

The Role of Protein L-isoaspartate O-methyltransferase (PIMT) in Infectious Disease Tolerance

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Abstract: Protein L-isoaspartate O-methyltransferase (PIMT, also known as PCMT) is the enzyme responsible for catalyzing the partial repair of abnormal L-isoaspartate and D-aspartate residues. These damaged proteins typically accumulate with age, but may also build up during an immune response and impact the organism's disease tolerance. A previously published screen showed that *Drosophila melanogaster* with mutated *pimt* have increased mortality during *Listeria monocytogenes* infection, even though they were able to limit pathogen growth just as well as wild-type flies. We hypothesize that PIMT is important for repair during infection due to damage caused by both the pathogen directly and the fly's own immune response. Here, we utilize *D. melanogaster* overexpressing *pimt*. Using *Staphylococcus aureus* and *Streptococcus pneumoniae* as model bacterial infection, we analyze whether changes in PIMT level impact the animal's ability to survive, limit pathogen load, and maintain health as measured by performance during negative geotaxis and chill-coma recovery assays during infection. We then plan to analyze their ability to regulate melanization at the area of injury and their resistance to oxidative stress using paraquat, as a test of the animal's ability to limit and repair damage done by non-infectious stresses.