Genetics Day Poster Submission

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Title: LOSS OF ATAXIA-TELANGIECTASIA MUTATED EXACERBATES MOTOR COORDINATION DEFECTS FOLLOWING OXIDATIVE INSULT

Abstract: Ataxia telangiectasia (AT) is a pediatric neurological disorder that is characterized by mutations in multifunctional kinase, ATM (Ataxia Telangiectasia, Mutated), that lead to progressive neurodegeneration and ataxia. Several mouse models with mutations in the Atm gene homolog have been generated that recapitulate many symptoms of AT, such as immunodeficiency and infertility, but not motor defects. While a majority of research has focused on the question of why mouse models do nor develop the end stage pathology that is defined by neuronal loss, we focus on understanding the early stages of the disease that precede neuronal loss. Recent data in patients suggest that demyelination and oxidative stress occurs in early stages and might contribute to disease progression. Whether this progression is due to loss of myelination oligodendrocytes, a defect in remyelination or both is not known. To address this knowledge gap, we used cuprizone, a commonly-used oxidizing insult, that allows us to identify processes during de-and remyelination. We specifically hypothesized that loss of ATM induces an exacerbated inflammatory response upon oxidation and renders oligodendrocytes highly vulnerable to stressors and impairs the repair ability of oligodendrocyte progenitor cells. To test our hypothesis we used behavioral and histological assessment during de- and remyelination. We present data that demonstrate the increased vulnerability of AT animals and provide a new and exciting model to study the early onset of the disease and processes that lead to progressive loss of function.