staphylococcus aureus (MRSA). The research will determine the stabilities of penicillin nanoparticles under various chemical and biological conditions, evaluate potential in vitro and in vivo toxicity of the nanoparticles, examine the biodistribution of the two most active nanoparticles in healthy mice, and assess the effectiveness in treating early stage (skin) and advanced (systemic) MRSA infections in mice. The results from this project will provide both fundamental data to the scientific community on these polyacrylate nanoparticles as a drug delivery platform, as well as animal testing data needed to advance this nanoparticle technology towards IND and FDA approval.

The broader impact of this research will be to demonstrate that nanoparticle technology can be applied to treatment of MRSA infections and provide essential data on the use of polyacrylate nanoparticles as a drug delivery platform. Use of nanoparticles in anti-infectives is essentially unexplored. These novel nanoparticles will enable characterization of the properties for creating FDA guidelines on the use of nanoparticles in medicine. In addition, the training of students at the graduate and undergraduate level in bio-nanotechnology is a central element of this joint project between industry and academia. The precipitous loss in the ability of antibiotics to treat bacterial infections is already having enormous societal implications. The number of deaths and serious illnesses due to clinical complications from drug-resistant infections is staggering. This research will establish a new treatment protocol for these types of infections through use of cutting-edge nanotechnology, both as a drug-delivery platform and as an effective way to recover the therapeutic effectiveness of antibiotics like penicillin. There are currently no existing technologies like this in the anti-infectives area, indication of an unmet health need and a large commercial market.

Title: SBIR Phase II: High-Density Microcapillary Bioplate

Award Number: 0548332
Program Manager: Ali Andalibi

Start Date: February 7, 2006
Expires: February 29, 2008
Total Amount: $500,000
Investigator: Joseph Krans, jak@incomusa.com
Company: Incom Inc
PO Box G
Southbridge, MA 01550
Phone: (508)765-9151

Abstract:

This Small Business Innovation Research (SBIR) Phase II research project will aid in the development of high-density glass microcapillary bioplates that will offer complete flexibility in the choice of diameter and thickness of the capillaries. These features are not currently available in an exiting product. Through an innovative low-cost fabrication approach, the disposable bioplate will allow for massive parallel experimentation that is crucial for large-scale high-integrity measurements.

The proposed research will provide for a dramatic and cost effective increase in high-throughput screening programs in all phases of drug discovery and target validation. The ability to accelerate the analysis of targets in a cost effective manner will provide for more effective screening programs.

Title: SBIR Phase II: Device for the Activation of Nanoparticle-Based Cancer Therapies

Award Number: 0548741
Program Manager: F.C. Thomas Allnutt

Start Date: February 7, 2006
Expires: January 31, 2008
Total Amount: $500,000
Investigator: Patrick O'Neal, poneal@nanospectra.com
Company: Nanospectra Bio, Inc.
8285 El Rio St Suite 130
Houston, TX 77054
Phone: (713)842-2720

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims at developing a minimally invasive, image-guided cancer therapy for the optimum activation of nanoparticle based, photo-thermal cancer therapies. This will allow for the treatment of deep-seated tumor, irregular shaped tumors as well as regional metastatic spread and tumors situated near or within sensitive tissues.

This technology will impact the current therapies for cancers, especially those of the brain and other sensitive areas. The technology will provide a minimally invasive therapy with a high safety profile that allows treatment of poorly defined tumors margins without damage to surrounding, often sensitive tissues. This would make the treatment not only more effective but will also limit damage to healthy tissue and as such, limit side effects and other organ dysfunction. Additionally, this therapy is compatible with and potentially synergist with existing treatment modalities.

Title: SBIR Phase II: Chiral Polymers for Pharmaceutical Purification

Award Number: 0620587
Program Manager: F.C. Thomas Allnutt

Start Date: August 8, 2006
Expires: July 31, 2008
Total Amount: $496,939
Investigator: Alexander Gorkovenko, agorkovenko@materialmethods.com
Company: Material Methods
30 Hughes, Suite 205
Irvine, CA 92618
Phone: (949)206-0967

Abstract:

This Small Business Innovation Research (SBIR) Phase II project develops new chiral stationary phases for pharmaceutical purification. Drug manufacturers seek new chiral stationary phases with high throughput, extended chiral selectivity, high loading capacity, with the ability to tolerate a wide range of mobile phases. To meet this need, artificial saccharides will be synthesized and polymerized into a 100% stereo specific chiral stationary phase for liquid chromatography of enantiomers. These polymers have remarkable propertie such as stereo specificity, five asymmetric centers, functionality for tailoring phase/ligand recognition, extensive crosslinking capability, and ether bonding. This chemistry was demonstrated in Phase I and in Phase II will lead to a new family of chiral polymers to speed drug discovery and reduce the cost of drug manufacture.

The broader impact of this research will be to provide artificial polysaccharides to provide novel activities versus the natural products currently sold. Polysaccharides have multiple, chiral centers, unparalleled optical integrity; and the highest density of functional groups of all known molecules. Artificial polysaccharides are most readily functionalized and tailored to form desired chiral selectors. This project will molecularly design chiral selectors. The impact of this research extends beyond drug purification to sugar separations, high performance fibers, tissue scaffolds, and nano machinery.

Title: SBIR Phase II: Disposable pL Fluid Transfer/Microarray Printing Device

Award Number: 0646638
Program Manager: F.C. Thomas Allnutt

Start Date: March 15, 2007
Expires: February 28, 2009
Total Amount: $498,437
Investigator: Robert Haushalter, bob@parallel-synthesis.com
Company: Parallel Synthesis Technologies, Inc
3054 Lawerence Expy
Santa Clara, CA 95051
Phone: (408)749-8308

Abstract:

This Small Business Innovation Research (SBIR) Phase II project provides an inexpensive disposable polymer tool that will perform extremely accurate fluid transfer in the picoliter to nanoliter range. Research efforts have already demonstrated that the costs associated with fabricating molds employing a combination of silicon micromachining and electroforming will allow these tools to be disposable. Fabrication processes will be transitioned to injection molding by adapting the micromachined/electroformed molds to the injection process. The research will design the final generations of the printing and fluid transfer pin designs, use silicon micromachining and electroforming to prepare the injection molds for the 96 and 384 pin printheads, design new collimator / printheads for both microarray printing and fluid transfer applications and redesign and scale up the chemical surface treatment process to treat thousands of pins simultaneously. Because the polymer pins can be manufactured so inexpensively compared to current technology, the number of laboratories around the world that can utilize this nanoscale fluid handling will dramatically increase.

The broader impacts of this project will be to provide disposible plastic parts at less than ten percent of the least expensive current technology thereby enabling reductions in costs for high throughput technologies important to drug discovery and diagnostics. This could improve the delivery of healthcare to the nation and reduce its overall cost.

# Proteomics

Title: SBIR Phase II: Computer-Directed High Throughput Screening for Improved Enzymatic Activity

Award Number: 0091586
Program Manager: Om Sahai

Start Date: March 15, 2001
Expires: February 28, 2003
Total Amount: $499,986
Investigator: John R. Desjarlais, jrd@xencor.com
Company: Xencor
111 W. Lemon Ave.
Monrovia, CA 91016
Phone: (626)737-8065

Abstract:

This Small Business Innovation Research (SBIR) Phase II project focuses on the development of an enabling technology for computer- directed high-throughput screening of proteins with improved properties. Xencor's Protein Design Automation (PDA) predicts all the possible amino acid sequences that will fold into the three-dimensional structure of a protein. There should be molecules among those sequences that have the structure and function of the "parent "protein, together with additional novel properties such as increased thermo-stability or alkaline pH optima. In Phase I the company addressed this possibility using xylanase as a model protein. After targeting the active site of the enzyme for PDA re-design, the company found sequences that were more active than the wild-type protein and one that had a different pH profile. These results were achieved by testing only 260 of a possible 110,592 sequences. In Phase II the company will develop a high-throughput assay system that will allow testing the majority of the predicted sequences. The research will also improve electrostatic functions of the PDA algorithm, and then use this version of the program to re-design the entire xylanase molecule instead of just the active site, thereby finding mutations located away from the active site that effect the protein's characteristics.

The PDA technology improves enzyme efficiency and expands the reactions and process conditions where they can be applied. Major markets include polymer manufacturers, value extraction from waste streams and food processing.

Title: SBIR Phase II: Proteome Epitope Tags-Based Antibody Arrays for High-Throughput, Proteome-Wide Kinase Pathway Profiling

Award Number: 0522303
Program Manager: George B. Vermont

Start Date: September 1, 2005
Expires: August 31, 2007
Total Amount: $500,000
Investigator: Neal Gordon, ngordon@epitomebiosystems.com
Company: Epitome Biosystems, Inc.
100 Beaver Street
Waltham MA, 02453
Phone: (781)209-2369

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will develop a novel antibody microarray for high-throughput, multiplexed profiling of a large number of signaling proteins from multiple pathways by measuring protein phosphorylation. The antibody array will simultaneously measure kinase activities in Ras effector pathways including the Raf-MEK-ERK pathway, the P13K-Akt pathway, the p38 and JNK pathways. Current kinase profiling technologies such as Western blotting of flow cytometry are low throughput, not quantitative and difficult to multiplex and standardize. This novel technology (Proteome Epitope Tag or PET) creates antibodies with pre-defined specificity that can be multiplexed using standardized assays on antibody microarrays for measuring protein phosphorylation. The PET approach will be further developed to construct highly multiplexed antibody arrays for simultaneous measurement of a large number of kinase protein activities from multiple pathways. The ability to measure all signaling proteins from interconnected pathways will provide an unprecedented opportunity to decipher the complexity of cell signaling.

The commercial applications of this technology will be in large scale protein analysis relevant to basic biological research, drug discovery, and clinical medicine. Protein biochips hold great promise for biomarker discovery which is important in all these areas. Large-scale protein biochips capable of standardized and high-throughput protein measurement on differentially perturbed biological systems do not exist today. This is due primarily to the lack of highly specific antibodies for all human proteins predicted by gene sequences. The PET technology addresses this urgent, unmet need by generating antibodies for highly specific peptide tags of defined sequences in a proteome, representing a universal method for producing antibodies and standardized chip-based assays for any protein of interest. PET chips for profiling kinase signaling networks will have enormous utility for drug discovery by better characterizing drug efficacy, side effects and potential toxicity

Title: SBIR Phase II: High Speed Sequencing and Structure Analysis

Award Number: 0450640
Program Manager: George B. Vermont

Start Date: May 15, 2005
Expires: April 30, 2007
Total Amount: $462,352
Investigator: Jack Syage, jsyage@syagen.com
Company: Syagen Technology Inc
1411 Warner Ave Ste D
Tustin CA, 92780
Phone: (714)258-4400

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop new methods for achieving high-speed sequencing and structure analysis of drug and biological molecules . The benefits of high-speed Molecular Sequencing (MSn) will be broadly applicable to end users through compatibility with ion trap MS instruments in general and specifically for the proposed QitTof MS (quadrupole ion - trap, time - of - flight mass spectrometry), which will provide the highest potential analysis speeds. The technical objectives for Phase II research are to (a) to develop high-speed MSn algorithms, (b) to optimize accurate mass neutral loss performance, (c) to develop CE / ESI (capillary electrophoresis / electrospray ionization) interface, and (d) to demonstrate CE / ESI / QitTof MS/MS for high-speed peptide sequencing. The final outcome of this Phase II work will be an instrument that will clearly achieve the highest speeds for peptide sequencing and overall protein identification.

The commercial application of this project will be in the area of proteomics. The proteomics market is forecasted to grow from $ 0.7 billion to $ 5.8 billion over the next 5 years. There is a tremendous need to develop automated methods for the analysis of proteins and peptides linked to specific cells and tissues, in order to better understand global biological function for improved drug therapy and early detection of diseases such as cancer

Title: SBIR Phase II:  Membrane Protein Microarrays

Award Number: 0450262
Program Manager: George B. Vermont

Start Date: April 1, 2005
Expires: March 31, 2007
Total Amount: $500,000
Investigator: Athena Guo, athena@memsurface.com
Company: Microsurfacees Inc
4001 Stinson Blvd Suite 430
Minneapolis MN, 55421
Phone: (612)789-0104

Abstract:

This Small Business Innovation Research (SBIR) Phase II project proposes to develop a product platform based on polymer cushion coated glass slides with controlled surface charge density for membrane protein microarray fabrication. The key technical objectives for Phase II research are : (a) to complete quantitative studies on surface charge density in the formation of supported phospholipid bilayer (SPB) from charged lipids , (b) to develop the chemistry for the grafting / adsorption of polymer cushions,  (c) to measure the activities of membrane proteins in SPBs,  and (d) to fabricate membrane protein microarrays based on surface pre-patterning using soft lithography techniques.

The commercial application of this project will be in the area of protein microarrays for use in disease diagnostics and for drug discovery research. The proposed technology will  enable development of therapeutics aimed at membrane protein targets.

Title: SBIR Phase II: Overexpression of Membrane Proteins from Hyperthermophilic Bacteria - Refinement of a Novel Expression System

Award Number: 0349777
Program Manager: Om P. Sahai

Start Date: February 15, 2004
Expires: January 31, 2006
Total Amount: $500,000
Investigator: Hiep-Hoa Nguyen, hiephoa@its.caltech.edu
Company: TransMembrane Biosciences
145 N. Sierra Madre Blvd.
Pasadena, CA 91107
Phone: (626)536-0691

Abstract:

This Small Business Innovation Research (SBIR) Phase II Project proposes to continue the development and refinement of a novel membrane protein expression system utilizing a unique group of bacteria capable of synthesizing a vast amount of membrane proteins and supporting extensive internal membrane structures. Membrane proteins are of significant medicinal importance. However, efforts to study membrane proteins are often hampered by their low level of biosynthesis. An efficient membrane protein overexpression system will facilitate their biochemical and biophysical characterization. This will allow for the economical mass production of membrane proteins essential for large-scale structural genomics effort as well as for industrial applications.

The commercial impact of the project will be on drug discovery work by biotechnology and pharmaceutical companies. Additional impact will be in areas of biology and physiology where processes are modulated by membrane proteins (for example, in agriculture).

Title: SBIR Phase II: Innovative Protein Microarrays

Award Number: 0349712
Program Manager: Om P. Sahai

Start Date: February 1, 2004
Expires: January 31, 2006
Total Amount: $499,807
Investigator: Andrzej Drukier, akd@biotraces.com
Company: BioTraces Inc
13455 Sunrise Valley Dr. Ste 200
Herndon, VA 20171
Phone: (703)793-1550

Abstract:

This Small Business Innovation Research Phase II project proposes to develop a novel supersensitive multiphoton detection system for protein chips (P-chip/MPD) for applications in drug discovery and in early detection of prostate cancer and breast cancer. The commercial impact of the proposed work will be in the area of diagnostic proteomics. The diagnostics industry is large, currently estimated at around 10 billion dollars per year. The most profitable and dynamically growing fields are those that permit early detection of cancer and therapy monitoring, or provide toxicity assays for new drugs.

It is expected that the P-Chips/MPD developed in this project will eventually capture a significant share of the diagnostic proteomics market.

Title: SBIR Phase II: Automated 2D Protein Cell Mapping

Award Number: 0321763
Program Manager: Om P. Sahai

Start Date: November 15, 2003
Expires: October 31, 2005
Total Amount: $413,037
Investigator: Jack Syage, jsyage@syagen.com
Company: Syagen Technology
1411 Warner Avenue. Suite B&D
Tustin, CA 92780
Phone: (714)258-4400

Abstract:

This Small Business Innovation Research Phase I project will develop a method for conducting high-throughput, automated analysis of the protein content of cell lines using a novel mass analyzed two-dimensional liquid-phase separation method. The conventional method of two-dimensional poly-acrylamide gel electrophoresis (2D PAGE) has several limitations ; it is labor intensive, time consuming, difficult to automate and often not readily reproducible. In addition, quantitation, especially in differential expression experiments, is often difficult and limited in dynamic range. The proposed technology provides automated, faster, and more accurate 2D protein maps, and can be used to purify specific proteins and enact protein/peptide digest and sequencing information. These capabilities will prove valuable for studying drug-protein interactions for detecting early signs of cancer. Studies of cancer cell lines can reveal signatures of cancerous cells that can serve as markers for actual diagnosis. The proposed system is based on 2D liquid-phase protein separation using chromatofocusing (CF) in one dimension and non-porous silica, reverse-phase, high-performance liquid chromatography (NPS-RP HPLC) in the second dimension. The HPLC eluent is monitored in real-time by on-line electrospray ionization (ESI) mass spectrometry (MS) to provide molecular weight and intensity information.

The commercial application of this project is in the area of proteomics. The proteomics market is forecasted to grow from $ 0.7 billion to $ 5.8 billion over the next 5 years. There is a tremendous need to develop automated methods of protein analysis and peptide analysis of cell lines to better understand global biological function for improved drug therapy and early detection of disease, such as cancer.

Title: SBIR Phase II: New Convergent X-Ray Beam Based System for Protein Crystallography

Award Number: 0321581
Program Manager: Om P. Sahai

Start Date: December 1, 2003
Expires: November 30, 2005
Total Amount: $499,903
Investigator: Huapeng Huang, hhuang@xos.com
Company: X-Ray Optical Systems, Inc.
15 Tech Valley Drive
East Greenbush, NY 12061
Phone: (518)880-1500

Abstract:

This Small Business Innovation Research (SBIR) Phase II project will develop a new convergent x-ray beam based crystallography system for measurement of the quality and the structure of protein crystals in an effort to support crystal growth development efforts and as a prescreening tool for very small protein crystals prior to refined, high-resolution structure determination at dedicated synchrotron-based macromolecular structure facilities. Measurements of a broad range of crystal types, sizes, and degrees of perfection will be carried out in an active protein crystal growth and characterization laboratory at the Wadsworth Center of the New York State Health Department. Parallel measurements using the same crystals will be made in this laboratory with a conventional state-of-the-art protein diffraction system in order to examine the potential benefits and limitations of the convergent beam method (CBM). Measurements will also be made in an industrial laboratory to evaluate the potential of CBM as a commercial, compact, high-intensity, low-power, low-cost, protein screening instrumentation.

The commercial application of this project will be in the area of structural proteomics. Development of a compact, high-efficiency, high-sensitivity system for measurement of the quality and preliminary structure of small protein crystals is crucial to implementation of the huge opportunities offered by recent advances in human and non-human genomics, with far-reaching consequences in the areas of disease therapy and drug discovery. Furthermore, such a system could find broad applications in academic, scientific and industrial programs for high- resolution microscopy of structure, texture, and strain in metallurgical, geological, environmental and biological or other materials.

Title: SBIR Phase II: Antigen-Mediated Selection of Hybridomas

Award Number: 0078548
Program Manager: Om P. Sahai

Start Date: October 1, 2000
Expires: September 30, 2003
Total Amount: $510,714
Investigator: Yevgenya Akselband, yaks@onecell.com
Company: One Cell Systems Inc
100 Inman Street, Suite 200
Cambridge, MA 02139
Phone: (617)868-2399

Abstract:

This Small Business Innovation Research (SBIR) Phase II project aims to develop a rapid, sensitive and highly specific method for monoclonal antibody production and hybridoma cell line development by combining single cell gel microdrop (GMD) encapsulation technology, a novel protein capture format, and fluorescence activated cell sorting. Using insulin as a model antigen, Phase I studies demonstrated that individual cells, which comprised a 1% sub-population of a heterogeneous population, could be rapidly isolated based on both secretion level and antigen specificity of the secreted antibody. Phase II research will optimize the assay format by permitting simultaneous analysis of other antibody properties, including antibody isotype and blocking properties. Using newly fused hybridomas, Phase II research will isolate and enrich productive clones and compare results with conventional methods which require use of time consuming and labor intensive limiting dilution cloning.

Monoclonal antibodies are widely used as research, therapeutic, diagnostic, and imaging reagents, and are increasingly used in the emerging field of proteomics for discovering new drug targets and locating disease specific markers. The GMD method will reduce production time and costs, improve antibody quality and yield, and permit isolation of rare cells.