





Faculty and PostDoc Population, Health & Wellness

Between Immunity, Metabolism, and Development: A story of a Fly Gut!

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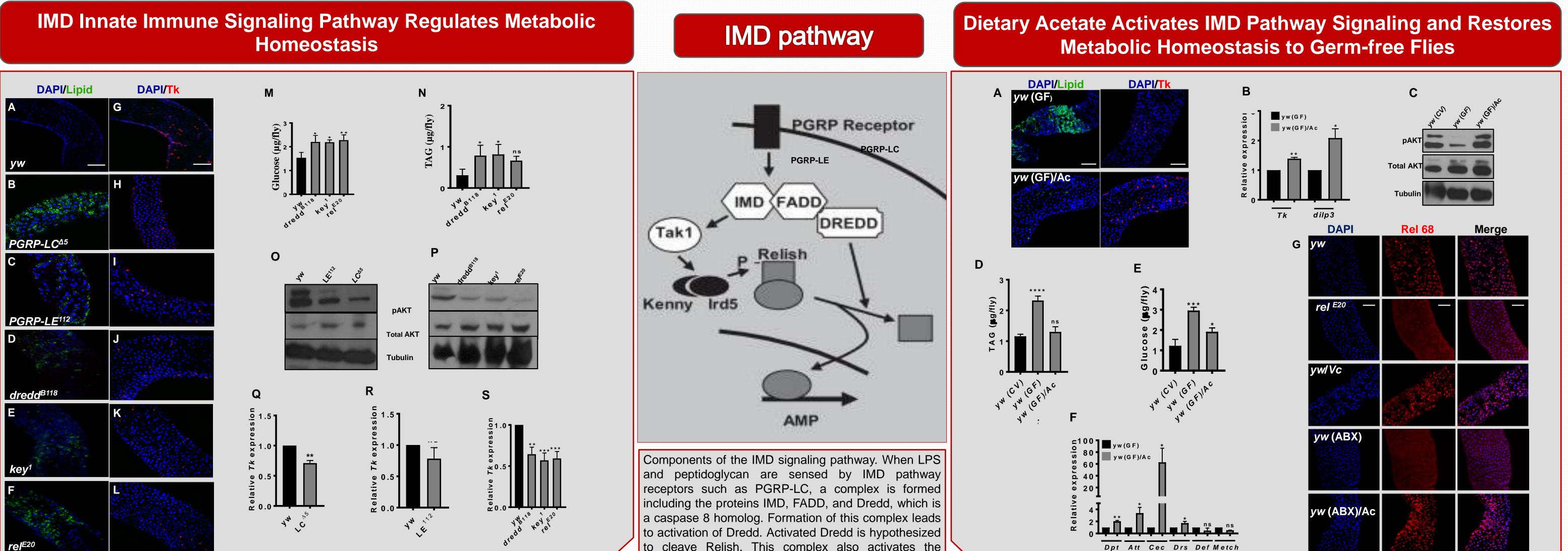
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In addition to its role in initiating immune response in the body, the innate immune system seems to also play a critical role in maintaining homeostatic balance in the gut epithelium. Our recent studies in the Drosophila melanogaster fruit fly model suggest that different innate immune pathways contribute to this homeostatic balance through activating the transcription of genes encoding antimicrobial peptides. We provide evidence that several metabolic parameters are altered in immune deficient flies. We also highlight a role of the gut flora, particularly through its short chain fatty acid, in contributing to this metabolic balance. Interestingly, our data suggest that impaired immunity and metabolic alteration, in turn, exhibit an effect on host development. Collectively, these findings provide evidence that innate immune pathways not only provide the first line of defense against infection but also contribute to host metabolism and development.

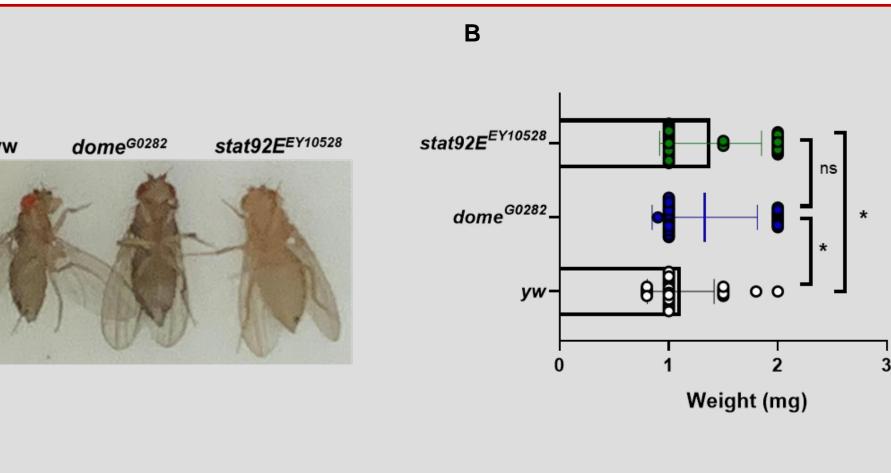


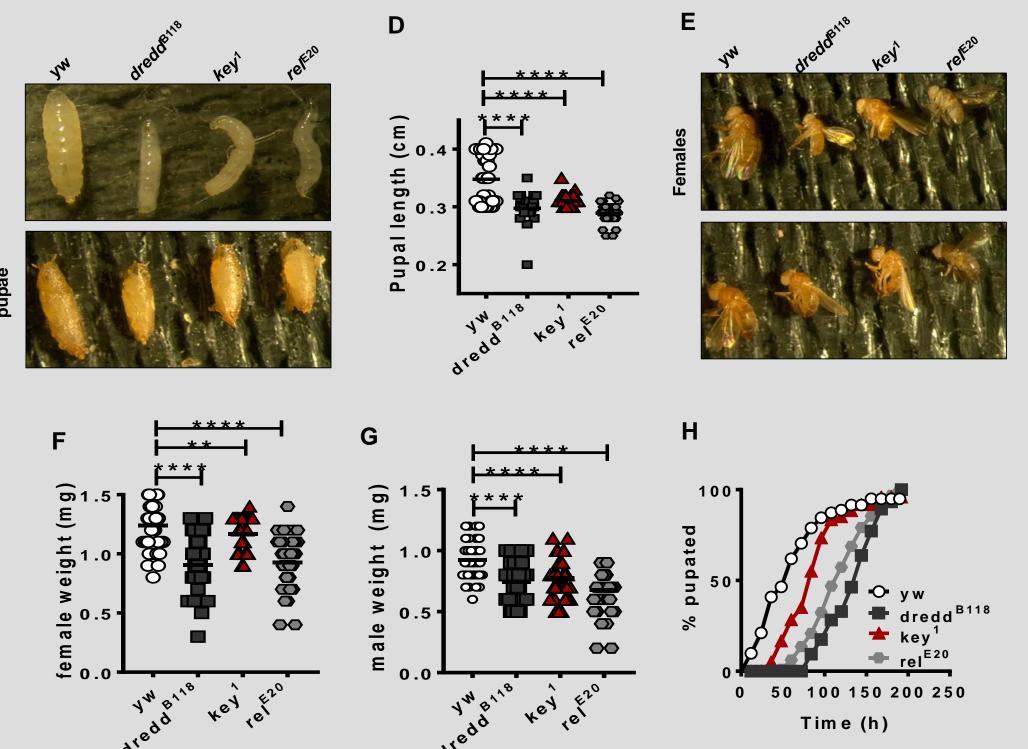
Lipid accumulation (A-F) and Tk peptide hormone expression (G-L) in the intestine of yw, PGRP- $LC^{\Delta 5}$, PGRP-LE¹¹², dredd^{B118}, key¹, and rel^{E20} IMD pathway mutants. (M) Glucose (N) Triacylglyceride (TAG) levels and **(O-P)** insulin signaling in the noted genotypes.(**Q-S)** qRT-PCR of *Tk* in the intestines of noted strains.

to cleave Relish. This complex also activates the MAP3kinase Tak1 [2] and then the IKK complex, leading to phosphorylation of Relish, a homolog of the mammalian transcription factor NF-kB [3]. The IKK complex includes IKKy, otherwise known as Kenny, and IKK β , otherwise known as IRD5. When Relish translocates to the nucleus it promotes the transcription and production of antimicrobial peptides in response to the bacterial infection.

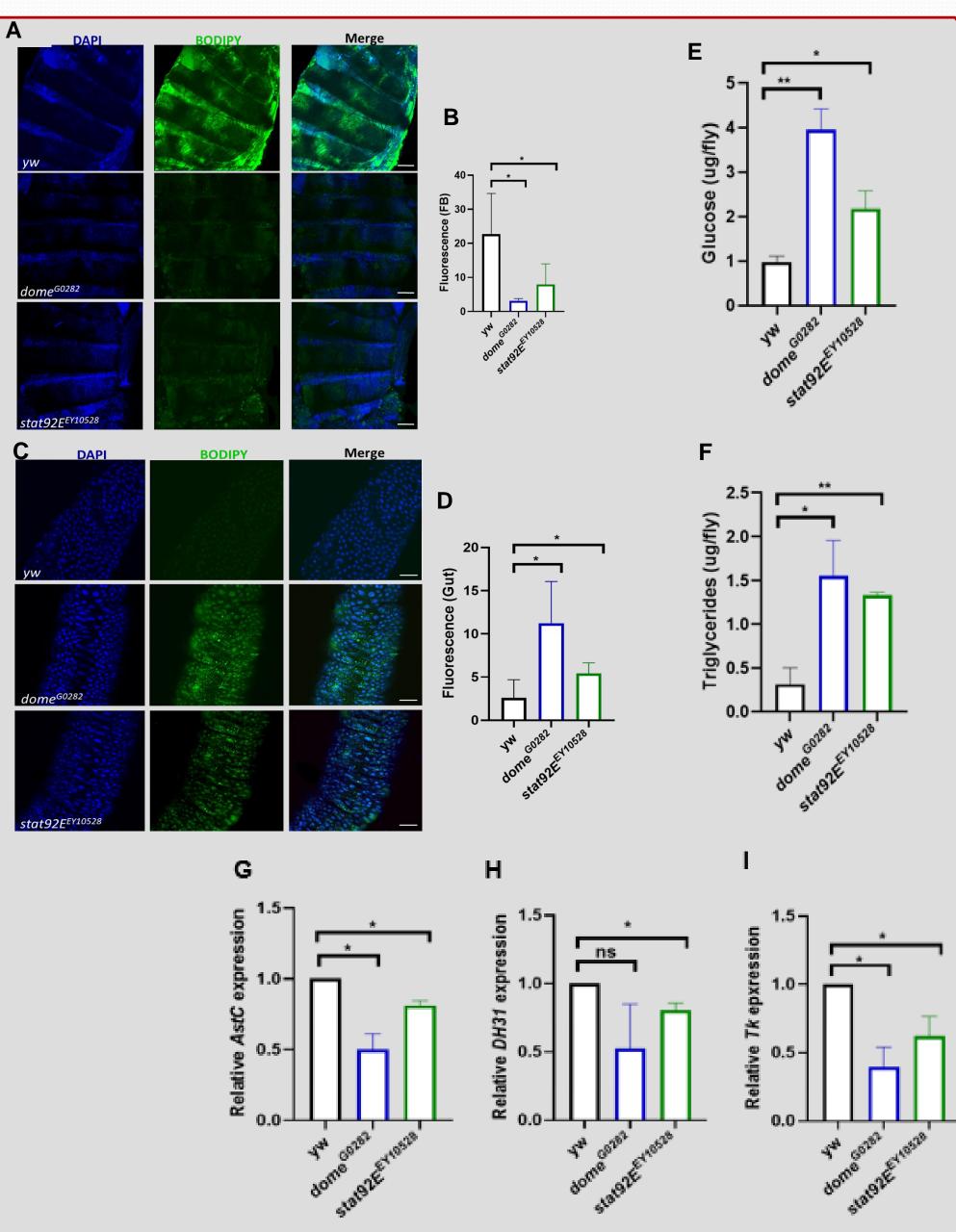
(A) Representative fluorescence images in the midgut of germ-free (GF) control flies (*yw*) fed fly food alone or supplemented with 50mM acetate (Ac). (B) qRT-PCR of Tk and dilp3 in the intestines of noted strains.(C) Insulin signaling (D) Triacylglyceride (TAG) and (E) Glucose levels in the noted genotypes.(F) qRT-PCR of anti-microbial peptides in the intestines of noted genotypes. (G) Immunofluorescence images of the intestines of flies using Rel 68 antibody and stained with DAPI.

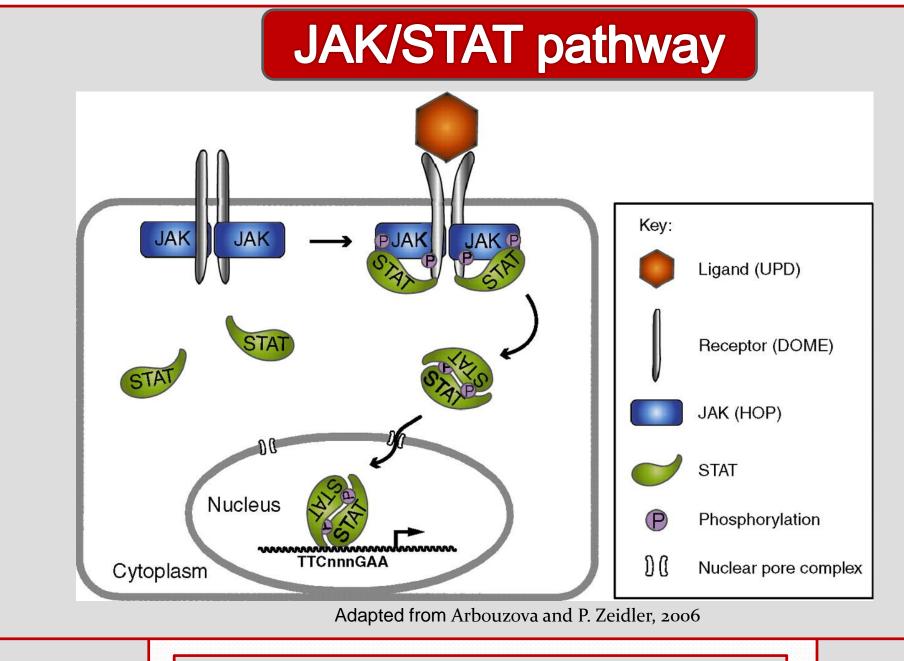
Impaired Immunity and Alerted Metabolism Affects Development





JAK/STAT Signaling Pathway Regulates Metabolic Homeostasis

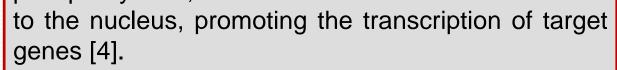




Upon ligand (red) binding, pre-dimerized complexes of the pathway including the receptor (grey) and JAKs (blue) are activated. The phosphorylation (purple circles) of the JAKs and the receptors, in turn, create docking sites for the normally cytosolic STATs that are recruited to the complex that have activated. Once these STATs get been phosphorylated, STAT dimers form and translocate

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(A,C) Representative fluoresce images of fat body tissues and gut of adult yw (control), dome^{G0282}, and stat92E^{EY10528} JAK/STAT mutant female flies, respectively, with DAPI (blue) staining nucleus on the left, BODIPY lipid staining (green) in the middle, and a merge of both on the right. Scale bar, 50µm. (B,D) Quantification of the normalized total BODIPY florescence in fat bodies tissues in the indicated fly genotypes in A. Measurements indicate the mean; error bars indicate the standard deviation. (E) Glucose (F) Triacylglyceride (TAG) levels in the noted genotypes. (G-I) qRT-PCR of AstC, DH31, and Tk peptide hormones in the intestines of noted strains.



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(A) Representative image of 5 days old *yw* (control), dome^{G0282}, and stat92E^{EY10528} JAK/STAT pathway mutant female flies. (B) Measurement of body weight of indicated fly genotypes. (C,E) Representative images of 5 days old *yw*, *dredd*^{B118}, *key*¹, and *rel*^{E20} IMD pathway mutants. (**D**) pupal length (**F,G**) weights of adult female and male flies, and (H) time to larval pupation of noted IMD mutant genotypes.