drop-dead and the formation of extracellular barriers in Drosophila

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The structural and chemical integrity of all organisms depends upon the presence of barriers that regulate the interaction of the organism with its environment. In insects, this barrier function is performed in part by extracellular structures such as the cuticle, the eggshell, and the peritrophic matrix (PM) of the gut. The Drosophila drop-dead (drd) gene encodes an integral membrane protein with homology to acyltransferases. drd mutants exhibit many severe phenotypes, including early adult lethality, female sterility, and gut dysfunction. While the cellular basis of some of these phenotypes remain unknown, in several instances the phenotypes have been shown to arise from a defect in extracellular barrier formation or stabilization. In the ovary, expression of drd in the somatic follicle cells is required for stabilization of the innermost layer of the eggshell, the vitelline membrane (VM). In drd mutant females, the VM proteins fail to become crosslinked by dityrosine bonds during ovulation and egg activation, resulting in early embryonic lethality. This crosslinking defect cannot be rescued by treatment of isolated egg chambers with exogenous peroxidase, suggesting that drd is required to make the VM proteins competent for crosslinking.

In the gut, drd expression in the cardia is required for formation of the PM. Because the pleiotropic nature of drd mutants makes these flies a poor model for studying PM function, we screened for other genes required for PM formation. Knockdown or mutation of multicopper oxidase 4 (mco4), which encodes a laccase and is expressed exclusively in the cardia, eliminates both the larval and adult PM. We have characterized two primary phenotypes of mco4 knockdown flies. First, they exhibit slow larval growth and reduced adult body mass due to a reduced larval digestive efficiency. Second, they exhibit an impaired ability to maintain the adult gut microbiome. Our data suggest that the PM both protects commensal bacteria from the fly’s immune system and enhances growth of the microbiome in an immune-independent manner.