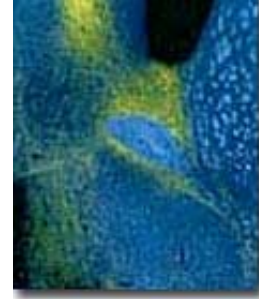




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Research Interests

Our laboratory studies inherited neurodegenerative diseases, with the goal of understanding the mechanisms underlying neurological dysfunction so as to develop effective treatments. We are particularly interested in the CAG repeat diseases, a group of nine genetically related disorders caused by expanded CAG/glutamine tracts in the coding regions of disease-causing genes. Among these disorders is Kennedy's disease, a degenerative disease that predominantly affects lower motor neurons and is caused by a mutation in the androgen receptor gene. The mutant protein misfolds, aggregates, and abnormally interacts with other proteins, leading to both a toxic gain-of-function and a partial loss of normal function. We have developed both a knock-in mouse model and cell culture models of Kennedy's disease. We are using these systems to understand the mechanisms by which the mutant androgen receptor causes selective neuronal dysfunction that is characteristic of this disorder.

Our laboratory also studies Niemann-Pick C, an autosomal recessive neurovisceral lipid storage disease for which there is no cure. Mutations in two genes, Npc1 and Npc2, produce a clinically heterogeneous disorder characterized by devastating neurodegeneration that often begins in childhood. Loss of function mutations in either gene disrupt lipid trafficking and lead to the predominant accumulation of glycosphingolipids within neurons. Most cases of Niemann-Pick C are caused by mutations in Npc1, a gene widely expressed in the brain. It is not currently known which cells are mechanistically involved in the neuropathology characteristic of this disease. We are using cellular and mouse models of Niemann-Pick C to address this question, and to study the mechanisms that lead to neuron death.



Selected References

Lieberman AP, Harmison G, Strand A D, Olson J M, Fischbeck K H. Altered transcriptional regulation in cells expressing the expanded polyglutamine androgen receptor. *Hum Mol Genet*, 11:1967-1976, 2002

Thomas M, Dadgar N, Aphale A, Harrell JM, Kunkel R, Pratt WB, Lieberman AP. Androgen receptor acetylation site mutations cause trafficking defects, misfolding and aggregation similar to expanded glutamine tracts. *J Biol Chem*, 279:8389-8395, 2004

Thomas M, Yu Z, Dadgar N, Varambally S, Yu J, Chinnaiyan AM, Lieberman AP. The unfolded protein response modulates toxicity of the expanded glutamine androgen receptor. *J Biol Chem*, 280:21264-21271, 2005

Yu Z, Dadgar N, Albertelli M, Scheller A, Albin RL, Robins DM, Lieberman AP. Abnormalities of germ cell maturation and Sertoli cell cytoskeleton in androgen receptor 113 CAG knock-in mice reveal toxic effects of the mutant protein. *Am J Pathol*, 168, 195-204, 2006

Thomas M, Harrell JM, Morishima Y, Peng HM, Pratt WB, Lieberman AP. Pharmacologic and genetic inhibition of hsp90-dependent trafficking reduces aggregation and promotes degradation of the expanded glutamine androgen receptor without stress protein induction. *Hum Mol Genet*, 15, 1876-1883, 2006

Yu Z, Dadgar N, Albertelli M, Gruis K, Jordan C, Robins DM, Lieberman AP. Androgen-dependent pathology demonstrates myopathic contribution to the Kennedy disease phenotype in a mouse knock-in model. *J Clin Invest*, 116, 2663-2673, 2006

Pacheco CD, Kunkel R, Lieberman AP. Autophagy in Niemann-Pick C disease is Beclin-1 dependent and responsive to lipid trafficking defects. *Hum Mol Genet*, 16, 1495-1503, 2007

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