

RESEARCH ADVANCES AT MIND

March, 2005

ALZHEIMER'S DISEASE

- Dr. Dora Kovacs demonstrated that a new approach to controlling blood cholesterol levels may be a potential treatment for Alzheimer's disease. This approach is different from the well-known statins and is already being investigated to prevent cardiovascular disease.
- Dr. Brad Hyman and Dr. Alberto Leo showed the mechanism by which ibuprofen reduces amyloid, the main component of the deadly plaques that accumulates in the brain of patients with Alzheimer's disease, pointing to a potential preventive agent.
- Dr. Rudy Tanzi and Dr. Lars Bertam announced the discovery of a new Alzheimer's disease gene called "ubiquilin", which increases risk for the disease by affecting how well nerve cells deal with the build up of abnormal protein aggregates.

AMYOTROPHIC LATERAL SCLEROSIS (ALS)

- Dr. Piera Pasinelli has generated new data concerning surprising ways in which SOD1 mutant protein created by the ALS gene binds tightly to one of the most important inhibitors of cell death, perhaps triggering the self-destruction of motor neurons.
- With Dr. John Lander, Dr. Robert Brown has opened a new complex genetics facility to look for gene variants that are significantly over- or under-represented in ALS patient populations, to identify genes that, combined with environmental factors, could trigger the disease. The center includes state-of-the-art robotic DNA analysis machines and relies on thousands of DNA samples from an international consortium of ALS researchers.
- Dr. Robert Brown and Dr. Michele Maxwell published data showing that a new technique, known as RNA interference or RNAi, can reduce SOD1 protein levels (the dangerous proteins encoded by the ALS gene) in a Petri dish. They are now pursuing collaborations to try this therapy in the ALS mice.

HUNTINGTON'S DISEASE

- MIND's high throughput drug screening laboratory, under the direction of Dr. Anne Young and Dr. Alex Kazantsev, has successfully identified a new potential treatment for Huntington's disease, the first such compound not based on an existing medication. This drug like compound shows powerful effects in cells and in fruit fly models of the disease. The MIND team is now preparing to test this compound in HD mouse models.
- Dr. Jang-Ho Cha's laboratory has continued its work on the role of transcription in HD—the process by which genes are selectively read or transcribed in a brain cell to allow normal functioning. Using an innovative technique called chromatin immunoprecipitation (ChIP), Dr. Cha's lab has found that histones—the proteins that control gene expression—are specifically altered by the mutant huntingtin protein. This observation paves the way for using histones as a potential therapeutic target in HD.

PARKINSON'S DISEASE

- Dr. Michael Schwarzschild's laboratory has engineered a mouse to be resistant to the features of Parkinson's disease. These genetically modified mice are expected to provide new insights into what goes wrong in Parkinson's disease and how new therapies may help. Dr. Schwarzschild also published his group's preliminary mouse research findings that helps explain the relationship between Parkinson's risk and prior caffeine and estrogen exposures.
- In order to improve existing treatment options, Dr. David Standaert's laboratory is studying the effects of l-dopa – the one effective treatment for PD – and why it wears off. Using new state-of-the-art confocal microscopes, the team replicated their work on rodent brains with primate brain samples, showing strikingly similar results on brain signaling mechanisms.