ESR Project Information Sheet

Project title	Generation & Characterisation of Sustained Release Ocular Implants for Neuroprotective Drug Efficacy
Reference number	ORBITAL_ESR_2019_Project 6
Host Institution/University	UNIVERSITY COLLEGE DUBLIN
Supervisor(s)	**Breandán Kennedy (UCD),** Alison Reynolds (UCD), Irene Bravo Osuna (UCM), Niall O'Reilly (WIT) & Sabrina Surrey (NEU).
Research Group	UCD OCULAR PHARMACOLOGY & GENETICS (OPGG)
Department / School	UCD SCHOOL OF BIOMOLECULAR & BIOMEDICAL SCIENCES
Duration	36-month employment contract provided and ESR enrolled on 4-year structured PhD. ESR will be required to self-fund after the initial 36 months
Status: Full-time / part-time	Full time
Funding information	Funding agency: H2020-MSCA-ITN-2018
Early Stage Researcher Allowances:	Living allowance: €45,361 p/a + mobility allowance of €7,200 p/a + family allowance where applicable (**all values before tax and social security payments**) Fees: €7,120-8,009
Closing date and time	5 p.m. (CET) Friday 28th June, 2019
Commencement date	2nd September 2019

Post summary

There is an unmet clinical need to develop effective treatments for blindness due to retinal dysfunction. Notably, in Europe, 0.7 million citizens are considered blind and an additional 34 million citizens affected by vision loss. This translates to 123 million workdays lost per year and an annual economic cost to European society of €7.1 billion. At a personal level, patients are impacted by loss of independence (e.g. driving, reading, writing) and inability to recognize loved ones. Retinal diseases are the most common cause of childhood blindness worldwide (*Gilbert et al. 2001*). Rare inherited retinal degenerations affect 1/3000 of the population. Research on these rare conditions has proven very informative to understand the mechanism of more common diseases such age-related macular degeneration which worldwide affects one in ten over the age of 50. Thus, improving therapeutic outcomes for blinding eye diseases represents a clinical challenge and a commercial opportunity.

An approach to preserve or restore vision is to identify neuroprotective drugs that prevent loss of visual function (Scholl et al 2016, Zhang et al. 2012). As neuroprotectants can modulate cell survival or cell death pathways common to all retinal disease, they have potential widespread applicability, irrespective of the risk factor. Recently, we demonstrated that phenotype-based visual behaviour assays in zebrafish can identify drugs preventing loss of visual function (Ward et al. 2019, Daly et al. 2017). Significantly, pathway analyses demonstrated visual restoration was mediated by brain-derived neurotrophic factor/tropomyosin-related kinase B (BDNF/TrkB) signaling, a known neuroprotective pathway in mammalian eyes (Daly et al 2017). Notably, a small molecule BDNF mimetic was sufficient to restore visual function in zebrafish models of blindness. Key advances going forward are to identify additional effective analogs and to generate sustained release ocular implants (Galvin et al. 2016) for lead neuroprotectant BDNF mimetics by encapsulation into (hyaluronan) microparticles/needles.

Key Objectives in this PhD project are:

• To manufacture sustained release nano/micro-particle formulations of lead neuroprotective drugs and to characterise their physiochemical properties.

• To characterise the in vitro release profile of the formulations over a 6-12 month period and to validate the bioactivity of the released drug.

• To characterise the safety of the sustained release formulations

• To determine if the sustained ocular release formulation preserves visual function in pre-clinical models of blindness

References

Daly C, Shine L, Heffernan T, Deeti S, Reynolds AL, O'Connor JJ, Dillon ET, Duffy DJ, Kolch W, Cagney G, Kennedy BN. A Brain-Derived Neurotrophic Factor Mimetic Is Sufficient to Restore Cone Photoreceptor Visual Function in an Inherited Blindness Model. Sci Rep. 2017 Sep 12;7(1):11320.

Galvin O, Srivastava A, Carroll O, Kulkarni R, Dykes S, Vickers S, Dickinson K, Reynolds AL, Kilty C, Redmond G, Jones R, Cheetham S, Pandit A, Kennedy BN. A sustained release formulation of novel quininib-hyaluronan microneedles inhibits angiogenesis and retinal vascular permeability in vivo. J Control Release. 2016 Jul 10;233:198-207.

Gilbert C, Foster A. Childhood blindness in the context of VISION 2020--the right to sight. Bull World Health Organ. 2001;79(3):227-32

Scholl HP, Strauss RW, Singh MS, Dalkara D, Roska B, Picaud S, Sahel JA. Emerging therapies for inherited retinal degeneration. Sci Transl Med. 2016 Dec 7;8(368):368rv6

Ward R, Ali Z, Slater K, Reynolds AL, Jensen LD, Kennedy BN. Pharmacological restoration of visual function in a zebrafish model of von-Hippel Lindau disease. Dev Biol. 2019 Feb 27. pii: S0012-1606(18)30731-0.

Zhang K, Zhang L & Weinreb RN. Ophthalmic drug discovery: novel targets and mechanisms for retinal diseases and glaucoma. Nature Reviews Drug Discovery 11, 541-559 July 2012.

Standard duties and responsibilities of the ESR

For the 36 months of employment contract the ESR will be required to work exclusively on the MSCA programme.

In all cases, all duties and responsibilities will be clearly outlined in the researchers Personal Career Development Plan, as determined in the early stages of the project between the ESR and their supervisory committee.

Person specification

Qualifications

Essential

Applicants should hold or expect to attain, as a minimum a 2:1 Honours degree, or equivalent, in Pharmacology, Neuroscience, Biomedical Science, Medicinal Chemistry, Pharmaceutical technology or related area.

Knowledge & Experience

Essential

- Research project carried out in one of the above disciplines
- A demonstrated knowledge of at least three of the following: phenotype-based drug discovery, computational drug discovery, drug delivery, zebrafish, human ocular cell culture, nanotechnology, neuroprotection, visual behaviour
- An understanding of research ethics
- Excellent time management skills

Desirable

- Work placement undertaken in an industry related to the above disciplines
- Experience using zebrafish or human cell lines as research models.

- An appreciation of retinal disease and ocular pharmacology
- Knowledge in microencapsulation and nanoencapsulation techniques

Skills & Competencies

Essential

- Applicants whose first language is not English must submit evidence of competency in English, please see UCD English Language Requirements http://www.ucd.ie/international/study-at-ucd-global/ucdenglishlanguagerequirements/ for details.
- Evidence of interest, aptitude and research experience in the above disciplines

Further information

For any informal queries, please contact Professor Breandán Kennedy on +353 1 7166740 or by email on brendan.kennedy@ucd.ie

For queries relating to the application and admission process please contact Dr Laurence Fitzhenry at orbital@wit.ie or by telephone at +353 (0)51 302624.

Website: www.orbital-itn.eu

The Institute may decide to interview only those applicants who appear from the information available, to be the most suitable, in terms of experience, qualifications and other requirements of the position.

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