

CURRICULUM VITAE

Name: **Graham Simmons**
Position: Associate Investigator
 Blood Systems Research Institute
 Assistant Professor (Adjunct)
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EDUCATION:

1988-91	University of Warwick, United Kingdom	B.Sc	Microbiology
1992-94	King’s College London, United Kingdom	M.Sc (Distinction)	Immunology
1995-2000	Institute of Cancer Research, University of London, United Kingdom (Advisors: Robin Weiss, Paul Clapham)	Ph.D.	Molecular Virology

PRINCIPAL POSITIONS HELD:

1999-2000	University College London, UK	Research Fellow	Wohl Research Centre
2000-2002	University of Pennsylvania, PA	Post-doctoral fellow	Microbiology
2002-2005	University of Pennsylvania, PA	Research Associate	Microbiology
2006-Present	Blood Systems Research Institute	Associate Investigator	

OTHER POSITIONS HELD CONCURRENTLY:

2007-Present University of California, San Francisco Assistant Professor (Adjunct)

KEYWORDS/AREAS OF INTEREST:

Emerging Viruses, Blood Transfusion, Viral Entry, Viral Receptors, Chikungunya, SARS-CoV, HIV, HCV, Ebolavirus, Glycoproteins

PROFESSIONAL ACTIVITIES

PROFESSIONAL ORGANIZATIONS

Memberships

American Society of Virology
American Association of Blood Banks
American Society for Microbiology

SERVICE TO PROFESSIONAL PUBLICATIONS:

1998-2010 Ad hoc reviewer for AIDS, Lancet, Journal of Virology, Virology, Transfusion, PLOS pathogens, PLOS One, Blood

INVITED PRESENTATIONS

FASEB conference, Chemokines and Lipid Mediators, Vermont, 2000 (Invited plenary speaker)
Keystone Symposia, Cytokines and Disease, Utah, 2000 (Invited plenary speaker)
Pathological Mechanisms of H5N1 influenza, Shantou, China, 2006 (Invited speaker)
Food and Drug Administration, Blood Products Advisory Committee, July 2010 (Invited speaker)
America's Blood Centers Interim Meeting, 2010 (Invited speaker)

OTHER INVITED PRESENTATIONS

1999 Heinrich-Pette Institut, Hamburg, Germany (Invited Speaker)
2005 University of Erlangen, Erlangen, Germany (Invited Speaker)
2010 CaridianBCT Emerging Pathogens Workshop (Invited Speaker)

OTHER PRESENTATIONS

European Community Experimental AIDS Research Conference, France, 1995 (Selected speaker)
European Union Concerted Action on HIV, Germany, 1996, (Selected speaker)
International workshop on HIV and cells of macrophage lineage, Italy, 1996 (Selected speaker)
Cold Spring Harbor, Retrovirology Conference, New York, 1998 (Selected speaker)
American Society for Virology, Wisconsin, 2001 (Selected speaker)
Keystone Symposia, Bioterrorism and emerging infectious agents, Colorado, 2004 (Selected speaker)
American Society for Virology, Penn State, 2005 (Selected speaker)
International Nidovirus Symposium, Colorado, 2005 (Selected speaker)
Regional centers of excellence for biodefense, Texas, 2005 (Selected speaker)

GOVERNMENT and OTHER PROFESSIONAL SERVICE

NIAID Special Emphasis Panel, ZAI1 ESB-M Biodefense Therapeutics, Feb 11-13, 2008
NIAID Special Emphasis Panel, ZAI1-DDS-M-J1 Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases, Sep 22-24, 2008
NIAID Special Emphasis Panel, ZAI1 AR-M (C2) Application of Platform Technologies for the Development of Therapeutics for Biodefense, Oct 16-17, 2008

NIAID Special Emphasis Panel, ZAI1 FDS - M(M1) Partnerships for Biodefense Viral Pathogens (Part I), Jan 29, 2010
NIH Special Emphasis Panel, ZRG1 F13-C (20) L Fellowships: Infectious Diseases and Microbiology, July 12-13, 2010

UNIVERSITY SERVICE

UCSF CAMPUS-WIDE

Reviewer - UCSF-GIVI Center for AIDS Research Pilot and Basic Science Awards, Nov 2006
Reviewer - UCSF-GIVI Center for AIDS Research Pilot and Basic Science Awards, Apr 2010

RESEARCH AND CREATIVE ACTIVITIES

RESEARCH AWARDS AND GRANTS

ACTIVE

5R01AI74986 (Simmons)

12/15/07-11/30/12

NIH/NIAID

Modeling viral entry and its inhibition using SARS-CoV

We aim to elucidate the mechanisms by which enveloped viruses, such as SARS-CoV, mediate membrane fusion during the process of entry, seek inhibitors of entry through targeted and general screening of compound libraries, and identify novel targets for the development of new antivirals.

Role: PI

HHSN272200900055C (Doranz)

9/30/09-9/29/14

NIH/NIAID

B Cell Epitope Discovery and Mechanisms of Antibody Protection

The primary objective of the study is to discover and characterize B cell epitopes on the surface of enveloped viral pathogens, and to determine their contribution to humeral protection or viral pathogenesis.

Role: Subcontract PI

N01 HB-057181 (Busch)

03/15/05 - 08/31/10

NIH/NHLBI

Retrovirus Epidemiology Donor Study (REDS) - II Central Laboratory

BSRI will establish and maintain a central laboratory for all REDS specimen testing. Specific project for the development of analytical and clinical panels for the study of XMRV in whole blood.

Role: Co-Investigator

Investigator Support (Simmons)

1/1/09-onward

Blood Systems, Inc.

Viral Entry

General support for investigators to run a laboratory. Utilized for equipment, salaries and consumables to further work characterizing the determinants of viral entry and attachment.

Role: PI

U19 AI088790 (McCune)

4/1/10-3/31/15

NIH

(Years 3 to 5 only)

Bay Area Hepatitis C Cooperative Research Center

The goals of this Center are to define the biology of the innate and adaptive immune responses to HCV in the setting of chronic infection, to understand how these responses are modulated by treatment, and to discern which parameters of the immune response are associated with (and possibly predictive of) an effective antiviral response to therapy.

Role: Project 2 Consortium Co-PI.

PAST

1. U54 AI057168 (Career Development Award recipient) 3/1/04-2/28/07
NIH
Hemorrhagic Fever and emerging viruses
2. R21 AI053653-01 (Co-Investigator; PI: H Shen) 9/1/02-8/31/04
NIH/NIAID
Modulation of T cell responses by Ebola Glycoprotein
3. Long-term EMBO Fellowship award ALTF-236-2001 7/1/01-7/31/02
EMBO
Ebola virus glycoprotein mediates changes in cell morphology: a potential role in immune evasion

PEER REVIEWED PUBLICATIONS:

1. **Simmons G**, McKnight A, Takeuchi Y, Hoshino H, Clapham PR. Cell-to-cell fusion, but not virus entry in macrophages by T-cell line tropic HIV-1 strains: a V3 loop-determined restriction. *Virology* (1995) 209:696-700.
2. **Simmons G**, Wilkinson D, Reeves J, Dittmar MT, Beddows S, Weber J, Carnegie G, Desselberger U, Gray PW, Weiss RA, Clapham PR. Primary, syncytium-inducing human immunodeficiency virus type 1 isolates are dual-tropic and most can use Lestr or CCR5 as coreceptors for virus entry. *J. Virol.* (1996) 70:8355-60.
3. McKnight A, Shotton C, Cordell J, Jones I, **Simmons G**, Clapham P. Location, exposure, and conservation of neutralizing and nonneutralizing epitopes on HIV-2 SU glycoprotein. *J Virol.* (1996) 70:4598-606.
4. **Simmons G**, Clapham P, Picard L, Offord R, Rosenkilde M, Schwartz T, Buser R, Wells T, Proudfoot A. Potent inhibition of HIV-1 infectivity by a novel CCR5 antagonist. *Science* (1997) 276:276-279.
5. Dittmar MT, McKnight A, **Simmons G**, Clapham PR, Weiss RA, Simmonds P. HIV-1 tropism and co-receptor use. *Nature* (1997) 385:495-496.
6. Dittmar MT, **Simmons G**, Hibbitts S, O'Hare M, Louisirirochanakul S, Beddows S, Weber J, Clapham PR, Weiss RA. Langerhans cell tropism of human immunodeficiency virus type 1 subtype A through F isolates derived from different transmission groups. *J. Virol.* (1997) 71:8008-8013.

7. Dittmar MT, **Simmons G**, Donaldson Y, Simmonds P, Clapham PR, Schulz TF, Weiss RA. Biological characterization of human immunodeficiency virus type 1 clones derived from different organs of an AIDS patient by long-range PCR. *J Virol.* (1997) 71:5140-5147.
8. Kledal TN, Rosenkilde MM, Coulin F, **Simmons G**, Johnsen AH, Alouani S, Power CA, Lutichau HR, Gerstoft J, Clapham PR, Clark-Lewis I, Wells TNC, Schwartz TW. A broad-spectrum chemokine antagonist encoded by Kaposi's sarcoma-associated herpesvirus. *Science* (1997) 277:1656-1659.
9. McKnight A, Wilkinson D, **Simmons G**, Talbot SJ, Picard L, Ahuja M, Marsh M, Hoxie JA, Clapham PR. Inhibition of human immunodeficiency virus fusion by a monoclonal antibody to a coreceptor (CXCR4) is both cell type and virus strain dependent. *J Virol.* (1997) 71:1692-1696.
10. Picard L, **Simmons G**, Power CA, Meyer A, Weiss RA, Clapham PR. Multiple extracellular domains of CCR-5 contribute to human immunodeficiency virus type 1 entry and fusion. *J Virol.* (1997) 71:5003-5011.
11. Reeves JD, McKnight A, Potempa S, **Simmons G**, Gray PW, Power CA, Wells TNC, Weiss RA, Talbot SJ. CD4-independent infection by HIV-2 (ROD/B): use of the 7-transmembrane receptors CXCR-4, CCR-3, and V28 for entry. *Virology.* (1997) 231:130-134.
12. **Simmons G**, Reeves JD, McKnight A, Dejuq N, Hibbitts S, Power CA, Aarons E, Schols D, De Clercq E, Proudfoot AE, Clapham PR. CXCR4 as a functional coreceptor for human immunodeficiency virus type 1 infection of primary macrophages. *J. Virol.* (1998) 72:8453-8457.
13. Mack M, Luckow B, Nelson PJ, Cihak J, **Simmons G**, Clapham PR, Signoret N, Marsh M, Stangassinger M, Borlat F, Wells TN, Schlondorff D, Proudfoot AE. Aminooxypentane-RANTES induces CCR5 internalization but inhibits recycling: a novel inhibitory of HIV infectivity. *J. Exp. Med.* (1998) 187:1215-1224.
14. Dejuq N, **Simmons G**, Clapham P. Expanded tropism of primary HIV-1 R5 strains to CD4(+) T-cell lines determined by the capacity to exploit low concentrations of CCR5. *J. Virol.* (1999) 73:7842-7.
15. Clapham PR, Reeves JD, **Simmons G**, Dejuq N, Hibbitts S, McKnight A. HIV coreceptors, cell tropism and inhibition by chemokine receptor ligands. *Mol Membr Biol.* (1999) 16:49-55.
16. Hibbitts S, Reeves JD, **Simmons G**, Gray PW, Epstein LG, Schols D, de Clercq E, Wells TNC, Proudfoot AEI, Clapham PR. Coreceptor ligand inhibition of fetal brain cell infection by HIV type 1. *AIDS Res Hum Retroviruses* (1999) 15:989-1000.
17. Reeves JD, Hibbitts S, **Simmons G**, McKnight A, Azevedo-Pereira JM, Moniz-Pereira J, Clapham PR. Primary HIV-2 Isolates Infect CD4- Negative Cells via CCR5 and CXCR4: Comparison with HIV-1 and SIV and Relevance to Cell Tropism In Vivo. *J Virol.* (1999) 73:7795-804.
18. Dejuq N, **Simmons G**, Clapham PR. T-cell line adaptation of human immunodeficiency virus type 1 strain SF162: effects on envelope, vpu and macrophage-tropism. *J. Gen. Virol.* (2000) 81:2899-2904.
19. Sabroe I, Peck MJ, Van Keulen BJ, Jorritsma A, **Simmons G**, Clapham PR, Williams TJ, Pease JE. A Small Molecule Antagonist of Chemokine Receptors CCR1 and CCR3. Potent inhibition of eosinophil function and CCR3-mediated HIV-1 entry. *J Biol Chem.* (2000) 275:25985-25992.
20. Stine JT, Wood C, Raport C, Epp A, Schweickart V, Endo Y, **Simmons G**, Boshoff C, Clapham PR, Chang Y, Moore P, Gray PW, Chantray D. The Kaposi's sarcoma-associated herpesvirus chemokine vMIP-III is a functional ligand for CCR4 and a selective chemoattractant for TH2 cells. *Blood* (2000) 95:1151-1157.
21. Elser J, Mack M, Bruh H, Dulk Y, Peter H, Kimmig D, **Simmons G**, Clapham P, Schlond D, Wells T, Proudfoot A. Differential activation of chemokine receptors by AOP-RANTES. *J Biol Chem* (2000) 275:7787-94.
22. Blanpain C, Buser R, Power CA, Edgerton M, Buchanan C, Mack M, **Simmons G**, Clapham PR, Parmentier M, Proudfoot AE. A chimeric MIP-1alpha/RANTES protein demonstrates the use of different regions of the RANTES protein to bind and activate its receptors. *J Leukoc Biol.* (2001) 69:977-985.

23. Vyakarnam A, Eyeson J, Teo I, Zuckerman M, Babaahmady K, Schuitemaker H, Shaunak S, Rostron T, Jones S, **Simmons G**, Clapham P. Evidence for a post-entry barrier to R5 HIV-1 infection of CD4 memory T cells. *AIDS*. (2001) 15:1613-26.
24. **Simmons G**, Wool-Lewis RJ, Baribaud F, Netter RC, Bates P. Ebola virus glycoproteins induce global surface protein down-modulation and loss of cell adherence. *J Virol*. (2002) 76:2518-2528.
25. **Simmons G**, Reeves, JD, Grogan CC, Vandenberghe JH, Baribaud F, Whitbeck JC, Burke E, Buchmeier MJ, Soilleux EJ, Riley J, Doms RW, Bates P, Pöhlmann S. DC-SIGN and DC-SIGNR bind Ebola glycoproteins and enhance infection of macrophages and endothelial cells. *Virology*. (2003) 305:115-123.
26. Lin G, **Simmons G**, Pöhlmann S, Baribaud F, Ni H, Leslie GJ, Haggarty BS, Bates P, Weissman D, Hoxie JA, Doms RW. Differential N-Linked glycosylation of Human Immunodeficiency Virus and Ebola Virus envelope glycoproteins modulates interactions with DC-SIGN and DC-SIGNR *J Virol*. (2003). 77:1337-1346.
27. **Simmons G**, Rennekamp A, Chai N, Vandenberghe LH, Riley JL, Bates P. Filoviruses do not require Folate receptor alpha for efficient entry. *J Virol*. (2003) 77:13433-13438.
28. **Simmons G**, Lee A, Rennekamp AJ, Fan X, Bates P, Shen H. Identification of murine T-cell epitopes in Ebola virus Nucleoprotein. *Virology*. (2004) 318:224-230.
29. **Simmons G**, Reeves J, Rennekamp A, Amberg S, Piefer A, Bates P. Characterization of severe acute respiratory syndrome-associated coronavirus spike protein mediated viral entry. *PNAS* (2004) 101:4240-5.
30. Marzi A, Gramberg T, **Simmons G**, Möller P, Rennekamp AJ, Krumbiegel M, Geier M, Eisemann J, Turza N, Saunier B, Steinkasserer A, Becker S, Bates P, Hofmann H, Pöhlmann S. DC-SIGN and DC-SIGNR interact with the glycoprotein of Marburg virus and the S protein of severe acute respiratory syndrome coronavirus. *J Virol*. (2004) 78:12090-12095.
31. Temperton NJ, Chan PK, **Simmons G**, Zambon MC, Tedder RS, Takeuchi Y, Weiss RA. Longitudinally profiling neutralizing antibody response to SARS Coronavirus with pseudotypes. *Emerg Infect Dis*. (2005) 11:411-416.
32. **Simmons G**, Gosalia DN, Rennekamp AJ, Reeves JR, Diamond SL, Bates P. Inhibitors of cathepsin L prevent SARS coronavirus entry. *PNAS*. (2005) 102:11876-11881.
33. Amberg SM, Netter RC, **Simmons G**, Bates P. Expanded tropism and altered activation of a retroviral glycoprotein resistant to an entry inhibitor peptide. *J Virol*. (2006) 80:353-359.
34. Qiu Z, Hingley ST, **Simmons G**, Yu C, Das Sarma J, Bates P, Weiss SR. Endosomal proteolysis by cathepsins is necessary for murine coronavirus mouse hepatitis virus type 2 spike-mediated entry. *J Virol*. (2006) 80:5768-5776.
35. Marzi A, Akhavan A, **Simmons G**, Gramberg T, Hofmann H, Bates P, Lingappa VR, Pöhlmann S. The signal peptide of the ebolavirus glycoprotein influences interaction with the cellular lectins DC-SIGN and DC-SIGNR. *J Virol*. (2006) 80:6305-6317.
36. Hofmann H, **Simmons G**, Rennekamp AJ, Chaipan C, Gramberg T, Heck E, Geier M, Wegele A, Marzi A, Bates P, Pöhlmann S. Highly Conserved Regions within the Spike Proteins of Human Coronaviruses 229E and NL63 Determine Recognition of Their Respective Cellular Receptors. *J Virol*. (2006) 80:8639-8652.
37. Kaletsky RL, **Simmons G**, Bates P. Proteolysis of the Ebola glycoproteins enhances virus binding and infectivity. *J Virol*. (2007) 81:13378-84
38. Salvador B, Zhou Y, Michault A, Muench MO, **Simmons G**. Characterization of Chikungunya pseudotyped viruses: Identification of refractory cell lines and demonstration of cellular tropism differences mediated by mutations in E1 glycoprotein. *Virology*. (2009) 393:33-41. PMID: 19692105
39. Chaipan C, Steffen I, Solomon Tsegaye T, Bertram S, Glowacka I, Kato Y, Schmokel J, Munch J, **Simmons G**, Gerardy-Schahn R, Pöhlmann S. Incorporation of podoplanin into HIV released from HEK-293T cells, but not PBMC, is required for efficient binding to the attachment factor CLEC-2. *Retrovirology*. (2010) 7:47. PMID: 20482880

40. Glowacka I, Bertram S, Herzog P, Pfefferle S, Steffen I, Muench MO, **Simmons G**, Hofmann H, Kuri T, Weber F, Eichler J, Drosten C, Pöhlmann S. Differential downregulation of ACE2 by the spike proteins of severe acute respiratory syndrome coronavirus and human coronavirus NL63. *J Virol.* (2010) 84:1198-205. PMID: 19864379
41. Switzer WM, Jial H, Hohn O, Zheng HQ, Tang S, Shankar A, Bannert N, **Simmons G**, Hendry RM, Falkenberg VR, Reeves WC, Heneine W. Absence of Evidence of Xenotropic Murine Leukemia Virus related Virus Infection in Persons with Chronic Fatigue Syndrome and Healthy Controls in the United States. *Retrovirology* (2010) 7:57. PMID: 20594299
42. Zhou Y, Lu K, Pfefferle S, Bertram S, Glowacka I, Drosten C, Pöhlmann S, **Simmons G**. A Single Asparagine-Linked Glycosylation Site of the SARS-Coronavirus Spike Glycoprotein Facilitates Inhibition by Mannose-Binding Lectin through Multiple Mechanisms. *J Virol* (2010) (Epub). PMID: 20573835
43. **Simmons G**, Bertram S, Glowacka I, Steffen I, Chaipan C, Agudelo J, Lu K, Rennekamp AJ, Hofmann H, Bates P, Pöhlmann S. Proteolytic activation of the SARS-coronavirus spike-protein: Evidence for an alternative cleavage site and for activation of cell-cell and virus-cell fusion by different host cell proteases. (2010). Submitted.

NON-PEER REVIEWED PUBLICATIONS:

1. Clapham PR, McKnight A, **Simmons G**, Weiss RA. Is CD4 sufficient for HIV entry? Cell surface molecules involved in HIV infection. *Philos Trans R Soc Lond B Biol Sci.* (1993) 342:67-73.
2. Reeves JD, and **Simmons G**. Chemokine inhibition of HIV infection, *Method Mol Biol.* (2000) 138:209-2.
3. **Simmons G**, Reeves JD, Hibbitts S, Stine JT, Gray PW, Proudfoot AEI, Clapham PR. Co-receptor use by HIV and inhibition of HIV infection by chemokine receptor ligands. *Immunol Rev.* (2000) 177:112-126.
4. **Simmons G**, Rennekamp AJ, Bates P. Proteolysis of SARS-associated coronavirus spike glycoprotein. *Adv Exp Med Biol.* (2006) 581:235-40.
5. Selvarajah S, Tobler LH, **Simmons G**, Busch MP. Host genetic basis for hepatitis C virus clearance: a role for blood collection centers. *Current Opinion in Hematology.* (2010). In Press.