

Professor Gregory John Towers

During my PhD (1991-95) I studied HIV-1 transcription at the Institute of Cancer Research with Mary Collins (ICR) and David Latchman (UCL). (1995-98) I was a Post Doc at the National Institute of Medical Research with Jonathan Stoye where we cloned Fv1, the first intracellular anti-retroviral restriction factor. I moved to the Genethon gene therapy institute in France in 1998 to study how intracellular innate immunity impacts gene therapy vector tropism. I joined UCL in 2000 and have been funded by Wellcome Trust fellowships since 2002. I was awarded a chair at UCL in Molecular Virology in 2006. My research is funded by a Wellcome Trust Senior Fellowship and a Wellcome Trust Collaborator Award. Research goals are to understand how lentiviruses, such as HIV-1, infect cells, despite the highly evolved defensive intracellular innate immune system. We aim to use this knowledge to design novel therapeutics, improve the use of lentiviruses for gene therapy and to understand cell and viral biology and their evolution.

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<http://www.ucl.ac.uk/towers-lab>

Professional History

2006 Professor of Molecular Virology, Division of Infection and Immunity, UCL

2005-2020 Wellcome Trust Senior Biomedical Research Fellowship, renewed in 2010 and 2015, held at Division of Infection and Immunity UCL.

2002 Sabbatical at Columbia University, College of Physicians and Surgeons, New York, USA
lab of Prof Stephen P. Goff.

2001-2005 Wellcome Trust Research Career Development Fellowship "Investigation of the early post entry events of the retrovirus life cycle and mechanisms of retrovirus restriction" held at Division of Infection and Immunity UCL.

2000-2001 Senior Post Doctoral Research Fellow, Wohl Virion Centre, Lab Head Prof Robin Weiss, Dept of Immunology and Molecular Pathology, UCL. Investigation of the retroviral lifecycle and mechanisms of retrovirus restriction.

1998-1999 Staff Scientist, "Genethon" Gene Therapy Institute, Evry, France. Investigation of the retroviral lifecycle and mechanisms of retrovirus restriction by fluorescent microscopy and quantitative PCR.

1995-1997 Postdoctoral Research Fellow, National Institute of Medical Research, lab of Dr Jonathan Stoye. Identification of the retroviral restriction gene Fv1 and investigation of its mechanism of action.

Education

1991-1994 Ph.D. The control of Human Immunodeficiency Virus Type 1 promoter activity by retinoic acid. Chester Beatty Labs, Institute of Cancer Research, Dept of Cellular Biology (Dr M.K. Collins) and University College London, Dept of Molecular Pathology, (Prof D.S. Latchman).

1988-1991 University of Surrey. B.Sc.(hons) Biochemistry, First Class

1990 1 year Industrial Placement Smithkline Beecham, Harlow, Dept Drug Metabolism.

Current Grants

Wellcome Trust Senior Biomedical Research Fellowship 2nd Renewal "Characterisation of innate immune DNA sensing and viral evasion strategies" 1/10/15-30/09/20 £2,121,162

National Institute of Health Research Development of broad specificity anti-viral drugs 15/8/2016-14/8/2019 £199,555

Wellcome Trust Public Engagement Grant associated with SRF 1/10/2016-30/09/2020 £25,000

Wellcome Trust Collaborator Award with Coapplicants Leo James Laboratory of Molecular Biology Cambridge, David Selwood UCL, Till Boecking and David Jacques University of New South Wales, Australia. What is special about pandemic HIV-1? How lineage specific capsid variation determines DNA synthesis, innate immune detection and pandemic potential £2,518,982 1/3/19-28/2/2024

MRC Project Grant Characterisation and therapeutic manipulation of flaviviridae innate immune evasion £414571.44 1/5/2019-31/4/2022

Recent Grants

Wellcome Trust Large Arts Award “Capsid” co-applicant with artist John Walter 09/2016-12/2018 £157,525.

ERC Advanced Grant “Characterisation and Manipulation of Primate Lentiviral Innate Immune Evasion Strategies” PI with co-applicant Prof David Selwood, Wolfson Institute of Biomedical Sciences, UCL, Feb 2014-Jan 2019 €2,499,643

Sponsor of Independent Fellowships

Sir Henry Wellcome Fellowship to Lucy Thorne, “Defining Pathogen-sensing in Human Skin-derived Dendritic Cells” 2015-2019, £250,000

Wellcome Trust Clinical PhD Fellowship to Dr Douglas Fink “Vpx antagonism of DNA sensing in determining cross-species transmission and epidemic potential of primate lentiviruses” 1/9/16-30/8/16. £250,000

Wellcome Trust Clinical PhD Fellowship to Dr Robert Lever “Species specificity of the lentiviral Vpr protein” 2018-2021. £250,000

Expert Review

Wellcome Trust Pathogen Biology and Disease Transmission Expert Review Group 5, Member 2014-2016
Chair 2017-2019

Editorial Boards Journal of Virology and Retrovirology

Ongoing Ad hoc Wellcome Trust senior science interview panel member since 2014

F1000 faculty member (HIV Infection and AIDS, Basic Science)

18 PhD students examined. 11 National, 7 International.

Invited Conferences 2015-18

German Austrian AIDS society annual meeting, Dusseldorf Germany, invited speaker **2015**. Barts and the London 7th HIV Symposium, session chair **2015**. European Congress of Clinical Microbiology and Infectious Diseases, Amsterdam, Invited speaker **2016**. Barts and the London 8th HIV Symposium, Co-Organiser and session chair **2016**. British Society of Immunology Annual Meeting, Liverpool, Invited speaker and session chair, **2016**. UCL Infection, Immunity and Inflammation Symposium speaker **2017**. International AIDS Society Invited speaker, **2017**. College of Medicine and Veterinary Medicine University of Edinburgh, Annual meeting, Keynote talk **2017**. Coldspring Harbor Retroviruses meeting Session chair **2018**.

Invited Seminars 2015-2018

2015 University of Heidelberg, Germany; The Pirbright Institute Compton; Amos Bursary London, **2016** Trinity College Dublin; Dunn school, University of Oxford; St Georges University of London; Vita-Salute San Raffaele University, Milan; Architects Association London **2017** University of Oxford Weatherall Institute of Molecular Medicine **2018** Adam Neville Lecture University of Dundee; Institute of Child Health Great Ormond Street Hospital London; University of Glasgow Centre for Virus Research; Division of Structural Biology University of Oxford.

Teaching

I teach several lectures considering retroviruses and innate immunity at UCL. My lab hosts undergraduate intercalated B.Sc. students (6 months) and M.Sc. students (3 months) for lab projects. I have been primary supervisor for 7 and second supervisor for 6 completed PhD students. I am currently primary supervisor for 4 and secondary supervisor for 5 UCL PhD students.

Favourite Publications

<http://scholar.google.co.uk/citations?user=m2mpiBUAAAJ&hl=en>

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Fletcher AJ, Vaysburd M, Maslen S, Zeng J, Skehel JM, Towers GJ, James LC. 2018 Trivalent RING Assembly on Retroviral Capsids Activates TRIM5 Ubiquitination and Innate Immune Signaling. *Cell Host Microbe*. Dec 12;24(6):761-775.e6.

Cyclosporine H Overcomes Innate Immune Restrictions to Improve Lentiviral Transduction and Gene Editing In Human Hematopoietic Stem Cells. 2018 Petrillo C, Thorne LG, Unali G, Schirolli G, Giordano AMS, Piras F, Cuccovillo I, Petit SJ, Ahsan F, Noursadeghi M, Clare S, Genovese P, Gentner B, Naldini L, Towers GJ, Kajaste-Rudnitski A. *Cell Stem Cell*. Dec 6;23(6):820-832.e9.

Mlcochova P, Sutherland KA, Watters SA, Bertoli C, de Bruin RAM, Rehwinkel J, Neil SJ, Lenzi GM, Kim K, Khwaja A, Gage MC, Georgiou C, Chittka A, Yona S, Noursadeghi M, Towers GJ, Gupta RK. 2017. A G1-like state allows HIV-1 to bypass SAMHD1 restriction in macrophages. *EMBO J*. 36: 604-16

Jacques DA, McEwan WA, Hilditch L, Price AJ, Towers GJ, James LC. 2016. HIV-1 uses dynamic capsid pores to import nucleotides and fuel encapsidated DNA synthesis. *Nature*. 536: 349-53.

Fletcher AJ, Christensen DE, Nelson C, Tan CP, Schaller T, Lehner PJ, Sundquist WI, Towers GJ. 2015 TRIM5 α requires Ube2W to anchor Lys63-linked ubiquitin chains and restrict reverse transcription. *EMBO J*. 34: 2078-95

Rasaiyaah, J., C. P. Tan, A. J. Fletcher, A. J. Price, C. Blondeau, L. Hilditch, D. A. Jacques, D. L. Selwood, L. C. James, M. Noursadeghi* and G. J. Towers*. 2013. HIV-1 evades innate immune recognition through specific co-factor recruitment. *Nature*. 503: 402-5 *Corresponding Authors

Price, A. J., A. J. Fletcher, T. Schaller, T. Elliot, K. Lee, V. N. Kewalramani, J. Chin, G. J. Towers, and L. C. James. 2012. CPSF6 defines a conserved capsid interface that modulates HIV-1 replication. *PLoS Pathogens* 8:e1002896

Schaller, T., K. E. Ocwieja, J. Rasaiyaah, A. J. Price, T. L. Brady, S. L. Roth, S. Hue, A. J. Fletcher, K. Lee, V. N. Kewalramani, M. Noursadeghi, R. G. Jenner, L. C. James, F. D. Bushman, and G. J. Towers. 2011. HIV-1 Capsid-Cyclophilin Interactions Determine Nuclear Import Pathway, Integration Targeting and Replication Efficiency. *PLoS Pathogens* 7:e1002439

Hué S, Gray ER, Gall A, Katzourakis A, Tan CP, Houldcroft CJ, McLaren S, Pillay D, Futreal A, Garson JA, Pybus OG, Kellam P, Towers GJ. 2010. Disease-associated XMRV sequences are consistent with laboratory contamination. *Retrovirology* 7:111.

Ylinen, L. M., Price, A. J., Rasaiyaah, J., Hue, S., Rose, N. J., Marzetta, F., James, L. C. & Towers, G. J. 2010. Conformational Adaptation of Asian Macaque TRIMCyp Directs Lineage Specific Antiviral Activity. *PLoS Pathogens* 6: e1001062

Gupta, K. R., S. Hué, T. Schaller, E. Verschoor, D. Pillay and G. J. Towers. 2009. Mutation of a single residue renders human tetherin resistant to HIV-1 Vpu-mediated depletion. *PLoS Pathogens* 5:e1000443

Wilson, S. J., Webb, B. L. J, Ylinen, L. M. J., Verschoor, E., Heeney, J. L., and G. J. Towers. 2008 Independent evolution of an antiviral TRIMCyp in Rhesus Macaques *Proc Natl Acad Sci USA*. 105: 35507-62

Keckesova, Z., Ylinen, L. M. J. Towers, G. J. 2004. The human and African green monkey TRIM5 α genes encode Ref1 and Lv1 retroviral restriction factor activities. *Proc Natl Acad Sci USA* 101: 10780-5

Towers, G. J., Hatzioannou, T., Cowan, S., Goff, S. P., Luban, J., and Bieniasz, P. D. 2003. Cyclophilin modulates the sensitivity of HIV-1 to host restriction factors. *Nature Med* 9: 1138-43

Best, S., Le Tissier, P., Towers, G, Stoye, J. P. 1996. Positional cloning of the mouse retrovirus restriction gene Fv1. *Nature* 382: 826-829