The Angel Fund for ALS RESEARCH

Benefiting ALS (Lou Gehrig's Disease)
at UMass Chan Medical School research

Brief Summary and Research Update   August 1, 2022
ALS Program – UMass Chan Medical School
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Over the last several months, ALS investigations at UMass Chan Medical School have had excellent momentum. Collaborating with Prof. Paul Greer in the Program in Molecular Medicine at UMass, Dr. Brown has further characterized roles that non-neuronal cells play in accelerating ALS. This work, spear-headed by two exceptional graduate students, Kit Mocarski and Abbi Hiller, has documented that some inflammatory cells in the spinal cord (known as "microglia") display progressively adverse properties as ALS progresses. Moreover, in mouse studies, there is evidence that suppressing these properties may slow the course of motor neuron death. In another collaboration, Prof. Job Dekker and the Brown Lab are conducting extensive studies of chromosome folding in motor neurons, with a focus on how this may be influenced by mutations in the C9orf2 gene. This study has been conducted experimentally for more than five years by a graduate student, Ozgun Uyan. Using stem cells to make motor neurons, Ozgun has documented that chromosome folding is distinctly different in different stages of development including skin cells, stem cells, and stem cell-derived motor neurons.

In addition to these more basic studies, the lab is continuing to develop therapies for forms of motor neuron disease induced by mutant ALS genes. While initial efforts focused on the C9orf72 and SOD1 genes, the present program, called The Accelerator Initiative, involves a pipeline to develop gene suppression therapy for multiple genes in parallel. Two important faculty members in this program are Professors Jonathan Watts and Anastasia Khvorova in the RNA Therapeutics Institute. Clinical aspects of these studies will be pursued jointly with Drs. Merit Cudkowicz and James Berry at the Massachusetts General Hospital.

Dr. John Landers, a former Angel Fund fellow and now a Professor of Neurology at UMass, continues to lead an international team that is discovering new ALS genes and is also initiating new programs to treat inherited ALS. Prof. Daryl Bosco, Co-Chief Scientific Advisor at the Angel Fund, is drawing upon her longstanding expertise in protein chemistry to understand how misbehavior of ALS proteins such as FUS and profilin-1 accentuate motor neuron pathology. Two other lead neuroscientists, Prof. Fen-Biao Gao and Assistant Prof. Sandra Almeida, are investigating why some forms of ALS are also associated with frontotemporal dementia (FTD). They have employed multiple models, using stem cells and fruit flies, to understand the biological overlap of ALS and FTD, and how this may point to possible new therapies.