Naomi Chadderton, PhD.

Ocular Genetics Unit, Department of Genetics, Trinity College Dublin, Dublin 2, Ireland.
Phone: +353 (0)1 896 2482 Email: chaddern@tcd.ie

Summary

My primary research interest is the delivery of gene based therapeutic strategies. I have ten years experience in viral delivery, encompassing retroviral, lentiviral, adenoviral and adeno-associated viral (AAV) approaches for a range of diseases. I have three first author publications in a portfolio of nine. The highest impact article, O'Reilly *et al*; 2007, was highlighted in Nature Reviews July 2007. I have authored a total of 23 published abstracts. I am a named inventor on two patents. I have been instrumental in developing the AAV core facility within the Ocular Genetics Unit at TCD, securing €250,000 of funding from Science Foundation Ireland in 2007. In total, I am the co-applicant on grants of over €450,000. As a previous FP7 Marie Curie research fellow I have benefited from an excellent postdoctoral programme and developed a positive working relationship with many of the best eye research laboratories in the EU.

Grants

Fighting Blindness Ireland
Exploration of Therapeutic Approaches for Leber's Hereditary Optic Neuropathy (LHON)
Chadderton N, Kenna PF and Farrar GJ.
Jan 2008 – Present (renewed Jan 2009), €100,000/annum.

Science Foundation Ireland
Viral Purification Equipment
Equipment call 2007, €247,700.

Irish Research Council for Science, Engineering and Technology (IRCSET)
Ulysses Travel Award
The Role of RdCVF in Photoreceptor Physiopathology using RNA Interference.
Chadderton N, Audo I, Humphries P and Leveillard T.
Jan 2007 – Dec 2007 (renewed 2008/2009), €5,000/annum.

Patents

Genetic Suppression and Replacement. US patent 10/651754 (Pending)
Millington-Ward S, Chadderton N, Palfi A, O'Reilly M, Tuohy G, Humphries P, Kenna PF & Farrar GJ.

Genetic Suppression and Replacement. PCT/GB2008/001310 (Pending)
Millington-Ward S, Chadderton N, Palfi A, O'Reilly M, Tuohy G, Humphries P, Kenna PF & Farrar GJ.

Publications

Tam LC, Kiang AS, Chadderton N, Kenna PF, Campbell M, Humphries MM, Farrar GJ, Humphries P (2010). Protection of Photoreceptors in a Mouse Model of RP10. Adv Exp Med Biol. 664:559-65.

McKee AG, Loscher JS*, O'Sullivan NC*, **Chadderton N***, Palfi A, Batti L, Sheridan GK, O'Shea S, Moran M, McCabe O, Fernández AB, Pangalos MN, O'Connor JJ, Regan CM, O'Connor WT, Humphries P, Farrar GJ, Murphy KJ (2010). AAV-mediated chronic over-expression of SNAP-25 in adult rat dorsal hippocampus impairs memory-associated synaptic plasticity. J Neurochem. 112(4):991-1004. ***equal contribution**

Palfi A, Millington-Ward S, **Chadderton N**, O'Reilly M, Goldmann T, Humphries MM, Wolfrum U, Humphries P, Kenna PF, Farrar GJ (2010). AAV-Mediated Rhodopsin

Replacement Provides Therapeutic Benefit in Mice with a Targeted Disruption of the Rhodopsin Gene. Hum Gene Ther. Mar;21(3):311-23.

Chadderton N, Millington-Ward S, Palfi A, O'Reilly M, Tuohy G, Humphries MM, Li T, Humphries P, Kenna PF, Farrar GJ (2009). Improved retinal function in a mouse model of dominant retinitis pigmentosa following AAV-delivered gene therapy. Mol Ther. 17(4):593-9.

Tam LC, Kiang AS, Kennan A, Kenna PF, **Chadderton N**, Ader M, Palfi A, Aherne A, Ayuso C, Campbell M, Reynolds A, McKee A, Humphries MM, Farrar GJ, Humphries P (2008). Therapeutic benefit derived from RNAi-mediated ablation of IMPDH1 transcripts in murine model of autosomal dominant retinitis pigmentosa (RP10). Hum Mol Genet. 17(14):2084-100.

O'Reilly M, Millington-Ward S, Palfi A, **Chadderton N**, Cronin TC, McNally N, Humphries MM, Humphries P, Kenna PF, Farrar GJ (2008). A transgenic mouse model for gene therapy of rhodopsin-linked Retinitis Pigmentosa. Vision Research 48(3):386-91.

O'Reilly M, Palfi A, **Chadderton N**, Millington-Ward S, Ader M, Cronin T, Tuohy T, Auricchio A, Hildinger M, Tivnan A, McNally N, Humphries M, Kiang AS, Humphries P, Kenna PF, Farrar GJ (2007). RNAi-mediated suppression and replacement of human rhodopsin *in vivo*. Am J Hum Gen. 81(1):127-35. **(See Research highlights - Nature Genetics Reviews July 2007).**

Chadderton N, Cowen RL, Sheppard FC, Robinson S, Creco O, Scott SD, Stratford IJ, Patterson AV, Williams KJ (2005). Dual responsive promoters to target therapeutic gene expression to radiation-resistant hypoxic tumour cells. Int J Radiat Oncol Biol Phys 62(1):213-22.

Chadderton NS, Stringer SE (2003). Interaction of platelet factor 4 with fibroblast growth factor 2 is stabilized by heparin sulphate. Int J Biochem Cell Biol 35(7):1052-5.

Oral Presentations

A therapeutic strategy for dominantly inherited Retinitis Pigmentosa
5th British Society for Gene Therapy (BSGT) Annual Conference 2008
Hum Gen Ther. 19(4):397

RNAi-based therapies for dominant retinal degenerations.
Irish Neurogenetics Symposium 2007.

RNAi-mediated suppression and replacement of human rhodopsin *in vivo.*
3rd Pro Retina Deutschland Research-Colloquium 2007.

A novel promoter enhancer for hypoxia selective gene therapy.
42nd British Association of Cancer Research (BACR) Meeting 2002.
Br J Cancer 86(S1): S29.

As a Marie Curie FP7 fellow I gave a further 8 presentations to a peer-review audience.

Experience

January '08 – Present Smurfit Institute of Genetics, Trinity College Dublin.

Postdoctoral Research Fellow

Development of therapeutic approaches for Leber's hereditary optic neuropathy.

- Investigation of a mutation independent gene replacement approach using adeno-associated virus delivery to rescue and enhance the longevity of retinal ganglion cells.

January '05 – Present Genable Technologies Ltd., Dublin.

Scientific Consultant

January '04 –Dec '08 Smurfit Institute of Genetics, Trinity College Dublin .
Marie Curie FP7 Postdoctoral Research Fellow
AAV delivery of suppression and replacement constructs for rhodopsin-linked autosomal dominant Retinitis Pigmentosa (RP).

- rAAV2/5 engineered to contain shRNAs targeting human Rho together with a replacement gene, consisting of human Rho cDNAs with degenerate nucleotide changes over the target sites for shRNA suppression, were evaluated for therapeutic effect in transgenic models of human retinal degeneration.

August '98–Oct '00 Paterson Institute for Cancer Research, Manchester.
Research Assistant
Gene therapy to increase the effectiveness of treatment in children undergoing chemotherapy.

- The expression of ATase and MDR-1 gene products in drug sensitive tissues was shown to circumvent the acute toxic and chronic carcinogenic effects of chemotherapy following *in vivo* retroviral delivery.

Education

2000-2004 PhD, The University of Manchester. Supervisor; Prof. I.J. Stratford
Biotechnology and Biological Sciences Research Council (BBSRC) Studentship
Thesis: The development of a transcriptional cascade to precisely control gene expression under hypoxic conditions.

1997-1998 MSc Biomedical Science, Manchester Metropolitan University
Thesis: The role of heparin sulphate proteoglycan (HS) and basic fibroblast growth factor (bFGF) in the modulation of platelet factor four (PF4).

1994-1997 BSc (Hons) Biochemistry and Molecular Biology, UMIST
Thesis: Adhesion of haemopoietic stem cells to the endothelium.

Awards

Best poster prize (€1200), 'Improved retinal function in two mouse models of Retinitis Pigmentosa following AAV-mediated gene delivery'.
European Science Foundation Rare Diseases II: Hearing & Sight Loss Conference.
Sant Feliu de Guixols, Spain, Nov 2009.

Best oral presentation, 'A therapeutic strategy for dominantly inherited Retinitis Pigmentosa'. FP7 RETNET Annual Meeting. Venice, Italy, Nov 2006.

Mentorship

I currently co-supervise two PhD students in the Ocular Genetics unit, TCD. I have previously co-supervised the six month final year projects of two senior sophisters.