

Automated Screening of *Drosophila* Neurodegenerative Disease Models Facilitates CNS Drug Development

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Neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, Huntington's disease and other polyglutamine repeat disorders together affect tens of millions of people worldwide. However, the development of drugs that stop or slow the progression of these CNS diseases has been challenging and requires new drug screening approaches. EnVivo Pharmaceuticals has developed an *in vivo*, high throughput screening platform using whole animal models. By expressing human disease genes in *Drosophila*, we generated models that demonstrate progressive, age-dependent neurodegeneration as well as other human disease hallmarks, such as protein aggregation and locomotor dysfunction. Integral to our proprietary platform is the mass industrialization of *Drosophila* production and their handling, compound dosing, and automated phenotypic assays. One exemplary assay uses robotics and video based motion tracking software to sensitively and rapidly measure multiple metrics of locomotor behavior. From these metrics, a Phenoprofile is generated, which reveals phenotypic impairment and improvements with drug treatment. As proof of concept, treatment of our *Drosophila* model of Huntington's disease with inhibitors of HDACs significantly improves their behavior, which is consistent with previous reports in other HD *Drosophila* and mouse models (Steffan et al., 2001; Ferrante et al., 2003). EnVivo is actively screening compound libraries through our various CNS models and has started to move hits from these screens forward in the drug discovery process. The output of such a discovery platform has the potential to generate information on the efficacy and toxicity of a compound in an intact nervous system, allowing hits to quickly advance into preclinical development.