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#### **ACCEPTED MANUSCRIPT**

# Metabolomic analysis of oxidative stress: *Superoxide dismutase* mutation and paraquat induced stress in *Drosophila melanogaster*

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#### Abstract

Oxidative stress results in substantial biochemical and physiological perturbations in essentially all organisms. To determine the broad metabolic effects of oxidative stress, we have quantified the response in *Drosophila melanogaster* to both genetically and environmentally derived oxidative stress. Flies were challenged with loss of *Superoxide dismutase* activity or chronic or acute exposure to the oxidizing chemical paraquat. Metabolic changes were then quantified using a recently developed chemical isotope labelling (CIL) liquid chromatography - mass spectrometry (LC-MS) platform that targets the carboxylic acid and amine/phenol submetabolomes with high metabolic coverage. We discovered wide spread changes in both submetabolomes in response to all three types of stresses including: changes to the urea cycle, tryptophan metabolism, porphyrin metabolism, as well as a series of metabolic pathways involved in glutathione synthesis. Strikingly, while there are commonalities across the conditions, all three resulted in different metabolomic responses, with the greatest difference between the genetic and environmental responses. Genetic oxidative stress resulted in substantially more widespread effects, both in terms of the percent of the metabolome altered,

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