RETINAS - Refinement of techniques for intravitreal injection to avoid side effects in rabbits

RETINAS aims to:

- Design, develop and validate a device to facilitate and standardise intravitreal drug delivery to rabbits with improved animal welfare.

Background

Treatment of degenerative disease of the eye such as age related macular degeneration is becoming more common. Many of these treatments require injection of the medicine directly into the eye. As a result of this intravitreal (IVT) injection is now a commonly used technique in pre-clinical research for drug administration. There were more than 60 papers published in 2011 which used this technique and many more unpublished experiments in contract research organisations and pharmaceutical companies. The use of this technique is likely to increase further with the success of new treatments using this method of administration in the clinic (e.g. Lucentis, Avastin and VEGF Trap-Eye).

Rabbits are often the species of choice for pre-clinical ocular studies due to the size and anatomy of their eyes which have a broad similarity to human eyes and the widespread use of rabbits as a species for toxicology studies. The pars plana (between the ciliary body and the start of the retina/choroid) is the optimal site for IVT injection. However, in the rabbit the pars plana is only approximately 1 mm in length and there are no obvious external features that can be reliably used to locate the correct area for injection. The very short pars plana (Figure 1) and large lens (Figure 2) in rabbits makes the angle of needle insertion of critical importance in this species.

The use of current techniques may lead to variation in dose delivery and adverse effects, ranging from mild inflammation to minor damage to the structure of the eye, particularly the lens and retina. While damage to the lens can be clinically diagnosed, retinal tears can only be picked up using techniques such as scanning laser opthalmoscopy with optical coherence tomography

A device to standardize IVT injection would eliminate variations in injection techniques and associated welfare problems. Such devices are available for clinical use[1,2] however, as rabbit eyes are around a third of the size of the average human eye, these are not directly applicable to this Challenge.

3Rs benefits

An IVT injection procedure for rabbits which minimises the risk of adverse effects associated with the angle and depth of needle insertion will improve data quality and animal welfare. A significantly large proportion of the rabbit eye is taken up by the lens which complicates

Sponsor
GlaxoSmithKline

Duration
Up to one year

Budget
£50,000 inclusive of VAT where applicable

Key words
Rabbit, intravitreal (IVT) injection, eye, refinement

IVT injection. For instance, the lens may be nicked by the needle during the procedure which can lead to a significant inflammatory response resulting in early euthanasia or exclusion of data. Improving drug delivery and avoiding the removal of animals from studies would reduce the number of animals needed per experiment.

Need for collaboration

To solve the challenge of IVT injection in rabbits, collaboration between scientists with extensive knowledge and expertise of carrying out the procedure and technical specialists with expertise in device development is needed to deliver appropriate prototypes. The need for an IVT injection device is not always recognised, as many of the side effects can be undetectable on cageside examination, and not all experiments include full ocular examinations. The device would also facilitate training of personnel carrying out the technique.

Overall aims

- Design a device to refine IVT injection in rabbits
- Produce and evaluate prototypes (*ex vivo* and *in vivo)*
- Select final design and manufacture device for commercial use

Full details of key deliverables and in-kind contributions for each Phase will be available from 12 September 2012.

Figures

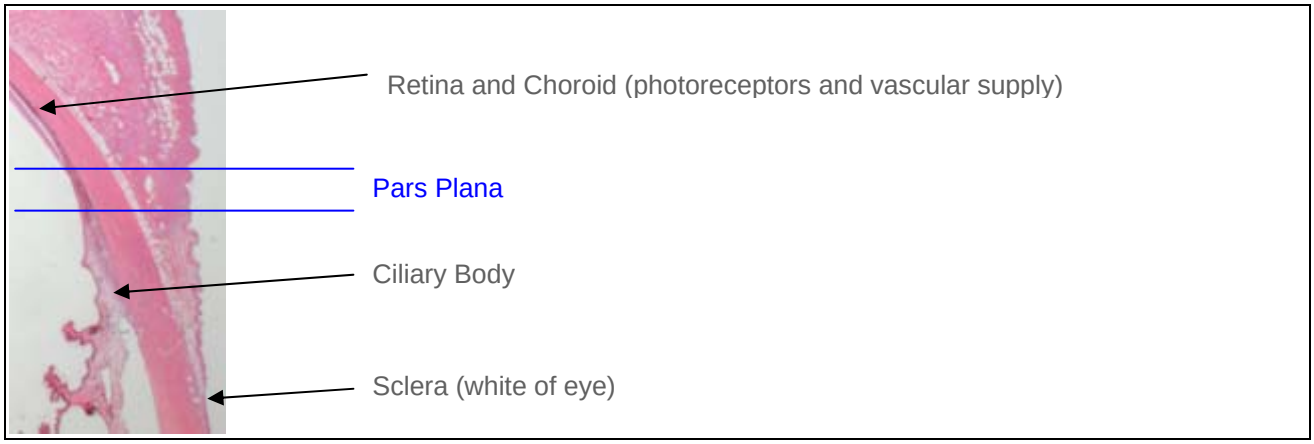

Figure 1: Histology of a pigmented rabbit eye showing site of the pars plana (between the end of the ciliary body and start of the retina/choroid). (Histology image, x 10 objective).

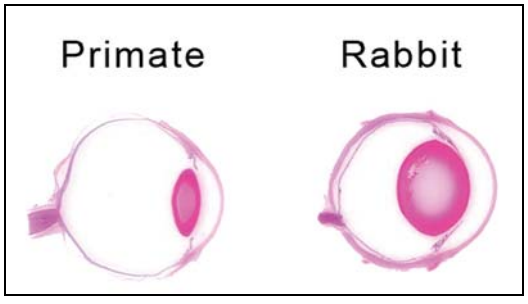

Figure 2: Comparison of lens size in primate (Cynomolgus monkey) and rabbit eyes (Image from B Short (2008) Safety Evaluation of Ocular Drug Delivery: Technical and Practical Considerations *Tox. Path.* 36 (1): 49 – 62).

References

1. www.fciworldwide.com/retina/invitria.html

2. www.duckworth-and-kent.com