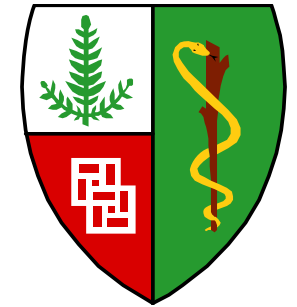


New Alzheimer's Therapies: Current Status

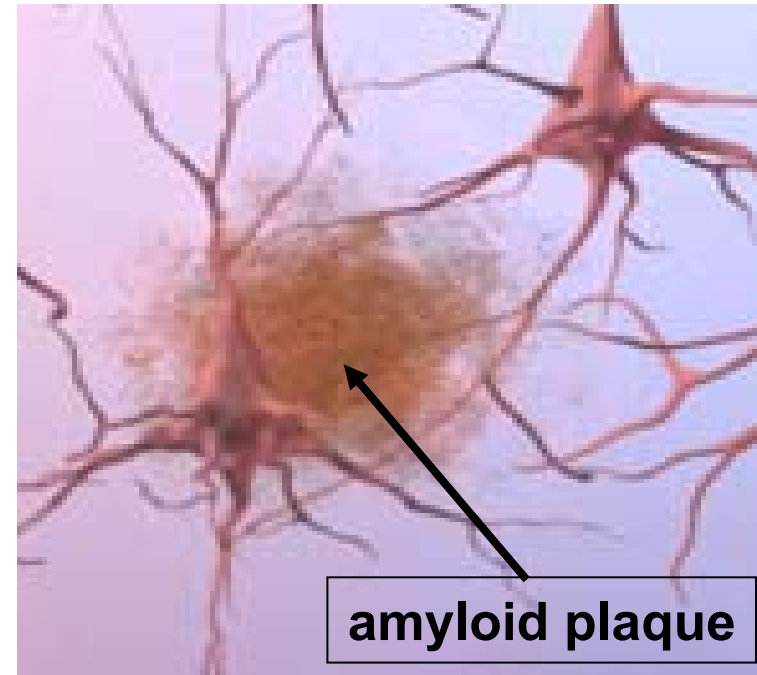


May 21, 2007



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Dementia & Alzheimer's Disease



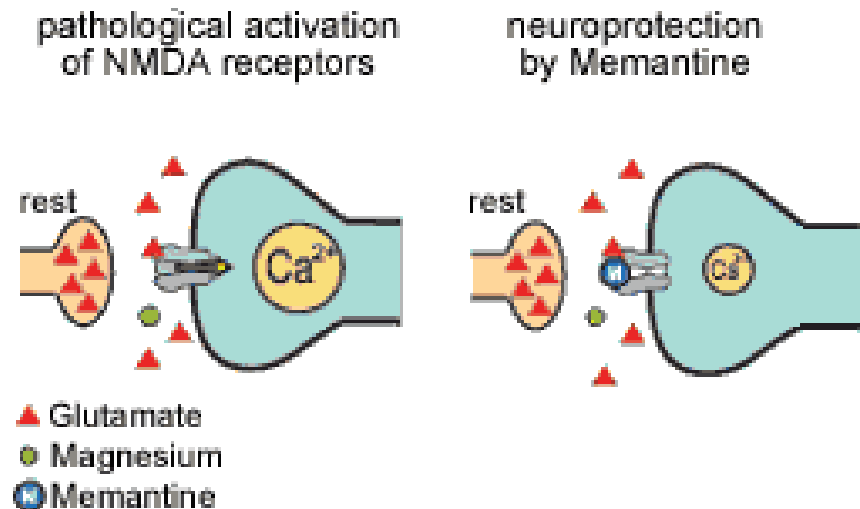
FDA-Approved Therapies

Cholinesterase Inhibitors

- Donepezil (Aricept)
- Galantamine (Reminyl, Razadyne)
- Rivastigmine (Exelon)

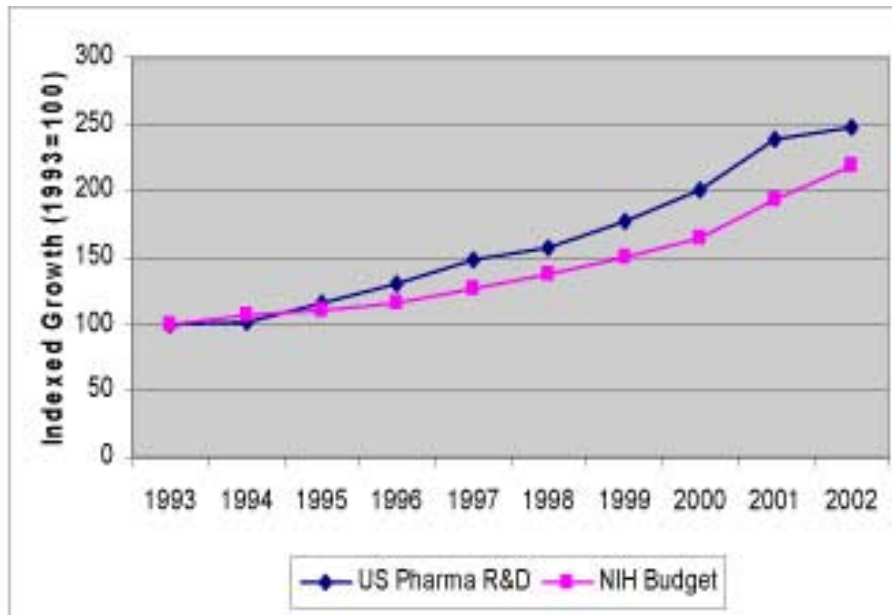
NMDA Receptor Antagonist

- Memantine (Namenda)

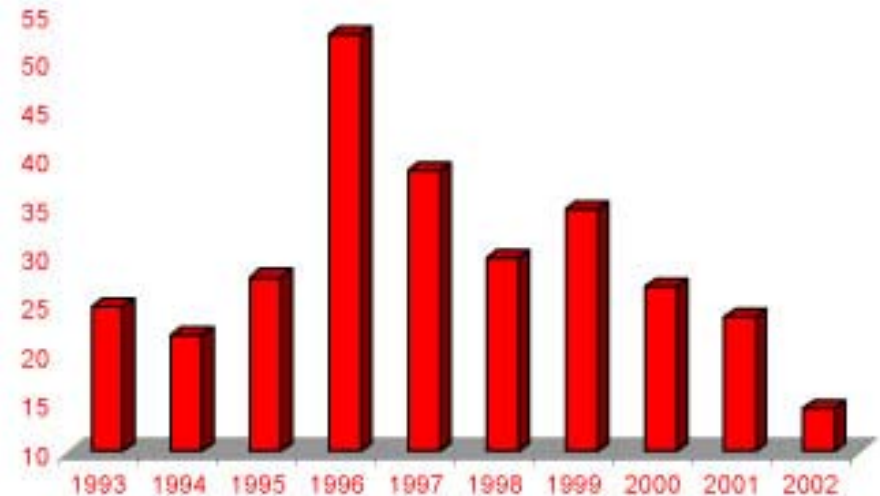


Accelerating Progress for Alzheimer's

Medical Therapy Investment

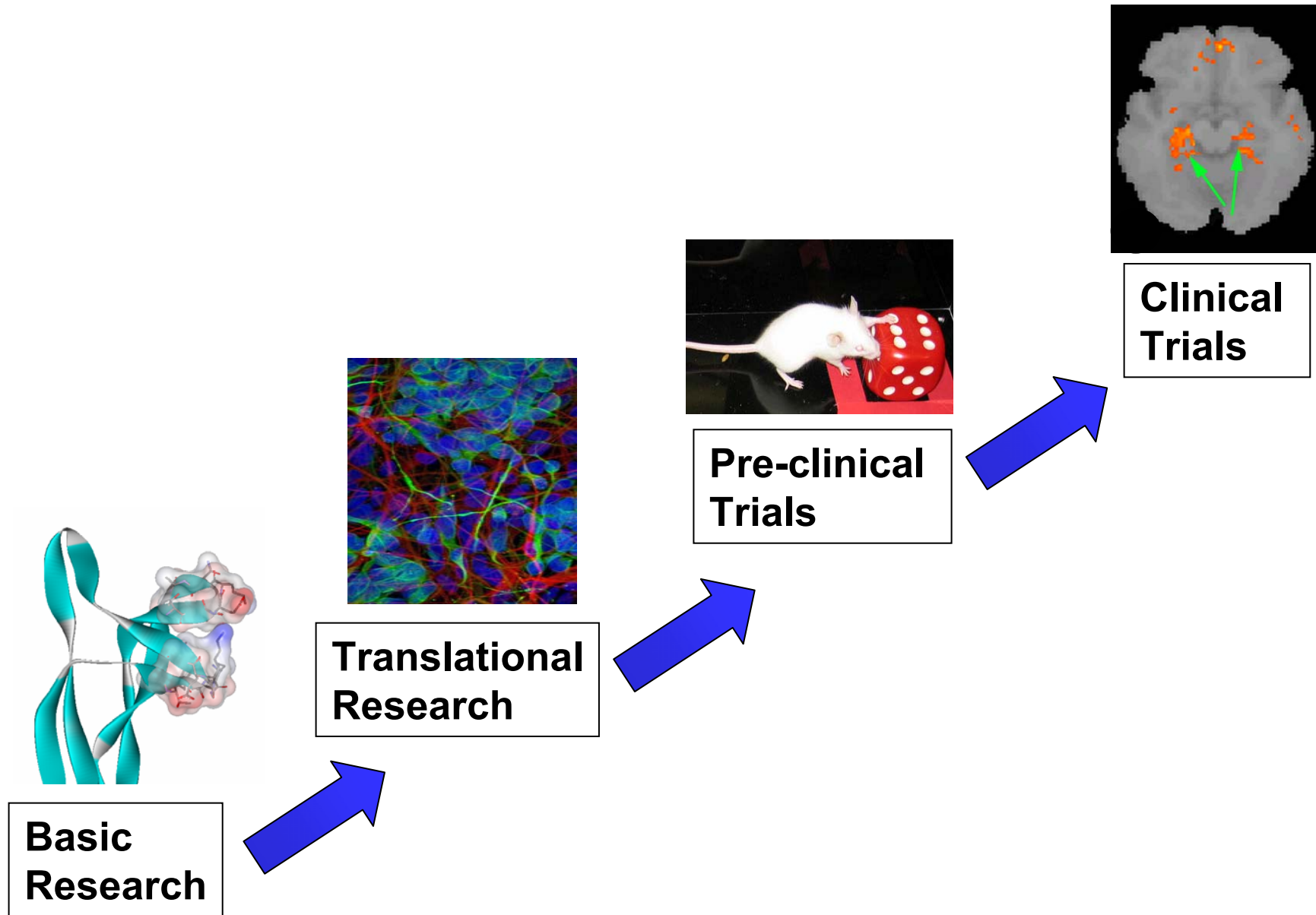


New Medical Treatments



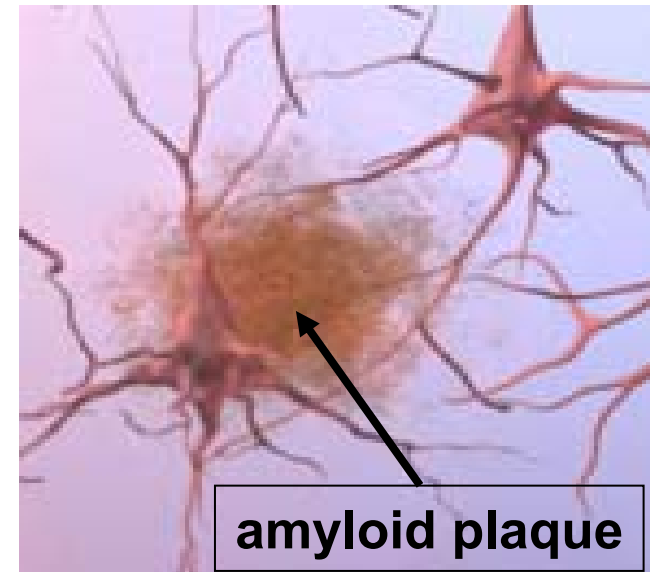
University Leadership

The Alzheimer's Pipeline



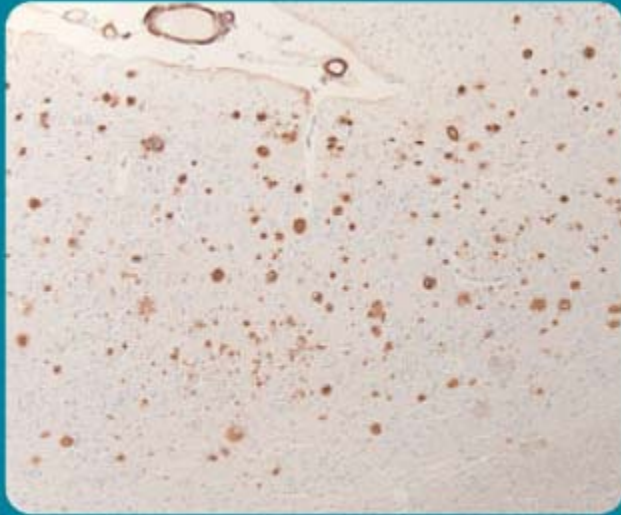
Emerging Alzheimer's Therapies

Treatment Strategy	Phase II or III Trials
Amyloid immunization	2
Drugs targeted to amyloid	2
Drugs lowering amyloid	3
Anti-inflammatory/Anti-oxidant	4
Neuron Protection	4
TOTAL	15
Exercise	Early
Cognitive Activity	Early



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Amyloid Immunization



AD



AD + AN-1792

J Nicoll, UK

Drug	Target	Sponsor	Phase
AN-1792	A β synthetic peptide immunization	Elan/AHP	IIA 2000-2002; discontinued, CNS inflammation
AAB-001-210	Passive A β immunization	Elan/AHP	IIA/IIB; 2005-2008

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Drugs Targeting Amyloid

Drug	Target	Sponsor	Phase
Tramiprosate (Alzhemed)	Bind soluble A β to decrease oligomer levels and fibrill/plaque formation	Neurochem Inc	Phase III North America/18 months 4-07: "adjustment to the initial statistical model, as set out in the statistical plan, (that) would be necessary to provide accurate results."
AZD-103	Neutralize A β oligomers; rescue LTP	Transition Therapeutics with Elan	Phase I; 2006-

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Drugs Lowering Amyloid

Drug	Target	Sponsor	Phase
r-flurbiprofen (Flurizan)	selectively modulating γ- secretase to lower $A\beta_{42}$ levels	Myriad	Phase III enrollment completed 3-07 (18mo) Phase II: positive ADAS-cog, global function; 42% pts had zero decline or improved function after 2 yrs
LY450139	γ-secretase inhibitor/NOTCH cleavage	Lilly	Phase I
Atorvastatin (Lipitor)	HMG-CoA reductase inhibitor; decreased cholesterol; possible decreased $A\beta$	Pfizer	Ia/IIb

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Mixed: A β /Anti-inflammatory/Anti-oxidant

Drug	Target	Sponsor	Phase
Leuprolide	GnRH agonist, lower LH, decrease A β production	Voyager	Phase III underway
DHA (Docosa- hexaenoic Acid) Omega 3 Fatty Acid	A β , antioxidant	Martek/NIA	Phase III 2-07 (18 mo)
Curcumin C3 complex	A β oligomers, antioxidant, anti- inflammatory	ISOA/ French Fdn	Phase II (12 mo)
Phenserine	ACI and decreased A β production	Axonyx; TorreyPines Therapeutics	3 Phase III trials; development dc'd; new partner?

Neuronal Protection

Drug	Target	Sponsor	Phase
Rosiglitazone XR (± ACIs)	Neuronal glucose use	GSK (REFLECT- 1/2/3)	III/24-54 weeks; 2006/2007-
Rasagiline + donepezil	Neuronal death	Teva/Easi	Phase II (12 mo); enrollment closed
NP12	GSK-3 inhibitor	NeuroPharma	Phase I
Dimebon (approved in Russia in 1983 as an antihistamine)	AchE and NMDA receptor inhibitor; inhibition of apoptosis by potential mitochondrial mechanisms	Medivation	Ia/Ib/6 months

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'Available' Drug Therapies

Treatment Strategy	Phase II or III Trials
Amyloid immunization	2
Drugs targeted to amyloid	2
Drugs lowering amyloid	3
Anti-inflammatory/Anti-oxidant	4
Neuron Protection	4
TOTAL	15
Exercise	Early
Cognitive Activity	Early

Statin
Leuprolide
DHA
Curcumin
Rosiglitazone
Rasagiline
Flurbiprofen (ibuprofen?)

Health for Life

Stronger, Faster, Smarter

Exercise does more than build muscles and help prevent heart disease. New science shows that it also boosts brainpower—and may offer hope in the battle against Alzheimer's.

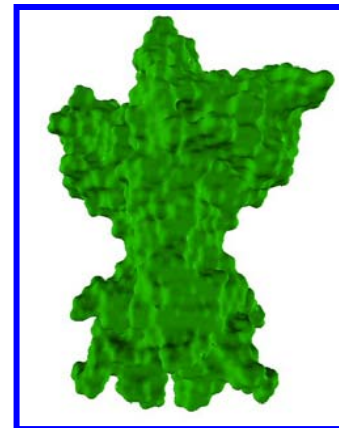
BY MARY CARMICHAEL

THE STEREOTYPE OF THE "DUMB JOCK" HAS NEVER sounded right to Charles Hillman. A jock himself, he plays hockey four times a week, but when he isn't body-checking his opponents on the ice, he's giving his mind a comparable workout in his neuroscience and kinesiology lab at the University of Illinois. Nearly every semester in his classroom, he says, students on the women's



Newsweek, March 2007

BDNF?

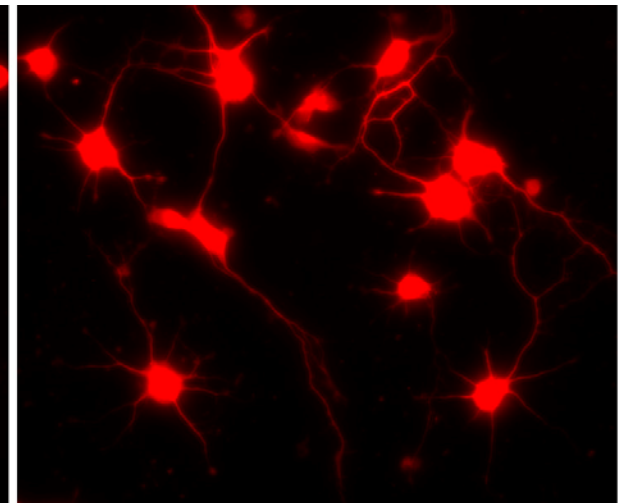
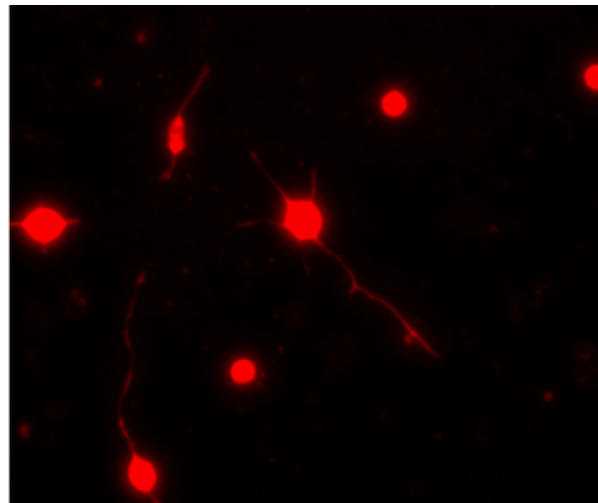
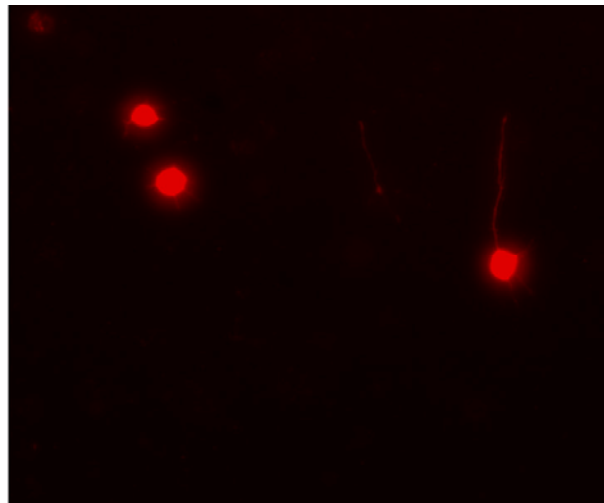


Translating BDNF to a Novel Therapy

No BDNF

BDNF

BDNF Mimetic



Dr. Frank Longo

Resveratrol – red wine polyphenol

The FASEB Journal • Research Communication

Moderate consumption of Cabernet Sauvignon attenuates A β neuropathology in a mouse model of Alzheimer's disease

Jun Wang,* Lap Ho,**[†] Zhong Zhao,* Ilana Seror,* Nelson Humala,*
Dara L. Dickstein,* Meenakshisundaram Thiyagarajan,* Susan S. Percival,[§]
Stephen T. Talcott,[§] and Giulio Maria Pasinetti**[†][‡][¶]



- Anti-oxidant
- A β clearance
- 600 Compounds?



Pinot Noir (resveratrol 1-5%)