

# Effects of Gut Microbiota on Drosophila Models of Parkinson's Disease

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Parkinson's Disease (PD) is a locomotor disease characterized by toxic aggregation of the protein  $\alpha$ -syn in neurons. In recent research, mice with a PD-causing mutation failed to exhibit disease symptoms when digestive-tract microbes were removed – however, this surprising effect has never been explored in other PD model organisms such as the fruit fly *Drosophila*. I investigated motor defects, the hallmarks of PD, in these flies both with and without their gut microbiota, using two PD-causing loss of function mutations for the proteins parkin and LRRK2. These mutations cause  $\alpha$ -syn aggregation (and thus loss of locomotion) as both proteins are needed to lyse  $\alpha$ -syn. However, parkin also is necessary for mitochondrial quality control, causing debate over which way it more strongly impacts locomotor activity. To create microbe-free flies, fly eggs were dechorionated, then added to sterile food; meanwhile flies were also cultured with a normal diet as controls. Fly homogenates were plated to ensure sterility. Flies were sorted by sex and then assayed to determine percentage that climbed up more than 8 cm in 10 seconds. Low climbing ability indicates PD-related neurodegeneration. LRRK2-mutant flies followed the pattern found in the mice study, with loss of gut microbiota causing the locomotor activity to increase (a drop in PD symptoms) – however, in parkin-mutant flies, the already poor locomotor activity decreased further with microbe loss. In summary, the results in LRRK2-mutants prove agreement between fly and mice models; however, the novel conclusion is reached that the mitochondrial activity of parkin is more crucial to its impact on locomotor ability than its breaking up of  $\alpha$ -syn, because parkin-mutant flies with no microbiota still had lower levels of locomotion.

## Awards Won:

Fourth Award of \$500