Strategic Promotion of Ageing Research Capacity

Ageing Flies

Glycation Analysis Fruitflies Ageing

Chemical Analysis of Ageing in *Drosophila Melanogaster*

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The Investigation

Objectives

We are using chemical techniques to study compounds (called Advanced Glycation Endproducts or AGEs) that form when sugar reacts with proteins, potentially stopping the protein working properly. We are examining the relationship between the rate of formation of AGEs and longevity in *Drosophila melanogaster* (fruitflies), in an attempt to establish whether these reactions play a causal role in, or are merely correlative markers of, ageing. We are currently establishing procedures to examine what effects factors that alter lifespan have on AGE status.

Background

The chemical species known as AGEs have been subjected to detailed investigation within the context of ageing in mammals, but their precise contribution to ageing pathologies still remains unclear. A major barrier to establishing (or disproving) causality in this system is the cost and time required to manipulate lifespan in mammals. In contrast, populations of fruitflies combine low maintenance costs with a short and easily manipulated lifespan. Despite this, there is only one scientific article1 describing the chemical analysis of fruitflies over their lifespan, and this work only described the measurement of fluorescent signals that commonly occur when AGEs are present, but that could arise for other reasons. In contrast, our work uses a battery of techniques to establish both the identity and the quantity of compounds present.

Plan

We have developed reliable methods for preparing samples suitable for analysis using a diverse range of techniques. Our first study, using samples collected weekly over the lifespan of a population, has resulted in data consistent with increasing levels of AGEs with age in *Drosophila*. We now need to confirm and quantify these observations, and attempt to characterise the molecular structures giving rise to the observed changes. Some pilot data are shown opposite.

Once we have established accurate baseline data for normal flies under standard conditions, we will then examine the effect of dietary restriction and changes in temperature on the kinetics of glycation. Finally we will examine the AGE status of the MNC-ablated flies2 and the long-lived mutant *chico*.3

Potential Benefits

For older people

Our work is designed to establish and apply analytical methods that will allow *Drosophila* to be used to determine directly the role that AGE formation plays in longevity. Understanding such basic ageing mechanisms will bring long-term benefits to older people, by allowing us to measure deleterious changes as they progress with age and to develop interventions that will prevent or remediate such changes.

For society

This research will contribute to new knowledge and thus to progress in general. More specifically, the scientific community will benefit from the development of *Drosophila* as a model system for studying the chemistry of ageing. New chemical mechanistic information and analytical methodology for the study of glycation processes will also result. Finally, the award of this grant establishes Dr Ostler as an independent PI, and provides funds to train Mrs Iqbal as a new researcher in the field of ageing.

References

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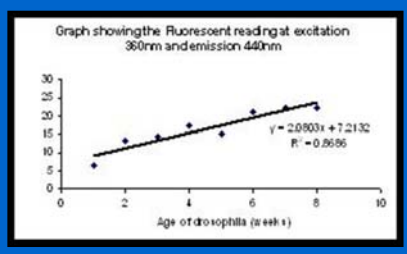

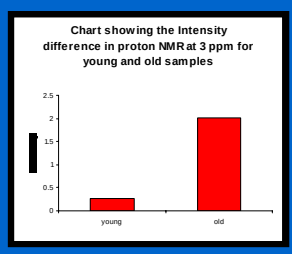

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