Life Sciences Division

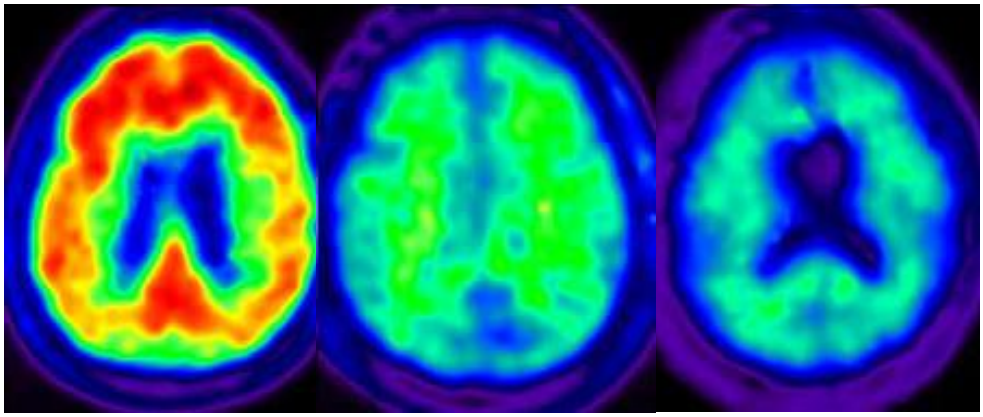
E-Newsletter June 22, 2007

Highlights

News from Neuroimaging

Life Sciences investigators in the **Department of Molecular Imaging and Neuroscience** are using a new method of imaging brain beta-amyloid in aging and Alzheimer's disease (AD). In AD, this beta-amyloid protein is deposited in the form of plaques, which are the hallmark of the disease. This amyloid protein is also neurotoxic, placing the protein at the center of the disease both diagnostically and etiologically. Using the new tracer with PET scanning, Pittsburgh Compound B (or PIB), LBNL investigators have begun studies using PIB to diagnose AD, and to examine the earliest stages of amyloid deposition. The figures below demonstrate studies in a patient with AD (left) and a normal older healthy individual. Note tracer uptake (red colors) throughout cortex in the AD patient, and minimal uptake of tracer in white matter in the normal.

On the right is a patient with another dementing illness, Frontotemporal Lobar Degeneration (FTLD), which is not associated with beta-amyloid deposition. This scan resembles the normal scan, in showing no tracer uptake because this individual has no beta amyloid in the brain. The appearance of these scans can therefore be used to diagnose the cause of the dementia, which is a major advance in clinical care.



AD **Normal** **Frontotemporal Lobar Degeneration**

Aspects of this research, using PIB as a diagnostic test to differentiate AD and FTLD, have been published in Rabinovici et al, *Neurology* 68: 1205-1212, 2007. . Future studies will include investigations of beta amyloid deposition in normal older individuals to see whether evidence of AD can be detected in those with normal cognitive function.

Gulliver's Travels: The Bioimaging Version

Just as Lemuel Gulliver, the narrator in the classic novel Gulliver's Travels by Jonathan Swift, observed a wide range of human physical scales, from the very small Lilliputians to the very large Brobdingnagians, so too are bioscientists eager to observe both small and large-scale structures in living systems. This desire has given rise to the Gulliver Initiative: Multiscale Bioimaging from Molecules to Organisms. The idea is to combine the latest in imaging technologies and labeling methods to advance investigations into the chemical composition, physical properties and molecular interactions within complex samples of biological materials.

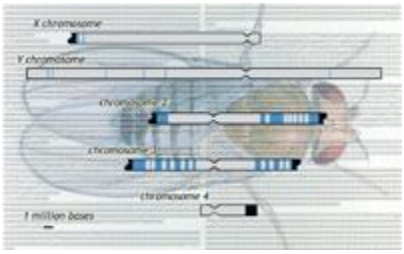
"Imaging techniques are dramatically accelerating biological research, revealing organizational and functional details at all levels of spatial and temporal resolution, ranging from single molecules to whole organisms," said **Joe Gray**, director of Berkeley Lab's Life Sciences Division (LSD).
Continue reading: http://www.lbl.gov/Publications/Currents/Archive/Jun-15-2007.html
Berkeley Lab View, 6/15/07

Shining a Light on the Dark Matter of the Genome

The Secrets of the Fruit Fly's Heterochromatin

Remember "junk DNA?" It's what biologists called the highly repetitive, gene-poor DNA in regions of the chromosomes known as heterochromatin. Like dark matter in the universe, the true nature of heterochromatin was unknown.

"Junk" will be heard less often after the appearance, in today's issue of Science, of two papers reporting the nearly complete assembly, mapping, and functional analysis of Drosophila melanogaster — fruit fly — heterochromatin.



The heterochromatin of Drosophila's centromere extends toward the center of the chromosomes from the gene-rich euchromatin (black). The sequenced regions are shown in blue. The gray regions are unsequenced "seas" of short repeats.

"Most researchers thought heterochromatin had little or no function, because it appeared to lack the protein-coding genes that occur so richly in the chromosomes' more accessible and better-studied euchro-matin," says **Gary Karpen** of the Life Sciences Division (LSD), an adjunct professor of cell and molecular biology at UC Berkeley and head of the Drosophila Heterochromatin Genome Project, whose members wrote the Science reports.
Continue reading: http://www.lbl.gov/Publications/Currents/Archive/Jun-15-2007.html#6
Berkeley Lab View, 6/15/07

More reading: Exploring the Dark Matter of the Genome: http://www.lbl.gov/Science-Articles/Archive/LSD-genome-darkmatter.html
Science at Berkeley Lab, 6/14/07

Creating a Pipeline of Space Scientists

Students and scientists from around the globe and from throughout the U.S. have come to New York this month to participate in the fourth annual NASA Space Radiation Summer School at Brookhaven National Laboratory. Berkeley Lab life scientist **Eleanor Blakely** is this year's school director. "Our goal is to attract the highest quality students from diverse scientific backgrounds and help train them to be the next wave of space radiation researchers," she said. Full story: http://www.huliq.com/24852/creating-pipeline-of-space-scientists

Today at Berkeley Lab, 6/20/07

Keep On Truckin'

A study of over 6,119 male and 2,221 female runners over a seven-year period showed that those who ran over 30 miles per week gained only half the weight of those who ran less than 15 miles per week. Keeping up exercise with age was particularly effective in preventing extreme weight gain, which is associated with high blood pressure, high cholesterol, Type 2 diabetes, and other diseases. While many studies have tracked exercise over time, the exercise habits of the people in those studies may have changed considerably. This is the first time the type and amount of exercise — running — have been controlled over a long period, according to **Paul Williams** of the Life Sciences Division, who published these latest results of the National Runners' Health Study in the May 3 Medicine and Science in Sports and Exercise.

News Round Up Berkeley View, 5/18/07

Recent publications (selected)

C. V. Sindelar and **K. H. Downing.** The beginning of kinesin's force-generating cycle visualized at nanometer resolution. J. Cell Biol. 177, 377-85(2007). Paper available online -- doi:10.1083/jcb.200612090

Schaber JA, Triffo WJ, Suh SJ, Oliver JW, Hastert MC, Griswold JA, **Auer M**, Hamood AN, Rumbaugh KP. Infect Immun. 2007 Jun 11; [Epub ahead of print], PMID: 17562773 [PubMed - as supplied by publisher]

> Biofilms are bacterial communities residing within a polysaccharide matrix that are associated with persistence and antibiotic resistance in chronic infections. We show that the opportunistic pathogen Pseudomonas aeruginosa forms biofilms within 8 hours of infection in thermally-injured mice, demonstrating that biofilms contribute to bacterial colonization in acute infections as well. Using light, electron and confocal scanning laser microscopy, P. aeruginosa biofilms were visualized within burned tissue surrounding blood vessels and adipose cells. Although quorum sensing (QS), a bacterial signaling mechanism, coordinates differentiation of biofilms in vitro, wild type and QS-deficient P. aeruginosa formed similar biofilms in vivo. Our findings demonstrate that P. aeruginosa forms biofilms on specific host tissues independent of QS.

The Release 5.1 Annotation of Drosophila melanogaster Heterochromatin

Christopher D. Smith, ShengQiang Shu, Christopher J. Mungall, and **Gary H. Karpen.** Science 15 June 2007 316: 1586-1591 [DOI: 10.1126/science.1139815] (in Research Articles)

The repetitive DNA that constitutes most of the heterochromatic regions of metazoan genomes has hindered the comprehensive analysis of gene content and other functions. We have generated a detailed computational and manual annotation of 24 megabases of heterochromatic sequence in the Release 5 Drosophila melanogaster genome sequence. The heterochromatin contains a minimum of 230 to 254 protein-coding genes, which are conserved in other Drosophilids and more diverged species, as well as 32 pseudogenes and 13 noncoding RNAs. Improved methods revealed that more than 77% of this heterochromatin sequence, including introns and intergenic regions, is composed of fragmented and nested transposable elements and other repeated DNAs. Drosophila heterochromatin contains "islands" of highly conserved genes embedded in these "oceans" of complex repeats, which may require special expression and splicing mechanisms.

Roger A. Hoskins, Joseph W. Carlson, Cameron Kennedy, David Acevedo, Martha Evans-Holm, Erwin Frise, Kenneth H. Wan, Soo Park, Maria Mendez-Lago, Fabrizio Rossi, Alfredo Villasante, Patrizio Dimitri, **Gary H. Karpen**, and **Susan E. Celniker**. Sequence Finishing and Mapping of Drosophila melanogaster Heterochromatin . Science 15 June 2007 316: 1625-1628 [DOI: 10.1126/science.1139816] (in Reports)

Genome sequences for most metazoans and plants are incomplete because of the presence of repeated DNA in the heterochromatin. The heterochromatic regions of Drosophila melanogaster contain 20 million bases (Mb) of sequence amenable to mapping, sequence assembly, and finishing. We describe the generation of 15 Mb of finished or improved heterochromatic sequence with the use of available clone resources and assembly methods. We also constructed a bacterial artificial chromosome–based physical map that spans 13 Mb of the pericentromeric heterochromatin and a cytogenetic map that positions 11 Mb in specific chromosomal locations. We have approached a complete assembly and mapping of the nonsatellite component of Drosophila heterochromatin. The strategy we describe is also applicable to generating substantially more information about heterochromatin in other species, including humans.