



**THE
LONGEVITY
FOUNDATION**

“Collaborative biomedical research of cancer and degenerative diseases associated with auto-immunity, inflammation and premature aging”

Christmas Season 2011

The “Holy Grail” of Neuronal Disease and Stem Cell Research?

Paul Wong and his team have done it again! They have come up with a discovery that is the first of its kind in the world. Building on their earlier ground-breaking experiments, Paul Wong, Ph.D. and the researchers in his lab at M.D. Anderson’s Science Park have found a treatment that prevents, and possibly even cures, the neurological effects of ataxia-telangiectasia or A-T. **The implications of this discovery are immeasurable**, considering that a whole array of neurodegenerative diseases, including Alzheimer’s, Parkinson’s, Lou Gehrig’s (or ALS), multiple sclerosis, and many others, will be impacted. **What has Paul’s lab done?** They have used A-T mice, as perhaps the best known genetic model for premature aging and neurodegeneration, to learn how both A-T and premature aging/neurodegenerative diseases can be counteracted by administering non-toxic drugs that promote neural stem cell (NSC) self-renewal and differentiation into neurons.

Paul and his team tested two drugs, one being monosodium luminal or GVT, a unique antioxidant manufactured by Bach Pharma Inc., and the other being an inhibitor of an enzyme called p38. These drugs prevent p38 from becoming over-activated when cells cannot handle oxygen exposure adequately. As cells are bombarded with oxygen molecules, they must be capable of neutralizing the toxic effects of stray electrons. Healthy organisms can control volatile electrons, or free radicals, with antioxidants or by activating their cellular antioxidant defenses. Animals whose antioxidant defenses are weakened by genetic defects or aging are unable to manage the reactive oxygen species (ROS) properly. A build up of ROS causes an activation of p38, which consequently prevents NSCs from renewing themselves and turning into neurons.

Paul’s team started its odyssey many years ago to get to this point. Team members conducted an untold number of experiments and literature reviews, beginning with the guidance and inspiration of Dr. Bill Lynn in the early ‘90’s. Building on that background, the team attempted an experiment in 2009, trying drugs to inhibit the production of p38 in NSCs in Petri dishes. As results came in, indications were that p38 could be inhibited with specific drugs. **The next step**, which began soon thereafter, **was to try to prove that these drugs would work in whole animals**. Now, just recently, initial results are in: Yes! The drugs work in live animals that exhibit the loss of balance and coordination found in human A-T patients. **The mice with A-T who received the drugs no longer exhibited Purkinje neuronal damage** when their cerebellums were examined. Predictably, the typical neuro-motor deficits were also prevented.



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Research News

HOPE FOR OUR FUTURE

What happens, now? Much work still needs to be done. A skeptical scientific community needs to be convinced of these landmark results so that they become universally accepted as game-changing discoveries. Papers must be published and grants must be awarded so that refinements and translational research can be conducted: What are the optimum doses of the drugs? When and how long should the drugs be administered? Are they best in combination and, if so, in what ratios?

Paul's group has submitted a grant to the NIH that is now pending approval. Given the current state of national research funding, however, we cannot be certain that the grant will be awarded. In the meantime, Paul's team has had to be detailed to other labs until more funding can be found. The team's spirit and desire remain intact and its members continue to pursue every opportunity to keep the research moving forward. We all believe that the progress they are making is much too important to be delayed. With your continued support, we will help keep the infrastructure in place until more financial resources become available.

More (Mind-Blowing!) A-T News

I distinctly remember Thanksgiving Day of 2000 for two reasons. For one thing, Patrick (meet Patrick on our website video) had just died that August. The other reason is that in the afternoon, I drove out to M.D. Anderson's Science Park to meet with Dr. Bill Lynn, who works every day of the year, and Mingshan Yan, a physician and scientist who had just arrived the day before from China.

We met in a trailer where Mingshan would be living on the campus. Mingshan spoke probably two indistinct words of English, but seemed able to understand scientific terms. At least he had to try, because Bill Lynn proceeded with giving him a non-stop three-hour lecture on A-T, of which Mingshan had never heard!

Fast-forward about four years and Mingshan had become the first and only scientist in the world to prevent lymphoma in A-T mice. Fast-forward a couple of more years and Mingshan had further perfected his treatment protocol and had it published. Fast-forward to the present and Mingshan, as a medical doctor, has returned to China to start his country's first A-T Clinic! We wish Mingshan and his wife, Leefung, all the best and thank them for their inspirational work. (They are pictured together in our rotating website banner.)

Another of our old friends is doing great things, too. Dr. Gerry Berry, with whom we started working over 15 years ago when he was at Children's Hospital in Philadelphia, is now planning an A-T clinical trial at Children's Hospital in Boston, which is affiliated with Harvard Medical School. Gerry, who is head of metabolic disease there, is organizing a comprehensive study into treating the causes and symptoms of A-T in children in locations throughout the world, including China. We thank him for his work and hope to help him along the way. *Robert Howard*

Wishing you a Healthy & Happy
Holiday Season