

our **vision** is
your **VISION**



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Summary of current research interests

The eye is outstandingly well suited for the development of novel therapeutic approaches. It is easily accessible and allows local application of therapeutic agents with reduced risk of systemic effects.

The main interest of my group is to develop gene and stem cell therapies for eye disease, particularly diseases of the retina.

Key achievements

- Demonstration of efficient transduction of photoreceptor cells (Hum Mol Genetics 1996)
- Proof of concept of gene therapy for photoreceptor defects (Nature Genetics 2000)
- Proof of concept of retinal repair by cell transplantation (Nature 2006)
- World's first clinical trial for inherited retinal degeneration (NEJM 2008)

Research Projects

Gene therapy

The primary focus of our work is to develop novel treatments for retinal disease. Over the past ten years we have been at the forefront of investigating the basic aspects of gene transfer to the eye with a broad programme of work to develop gene therapy for eye disease and in particular for disorders affecting the retina, including inherited retinal degeneration as well as complex diseases such as those associated with retinal and choroidal neovascularisation and posterior uveitis. We are now combining gene therapy approaches with that of stem cell transplantation (see below) and are particularly interested developing therapeutic approaches to treat age-related macular degeneration. We use a number of strategies including gene replacement and or siRNA to treat animal models of inherited retinal degeneration and delivery of genes encoding angiostatic, anti-apoptotic, immunomodulatory or neurotrophic molecules to treat a variety of animal models.

Viral vector development

We have extensive experience of a number of viral vector systems. Our main interest is in the development of vectors based on either adeno-associated virus or lentivirus.

Stem cell research

We are engaged in a programme of research to determine the local cues and transcription factors that might promote optimal integration and differentiation of transplanted stem cells, in order to generate functional photoreceptors and repair degenerating retinae. We are using viral vectors, carrying genes encoding key transcription factors or growth factors, to transduce retinal stem cells within the retina or transduce stem cells before transplantation.

Clinical trial ([Click here](#))

We have now started a clinical trial of gene therapy for a form of severe childhood-onset retinal dystrophy due to mutations in the gene encoding RPE65. This trial is one of the first in ocular gene therapy.

Publications [Click here for complete publication list](#)

Effect of gene therapy on visual function in Leber's congenital amaurosis. Bainbridge JW, Smith AJ, Barker SS, Robbie S, Henderson R, Balaggan K, Viswanathan A, Holder GE, Stockman A, Tyler N, Petersen-Jones S, Bhattacharya SS, Thrasher AJ, Fitzke FW, Carter BJ, Rubin GS, Moore AT, Ali RR. *N Engl J Med.* 2008 May 22;358(21):2231-9

Retinal repair by transplantation of photoreceptor precursors. MacLaren RE, Pearson RA, MacNeil A, Douglas RH, Salt TE, Akimoto M, Swaroop A, Sowden JC, Ali RR. *Nature* 2006 444(7116):203-7

Effective gene therapy with non-integrating lentiviral vectors. RJ Yáñez-Muñoz, KS Balaggan, A MacNeil, AJ Smith, Prateek Buch, Steven Howe, Yanai Durán, Robert E MacLaren, PN Anderson, C Kinnon, RR Ali, AJ Thrasher *Nature Med.* 2006 2 (3) :348-353

Restoration of photoreceptor ultrastructure and function in retinal degeneration slow mice by gene therapy. R. R. Ali, G. Sarra, C. Stephens, M.

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de Alwis, J. W.B. Bainbridge, P. M. Munro, S. Fauser, M. B. Reiche1, C. Kinnon, D. M. Hunt, S. S. Bhattacharya, A. J. Thrasher Nature Genet. 2000 25 (3): 306-310

Gene transfer into the mouse retina mediated by an adeno-associated viral vector. RR Ali, MB Reichel, AJ Thrasher, RJ Levinsky, C Kinnon, N Kanuga, DM Hunt and SS Bhattacharya Human Mol. Genet. 1996 5 (5): 591-594

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British Retinitis Pigmentosa Society
Fight for Sight
National Institute for Health Research
European Union

Useful Links:

For further information on Robin Ali's research and his group please see:

<http://www.ucl.ac.uk/ioo/research/ali.htm>