Identifying genetic modifiers in a *Drosophila* model of Inclusion Body Myopathy

Amber Follin1,2, Kyla Britson3, Thomas Lloyd3,4

Biology Department, Berea College1, Johns Hopkins Health Careers and Opportunities Program2, Johns Hopkins Department of Neurology3 and Neuroscience4

Inclusion body myopathy (IBM) is the most common myopathy in people over the age of 50. It causes slow progressive muscle weakness and is characterized by vacuolization, mitochondrial dysfunction, endomysial inflammation, and cytoplasmic deposition of TDP-43.   
Recently, whole exome sequencing has ~~recently~~ shown that valosin-containing protein (VCP) is a significant risk factor in sporadic forms of IBM. In addition, mutations in VCP are known to cause a hereditary form of IBM associated with Paget’s disease and frontotemporal dementia (IBMPFD). To better understand the disease pathology of IBM, the Lloyd lab expresses a mutant form of this gene in *Drosophila*, which recapitulates human IBM pathology. Importantly, this model shows TDP-43 depositions in the cytoplasm, and it has been shown that such aggregations are sufficient to interfere with nuclear cytoplasmic transport (NCT). As disruption of NCT is a key pathologic event in other TDP-43 proteinopathies, such as ALS, the purpose of this study was to identify if IBM pathology was driven by aberrant NCT. A genetic screen using Bloomington *Drosophila* lines and a mutant VCP line was performed, as well as subsequent climbing assays and thorax dissections. Two Bloomington lines contained genes that enhanced the IBM phenotype; future investigation into the NCT genes of each line may shed light on their role in IBM pathogenesis.

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