Dr Heping Xu, MD, PhD

Senior Lecturer

Centre for Vision and Vascular Science, Institute of Clinical Sciences School of Medicine, Dentistry and Biomedical Sciences Queen's University Belfast Grosvenor Road, BT12 6BA UK Tel: (44) 28 90633615 Fax: (44) 28 90632699 E-mail: <u>heping.xu@qub.ac.uk</u> Web: <u>www.qub.ac.uk/cvvs</u>

EDUCATION

1989-1994 Ph.D., Ophthalmology, Hunan Medical University, P.R.China.

1982-1987 M.D., Medicine, HengYang Medical College, P.R.China.

Membership of Professional Bodies

- > Member of British Society for Research into Aging
- > Member of Overseas Chinese Society of Ophthalmology and Vision Research
- > Member of Association for Research in Vision & Ophthalmology (ARVO)
- > Member of British Society of Immunology

EMPLOYMENT

Sept. 2009-Present	Senior Lecturer,
	Centre for Vision and Vascular Science, Queen's University Belfast.
Aug. 2008-Aug. 2009	Senior RCUK Fellow, Immunology and Infection, University of Aberdeen, UK
Apr. 2005-Jul. 2008	RCUK Fellow, Immunology and Infection, University of Aberdeen, UK
Feb. 2000-Mar. 2005	Post-doctoral Research Fellow Department of Ophthalmology, University of Aberdeen, UK
Sept. 1997-Jan. 2000	Post-doctoral Research Scientist
	Department of Exploratory Research, Tokyo Research Institute, Seikagaku Corporation, Japan.
Jul. 1994-Sept.1997	Assistant professor, senior trainee ophthalmologist
	Department of Ophthalmology, XiangYa Hospital, Hunan Medical University, Hunan, China
Jul. 1987-Aug. 1989	Trainee doctor (resident) Long Shang People's Hospital, Hunan, China

TEACHING EXPERIENCE

• 2009-present: Coordinate a SSC course: "Foundation in Ophthalmology and Visual Science", and also deliver 6 lectures in the module. Queen's University Belfast (QUB).

- 2009-present: Lecture "Age-related macular degeneration", level-3 Biomedical Science course. QUB.
- 2010-present: Lecture "Complement system in innate immunity", level-2 Biomedical Science course. QUB.
- 2009-present: Supervise 3-4 undergraduate students (annually) for their research projects. QUB.
- 2008-2009: Co-ordinate "Immunology Research Skills Tutorial" course for MSc in Molecular & Cellular Immunology. University of Aberdeen.
- 2007-2009: Lecturer on "Complement activation in age-related macular degeneration" for MSc student (Molecular & Cellular Immunology). University of Aberdeen
- 2004-2009: Tutorial for undergraduate students in Medical Immunology (Imaging Leukocyte Trafficking). University of Aberdeen.
- 2004-2009: Tutorial for Molecular & Cellular Immunology MSc students (In vivo and In vitro imaging immune responses). University of Aberdeen
- 2004-2009: Tutorial for Bio-Medical Technology MSc students (Bio-medical imaging techniques). University of Aberdeen.
- 1994-1997: Undergraduate course in Clinical Ophthalmology at Hunan Medical University, China.

PHD STUDENT SUPERVISION

- Currently acting as the primary supervisor for three PhD students and the 2nd supervisor for one PhD student at Queen's University Belfast.
- During my service with the University of Aberdeen: I supervised three PhD students and two of them have graduated and are doing their post-doc (one in US and one in Aberdeen). The other student is expected to graduate in early 2011.

REVIEW DUTIES

- 1. Journal referee for 1) Blood; 2) Brain Research; 3) Journal of Leukocyte Biology; 4) Experimental Eye Research; 5) Ophthalmology Research; 6) Molecular Vision; 7) Investigative Ophthalmology and Visual Science; 8) British Journal of Ophthalmology; 9)Biomarker Insights; 10) Gastroenterology; 11) Current Eye Research; 12) Graefe's Archive for Clinical and Experimental Ophthalmology; 13) Clinical Ophthalmology; 14) immunology.
- 2. **Grant referee** for 1) Medical Research Council (MRC), UK; 2) Biotechnology and Biological Sciences Research Council (BBSRC), UK; 3) the Wellcome Trust, UK; 4) Diabetes UK; 5) National Eye Research Center; 6) National Natural Science Foundation of China (NSFC).

DISTINGUISHING AWARDS

- 2005-2010: Research Council UK (RCUK) Fellowship Award.
- **Royal Society International Travel Awards** for the following years: 2005, 2008, 2010.
- **2005**: Uveitis Award (1st Prize): German Uveitis Patients Interests Group.
- **2000**: Patent: A new mouse IL-12 inhibitor, Japanese Patent No. JP 20658699, 1999; European Patent No. EP 1074260 A1, 2000
- **1997**: Zhang WenShang Eye Foundation Award (1st Prize): Chinese Society of Ophthalmology of Hunan Branch.
- **1996**: New Technology Award (2nd Prize): Science and Technology Committee,

Hunan Province, China.

• **1995**: Advanced Science & Technology Award (3rd award): Health Department of Hunan Province, China.

RESEARCH GRANTS

- 1. **2010-2015**: "Development of a Vision Science Research Building". £4.8 million. <u>Wellcome-Wolfson Capital Award</u>. Co-holder with other nine colleagues, Lead applicant: Prof A Stitt.
- 2. **2010-2013**: "Mechanism of inflammation-induced retinal angiogenesis". £60,000. PhD studentship. <u>National Eye Research Centre</u>. UK. **PI**
- 3. **2010-2013**: "RAGE is central to initiation and progression of pro-inflammatory pathway in diabetic retina". £159,628. Fight for Sight. Project grant. Co-holder with Prof A Stitt (lead applicant).
- 2009-1012. "Microglia and complement activation in age-related macular degeneration". £79,500. By <u>Age UK</u> (Former Research into Aging, Help the Aged. UK, PI.
- 5. **2009-2010.** "Monocyte malfunction and age-related macular degeneration". £12,000 National Health Service (NHS) Endowment. UK, **PI**.
- 6. **2008-2009.** "Endocannabinoid system in the ageing retina and age-related macular degeneration". £12,000. <u>NHS Endowment</u>. UK. **PI.**
- 7. **2008-2009.** "Oxidative damage and microglial activation in age-related macular degeneration". £10,000. <u>Tenovus Scotland.</u> PI.
- 2007-2009. "Complement regulation in age-related macular degeneration". \$100,000. By <u>American Health Assistance Foundation: Macular Degeneration</u> <u>Research</u>. USA. PI.
- 9. **2007-2008**. "Microarray analysis of retinal microglial gene expression in the rodent model of age-related macular degeneration". £14,100. By <u>NHS Endowment</u>. UK, **PI**.
- 10. **2007-2008**. "Complement factor H and factor B in retinal pigment epithelial cells". £10,000.By <u>Tenovus Scotland</u>. **PI**.
- 11. **2006-2007**. "Understanding the pathogenesis of fundus autofluorescence in the murine model of age-related macular degeneration". £12,000. By NHS Endowment. UK, **PI.**
- 12. **2005-2010.** "Imaging immune response in the eye". £125,000. <u>Research Council UK</u> (<u>RCUK</u>) fellowship award.
- 13. **2003-2005**: £228,536 "Does the CD200-CD200 receptor interaction signal altered trafficking or survival of migrating myeloid macrophages and dendritic cells *in vivo* either in the basal state or during organ specific autoimmune inflammation". <u>The Wellcome Trust</u>. Co-holder with Prof. J Liversidge, Dr IJ Crane.

PUBLICATIONS & PRESENTATIONS

Refereed Papers:

- 1. <u>Xu H</u>, Chen M, Forrester JV, Lois N. Cataract surgery induces pro-inflammatory gene expression and protein secretion. *Invest Ophthalmol Vis Sci.* 2010. August 18. [Epub ahead of print].
- 2. Ganesan PB, He S, Xu H. Modelling of pulsatile blood flow in arterial trees of retinal

vasculature. *Medical Engineering Physics*. 2010. Oct 31. [Epub ahead of print].

- 3. Chen M, Muckerise E, Forrester JV, **Xu H**. Immune activation in retinal aging: a gene expression study. *Invest Ophthalmol Vis Sci*. 2010. 51(11):5888-5896.
- Chen M, Muckersie E, Forrester JV, <u>Xu H</u>. Inhibition of the alternative pathway of complement activation reduces inflammation in experimental autoimmune uveoretinitis. *Eur J Immunol*. 2010. 40: 2870-2881
- Motulsky E, Koch P, Janssens S, Liénart M, Vanbellinghen A, Bolaky N, Chan CC, Caspers L, Martin-Martinez M, <u>Xu H</u>, Delporte C, and Willermain F. Aquaporins expression on blood retinal barrier cells during experimental autoimmune uveitis. *Mol Vis*. 2010. Apri 3 ; 16 :602-10.
- 6. Ganesan PB, He S, <u>Xu H</u>. Analysis of retinal circulation using an image-based network model of retinal vasculature. *Microvasc Res.* 2010, 80(1):99-109.
- 7. Ganesan PB, He S, <u>Xu H</u>. Development of an image-based network model of retinal vasculature. *Ann Biomed Eng*. 2010,38(4):1566-85.
- 8. Forrester JV, **Xu H**, Kuffova L, McMenamin P, Dick AD. (Review) Dendritic cell physiology and function in the Eye. Immunol Rev. 2010. 234(1)282-304.
- 9. Copland DA, Hussain K, Baalasubramanian S, Hughes TR, Morgan BP, <u>Xu H</u>, Dick AD, Nicholson LB. Systemic and local anti-C5 therapy reduces the disease severity in experimental autoimmune uveoretinitis. *Clin Exp Immunol*. 2010. 159:303-314.
- 10. Xu H, Chen M, Forrester JV. (Review) Para-inflammation in the aging retina. *Prog Retin Eye Res.* 2009. 28(5):348-368.
- 11. Dagkalis A, Wallace C, <u>Xu H</u>, Liebau S, Manivannan A, Stone M, Mack M, Liversidge J, Crane IJ. Development of experimental autoimmune uveitis with efficient recruitment of monocytes is independent of CCR2. *Invest Ophthalmol Vis Sci*. 2009, 50(9):4288-4294.
- 12. Forrester JV, <u>Xu H</u>, Lambe T, Cornall R, (Review). Immune privilege or privileged immunity? *Muscosal Immunol.* 2008,1(5):372-381.
- Chen M, Muckersie E, Robertson M, Forrester JV, <u>Xu H</u>. Up-regulation of complement factor B in retinal pigment epithelial cells is accompanied by complement activation in the aged retina. *Exp Eye Res.* 2008, 87(6):543-440.
- Xu H, Koch P, Chen M, Lau A, Reid DM, Forrester JV. A Clinical grading system for retinal inflammation in the chronic model of experimental autoimmune uveoretinitis using digital fundus images. *Exp Eye Res*. 2008, 87(4):319-326.
- Chen M, Muckersie E, Roberston M, Fraczek M, Forrester JV, <u>Xu H</u>. Characterization of a mouse retinal pigment epithelial cell line: B6-RPE07. *Invest Ophthalmol Vis Sci.* 2008, 49(8):3699-3706.
- Xu H, Manivannan A, Crane IJ, Dawson R, Liversidge J. Critical but divergent roles for CD62L and CD44 in directing monocyte trafficking in vivo during inflammation. *Blood*. 2008, 112(4):1166-74.
- 17. Kezic J, **Xu H**, Chinnery HR, Murphy C, McMenamin PG. Retinal microglia and uveal tract dendritic cells and macrophages are not CX3CR1 dependent in their homing and distribution. *Invest Ophthalmol Vis Sci.* 2008. 49;1599-608.
- Xu H, Chen M, Manivannan A, Lois N, Forrester JV. Age-dependent accumulation of lipofuscin in perivascular and subretinal microglia in experimental mice. *Aging Cell.* 2008. 7; 58-68.
- 19. Xu H, Chen M, Mayer EJ, Forrester JV, Dick AD. Turnover of retinal microglia in adult experimental mouse. *GLIA*. 2007. 55; 1189-98.
- Xu H, Cheng CL, Chen M, Manivannan A, Cabay L, Pertwee RG, Coutts A, Forrester JV. Anti-inflammatory property of the cannabinoid receptor-2-selective agonist JWH-133 in a rodent model of autoimmune uveoretinitis. J Leukoc Biol. 2007. 82; 532-541.
- 21. Xu H, Chen M, Reid D, Forrester JV. LYVE positive macrophages are present in normal murine eyes. *Invest Ophthalmol Vis. Sci.* 2007. 48: 2162-71.
- 22. Xu H, Dawson R, Forrester JV and Liversidge J. Identification of novel dendritic cell

populations in mouse retina. Invest Ophthalmol Vis. Sci. 2007. 48:1701-10.

- 23. Chen M, Forrester JV, <u>Xu H</u>. Synthesis of complement factor H in RPE cells is down-regulated by oxidized photoreceptor outer segment. *Exp Eye Res*. 2007. 84: 635-45.
- 24. Crane IJ, **Xu H**, Wallance C, Manivannan A, Mack M, Liversidge J, Marquez G, Sharp PF, Forrester JV. Involvement of CCR5 in the passage of Th1-type cells across the bloodretina barrier in experimental autoimmune uveitis. *J Leukoc Biol*. 2006. 79:435-45. (C.J.I. and X.H. shared first author)
- 25. Xu H, Manivannan A, Dawson R, Crane IJ, Mack M, Sharp P and Liversidge J. Differentiation to the CCR2+ Inflammatory Phenotype In Vivo Is a Constitutive, Time-Limited Property of Blood Monocytes and Is Independent of Local Inflammatory Mediators. J Immunol. 2005. 175:6915-23.
- 26. Xu H, Kurihara H, Ito T, Kikuchi H, Yoshida K, Yamanokuchi H, Asari A. The keratan sulfate disaccharide gal(6S03) b1,4 glcNAc(6S03) modulates IL12 production by macrophages in murine Thy-1 type autoimmune disease. J Biol. Chem. 2005. 280:20879-86
- 27. Xu H, Dawson R, Crane IJ and Liversidge J. Leukocyte diapedesis in vivo induces transient loss of tight junction proteins at the blood-retina barrier. *Invest Ophthalmol Vis. Sci.* 2005. 46:2487-94.
- Sharp FP, Manivannan A, <u>Xu H</u>, Forrester JV. (Review) The scanning laser ophthalmoloscope—a review of its role in bioscience and medicine. *Phys. Med. Biol*. 2004 (49) 1085-1096.
- 29. **Xu H**, Manivannan A, Jiang H-R, Liversidge J, Sharp PF, Forrester JV, and Crane IJ: Recruitment of IFN_γ-producing cells into the inflamed retina in vivo is preferentially regulated by P-selectin glycoprotein ligand 1:P/E-Selectin interactions. *J. Immunol.* 2004, 172:3215-3224.
- Xu H, Manivannan A, Goatman K, Jiang H-R, Liversidge J, Sharp PF, Forrester JV, and Crane IJ: Reduction in Shear Stress, Activation of the Endothelium and Leukocyte Priming are all required for Leukocyte Passage across the Blood-Retina Barrier. J Leukocl. Biol. 2004, 75: 224-232.
- 31. **Xu H**, Manivannan A, Liversidge J, Sharp PF, Forrester JV, and Crane IJ. Requirements for passage of T lymphocytes across non-inflamed retinal microvessels. *J. Neuroimmunol*. 2003, 142: 47-57.
- 32. Crane IJ, Xu H, Manivannan A, McKillop-Smith S, Lamont G, Wallace C, Liversidge J, Sharp PF, Forrester JV. Effect of anti-macrophage inflammatory protein-1 on leukocyte trafficking and disease progression in experimental autoimmune uveoretinitis. *Eur. J. Immunol.* 2003, 27: 402-410 (C.J.I. and X.H. shared first author)
- 33. Xu H, Forrester JV, Liversidge J, and Crane IJ. Leukocyte trafficking in experimental autoimmune uveitis: Breakdown of blood-retinal-barrier and up-regulation of cellular adhesion molecules. *Invest Ophthalmol Vis Sci.* 2003, 44: 226-234.
- 34. Rosenbaum JT, Planck SR, Crane IJ, <u>Xu H</u>, Martin TM, and Forrester JV. (Review) Imaging ocular immune responses by intravital microscopy (Review). *Int. Rev. Immunol.* 2002,21(2-3):255-272.
- Xu H, Manivannan A, Liversidge J, Sharp P, Forrester JV, and Crane IJ. Involvement of CD44 in leukocyte trafficking at the blood retinal barrier. J. Leukocl. Biol. 2002, 72: 1133-1141.
- 36. Jiang H-R, Muckersie E, Robertson M, <u>Xu H</u>, Liversidge J and Forrester JV. Secretion of interleukin-10 or interleukin-12 by LPS activated dendritic cells is critically dependent on time of stimulus relative to initiation of purified DC culture. *J. Leukol. Biol.* 2002, 72: 978-985.
- 37. **Xu H**, Manivannan A, Goatman K, Liversidge J, Sharp PF, Forrester JV, and Crane IJ: Improved leukocyte tracking in mouse retinal and choroidal circulation. *Exp Eye Res*. 2002, 74:403-410.
- 38. <u>Xu H</u>, Ito T, Tawada A, Maeda H, Hiroko Yamanokuchi H, Kyoko Isahara, Keiichi Yoshida, Yasuo Uchiyama, and Akira Asari. Effect of hyaluronan oligosaccharides on the expression

of heat shock protein 72. J. Biol. Chem. 2002, 277 (19):17308-17314.

- 39. Xu H, Manivannan A, Garry D, Liversidge J, Sharp PF, Forrester JV, and Crane IJ: Evaluation of leukocyte dynamic in mouse retinal circulation with scanning laser ophthalmoloscopy (Video report). *Br. J Ophthalmol.* 2001, July, available at http://bjo.bmjjournals.com/cgi/content/full/85/7/DC1
- 40. Xu H, Kurihara H, Ito T, Nakajima SI, Hagiwara E, Yamanokuchi H, Asari A. IL-12 Enhances Lymphoaccumulation by Suppressing Cell Death of T Cells in MRL- lpr/lpr Mice. *J Autoimmun*. 2001, 16(2):87-95.

Books & Chapters

- 1. **(2010)** Xu H, Liversidge J. "Quantitative in site analysis of claudin expression at the blood-retinal barrier" in "Claudins: Methods and Protocols". Kursad Turksen (Editor). Springer. (In press).
- 2. (2009) Xu H, Forrester JV. Chapter 7 "Inflammation in age-related macular degeneration: what is the evidence?" in "Essentials in Ophthalmology". Uwe Pleyer and John V Forrester (Editors). Springer. Pages 61-71.
- 3. **(2009)** Xu H. Chapter "Lipofuscin and aurofluorescence in experimental models". In "Fundus Autofluorescence". Dr Noemi Lois and JV Forrester (Editors). Lippincott. Pages 38-47.
- 4. **(2002)** Xu H, Asari A. HA oligosaccharides accelerate heat shock protein 72 expression. In "Hyauluronan (Vol 1): Biochemical and Biological Aspect" P435-446. Kennedy JF and Phillips GA, (Editors). Woodhead publishing Ltd.
- 5. **(1997)** Xu H and Wang CY. Chapter "Macular tumors". In "Macular diseases" p278-335. Nie AG and Chen S (Editors). Hunan Science & Technology Publishers. China.
- 6. **(1996) Xu H.** Chapter "Corneal surgery complications". In Ocular surgery complications: symptoms and managements". Wang CY (Editor). Human Science and Technology Publisher. China.

Invited presentations/lectures

1. Immune response and age-related macular degeneration. The Royal College of Ophthalmologists seminar: Benchside Spectrum of Translational Research in

Ophthalmology. Nov. 2010. London, UK

2. Innate immunity and retinal aging. XIX biennial Meeting of the Internatinal Society

for Eye Research (ISER 2010). July 2010. Montreal. Canada

- 3. In vivo imaging retinal inflammation in experimental autoimmune uveoretinitis. *European Association for Vision and Eye Research (EVER)*. Sept 30-Oct. 3, 2009. Portoroz. Slovenia.
- Macrophage and complement in EAU and retinal degeneration. 10th Congress of international Ocular Inflammation Society (IOIS). May 30-June 2 2009. Prague. Czech Republic.
- 5. Leukocyte trafficking at the neuroretina in patho-physiological condition. **European Frontiers in Ocular Pharmacology**. University of Catania, 4th December 2008. Italy.
- 6. Leukocyte trafficking at the blood retinal barrier. **Singapore National Eye Research Center.** Oct. 22, 2008. Singapore.
- 7. Para-inflammation in the ageing retina and in age-related retinal degeneration. **NHG Eye Institute International Ophthalmology Congress,** Oct. 23-25, 2008 Singapore.
- 8. Complement activation in retinal pigment epithelial cells. In Educational section of **World Ophthalmology Congress 2008.** Hong Kong, China.
- 9. Complment activation in the aging retina in physio-pathological conditions. 2008

Annual Meeting of European Association for Vision and Eye Research (EVER). Portoroz, Slovenia.

- 10. Leukocyte trafficking in the neuroretina in patho-physiological conditions. **2008 Annual Meeting of ARVO.** Fort Lauderdale, USA.
- 11. Leukocyte trafficking in experimental autoimmune uveoretinitis. **The 1st International Symposium on Uveitis in China.** Oct. 2007 GuangZhou, China.
- 12. Complement activation in the retina. **Aberdeen Inflammation & Immunity Theme Symposium.** 2007, Aberdeen.
- 13. Macrophage, complement and age-related macular degeneration. **Aberdeen Royal Infirmary, Eye Clinic.** 2007, Aberdeen.
- 14. Comparison of monocyte and T lymphocyte trafficking at the blood-retina barrier in vivo. **International Society of Neuroimmunology Congress**. Oct. 2006, Nagoya, Japan.

Other conference presentations

I have delivered over 40 oral/poster presentations in national and international conferences.