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Project Title: Investigating androgen receptor acetyltransferases as therapeutic targets for the treatment of spinal and bulbar muscular atrophy

The nature of the nuclear events that transform the polyglutamine(polyQ)-expanded androgen receptor (AR) into a toxic species are a major focus of study in the field of spinal and bulbar muscular atrophy (SBMA). It is unknown at what point in its metabolism the mutant AR becomes toxic to motor neurons and skeletal muscle. However, Dr. Montie's work, along with studies from other laboratories, has begun to dissect a number of potential pathological pathways, with the intention of defining therapeutic targets for SBMA. Dr. Montie has demonstrated that inhibition of mutant AR acetylation decreases its aggregation and toxicity in cell models of SBMA (Montie HL, et al. SIRT1 modulates aggregation and toxicity through deacetylation of the androgen receptor in cell models of SBMA. *J Neurosci.* 2011. 31(48):17425-36). She is in the process of generating mouse models that will enable continued investigations into the role of polyQ-expanded AR acetylation *in vivo*.

Dr. Montie is interested in targeting the AR acetyltransferases, Tip60 and ARD1 as potential lines of therapy for SBMA. Support of this project by the Kennedy's Disease Association will enable Dr. Montie to generate preliminary data for grant applications to the National Institutes of Health (NIH) and the Muscular Dystrophy Association to support her new, independent research laboratory at Philadelphia College of Osteopathic Medicine.