

AFTD is very pleased to announce that the Association has exceeded its goal to raise \$100,000 for FTD drug discovery research in 2007, the first year of a three-year effort to raise a total of \$300,000. As previously announced, this is a collaborative Program with the Alzheimer's Drug Discovery Foundation that will provide a total of \$900,000 to support academic and biotechnology industry scientists worldwide conducting drug discovery research on innovative therapies for frontotemporal dementias (FTD).

An initial round of grant applications was received last fall and the submissions were reviewed by a panel of specialists in the field of dementia drug discovery. The scientific panel, charged with reviewing the 21 proposals submitted from the USA, Hong Kong, Portugal and Israel, was very pleased with the quality of applications received. The winner of this year's grant competition and a brief description of their research programs are as follows:

**David Vocadlo, PhD, Assistant Professor of Chemistry**  
*Simon Fraser University, British Columbia, Canada*

One of the principal disease mechanisms at work in FTD involves the molecule tau, which plays an important role in normal brain cells by stabilizing microtubules in the neurons so they can get nutrients and function normally. In tau-related FTD, tau molecules have phosphate attached to them, which causes tau to fall off microtubules and prevents them from playing this key role. The result is the development of neurofibrillary tangles, hallmarks of FTD, and the death of brain cells.

Dr. Vocadlo's lab has developed compounds that inhibit the excess phosphorylation of tau, and thus enable this molecule to retain its important role in brain function. Dr. Vocadlo has tested these compounds in rats that have tau-related FTD, and has documented a marked decrease in the formation of neurofibrillary tangles.

This grant will enable Dr. Vocadlo to further test these compounds, and determine their mechanism of action. The goal is to identify an optimal form of these compounds that will be suitable for clinical testing as an FTD therapeutic.

**Ben Bahr, PhD, Associate Professor of Pharmaceutical Sciences**  
*University of Connecticut*

Dr. Bahr's approach to FTD therapy also targets the tau disease mechanism. Scientists know that our brain cells are equipped with a system to remove altered or misfolded tau so the cells can continue to serve their normal function. The problem in FTD and other dementias is that these altered tau molecules build up quickly, and to such an extent that the system can't keep up, and the brain cell eventually dies because it is literally filled up with these non-functional proteins.

Dr. Bahr plans to test a number of compounds that have already been proven to enhance the function of the normal garbage "disposal" system in brain cells. His hypothesis is that if he can find a compound that works within the brain to speed removal of this altered tau, the brain cell will be able to continue functioning and the FTD-related damage will not occur.

**Larry Baum, PhD, Assistant Professor of Medicine and Therapeutics**  
*Chinese University, Hong Kong*

Dr. Baum's project also involves enhancement of a protective process that occurs naturally in brain cells. When a cell undergoes stress (trauma, lack of nourishment or oxygen, for example) the proteins that perform the work of the cell begin to degrade and fold abnormally, which renders them nonfunctional. The cell has developed a natural response system which enables it, in times of such stress, to produce chaperone molecules which bind with the altered proteins to

either re-fold them into their functional shape or remove them from the cell. Dr. Baum proposes to use these naturally-occurring chaperones to re-fold, or “fix” the nonfunctional tau in FTD brain cells.

**Tara Spires-Jones, PhD, Instructor of Neuroscience**  
*Harvard Medical School*

Dr. Spires-Jones is working with a family of proteins called sirtuins that are known to be involved in cell survival. Previously, researchers have shown that they can minimize brain cell death from Alzheimer and Parkinson disease processes by changing the activity of sirtuins in the cell. Dr. Spires-Jones will be testing a compound that affects the level of activity of sirtuins in a mouse model of FTD, to see if she can replicate this effect in FTD.

**Thanks to all of our generous donors** we have met our goal for the first year of this exciting research effort. We look forward to exceeding our goal once again in 2008. If you wish to make a donation to help us on our way to our second \$100,000 or want to learn more about our partnership with ADDF, [click here](#).