Strategic Promotion of Ageing Research Capacity

Ageing Flies

Chemical Analysis of Ageing in *Drosophila Melanogaster*

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The Investigation

Objectives

We are using chemical analysis to examine the relationship between the rate of formation of Advanced Glycation Endproducts (AGEs) and longevity in *Drosophila melanogaster*, in an attempt to establish whether glycation plays a causal or merely correlative role in 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 characterisation within the context of mammalian ageing. However their precise role (ie causal agents of ageing or simply correlative markers of pathology) remains unclear. A major barrier to establishing (or disproving) causality is the cost and time required to manipulate lifespan in mammals (whether by environmental or genetic modifications). In contrast, populations of *Drosophila* combine low maintenance costs with a short and easily manipulated lifespan. Despite this, there is only one publication1 describing the chemical analysis of *Drosophila* over their lifespan, and this only described simple fluorimetry conducted at a single wavelength (as a marker of the probable levels of common AGEs).

Plan

Acid-digests of the kind commonly used for AGE analysis are suitable for use on whole *Drosophila*, and represent a simple method of preparing analytical samples for use in Nuclear Magnetic Resonance spectroscopy (NMR), fluorimetry and HPLC with UV and fluorescent detection. Our pilot 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.

Pilot Data

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References