

News from the FAL

The FRAME Alternatives Laboratory (FAL) was founded in 1983 at the University of Nottingham Medical School. Now under the leadership of Dr Andy Bennett, the FAL is continuing to discover and develop real alternatives to the use of animals in research and testing. Here, Andy outlines another of his current key projects, in a discussion with Rita Seabra:

Development of an age-related macular degeneration *in vitro* model

1. What will you be studying in the project?

We will be studying age-related macular degeneration (AMD), a complex eye disease that mainly affects older adults and causes a gradual loss of sight. AMD is a complex disease, in which both genetic and environmental factors play a part. Since there is an association between diabetes and the risk of developing retinal disease, the prevalence of retinopathies may increase over time, due to the increasing incidence of diabetes in the general population.

2. What is the focus of the project?

The exact causes of AMD are not known, and a lack of models that adequately reproduce the pathological features of AMD might be contributing to the poor understanding of the disease.

We plan to develop an *in vitro* model of AMD, with the ultimate aim of understanding the mechanisms behind disease progression and identifying potential targets for therapy.

3. What is the medical significance of the research?

Increasing levels of obesity are linked to the rising number of cases of Type 2 diabetes. Together with higher life expectancy, this means that more individuals are likely to suffer from retinopathies at some point in their lives.

In the UK, there are currently an estimated 3.1 million people with diabetes (about 7.4% of the population). Figures issued by the National Health Service suggest that this will rise to 4.6 million, or 9.5% of the population, by 2030 (NHS Online; www.diabetes.nhs.uk).



4. What alternative methods are you using in the study?

A recent paper¹ described the development of a cell culture model that replicated some of the characteristics of AMD, including the accumulation of globular structures that contained known constituents of drusen (which are extracellular deposits present in the early stages of the disease). In this case, fetal eyes were the source of human retinal pigment epithelial (RPE) cells, but stem cells could prove to be an adequate alternative. In the USA² and in the UK,³ human embryonic stem cell (hESC)-derived RPE cells have been transplanted into patients as part of a prospective clinical study to assess tolerability and safety — an achievement that also highlights the usefulness of hESCs for the development of *in vitro* disease models.

We will use RPE cells derived from embryonic human stem cells, as this eliminates the need for any animal tissue. In order to obtain three-dimensional cell cultures that can be used for *in vitro* studies, we plan to grow human RPE cells in a transwell system. We will then be able to use microarray technology to monitor gene expression and to identify changes associated with disease progression. In the case of AMD, the formation of drusen-like deposits, which include protein and lipid constituents, can be detected by histological analysis with specific dyes.

¹ Johnson, L.V., Forest, D.L., Banna, C.D., Radeke, C.M., Maloney, M.A., Hu, J., Spencer, C.N., Walker, A.M., Tsie, M.S., Bok, D., Radeke, M.J. & Anderson, D.H. (2011). Cell culture model that mimics drusen formation and triggers complement activation associated with age-related macular degeneration. *Proceedings of the National Academy of Sciences of the USA* **108**, 18,277–18,282.

²Schwartz, S.D., Hubschman, J-P., Heilwell, G., Franco-Cardenas, V., Pan, C.K., Ostrick, R.M., Mickunas, E., Gay, R., Klimanskaya, R. & Lanza, R. (2012). Embryonic stem cell trials for macular degeneration: A preliminary report. *Lancet* **379**, 713–720.

³Anon. (2011). *New trial for retinal stem cell treatment gets go-ahead at Moorfields Eye Hospital*. [Moorfields Eye Hospital NHS Foundation Trust latest news, 22.09.11]. Available at: <http://www.moorfields.nhs.uk/aboutus/mediaoffice/mediareleases/sqhq> (Accessed 17.07.12).