

BIOGRAPHICAL SKETCH

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NAME Higgs, Stephen	POSITION TITLE Professor		
eRA COMMONS USER NAME sthiggs			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
King's College, London University, UK	B.Sc. (Honors)	1980	Zoology
Reading University, Reading, England UK	Ph.D.	1985	Parasitology

A. Positions and Honors

Professional Experience

- 1983 **Lecturer**, North East Surrey College of Technology.
- 1986-1988 **Postdoctoral Research Fellow**, London School of Hygiene and Tropical Medicine, London University.
- 1988-1991 **Higher Scientific Officer**, Natural Environment Research Council's Institute of Virology and Environmental Microbiology, Oxford, UK.
- 1991-1992 **Research Associate**, Arthropod-Borne and Infectious Diseases Laboratory (AIDL), Colorado State University (CSU).
- 1992-2000 **Assistant Professor (and Assistant Director for Laboratory Sciences)**, AIDL, CSU.
- 2000-2006 **Associate Professor**, Dept. of Pathology, UTMB, Galveston, Texas
- 2006-present **Professor**, Dept. of Pathology, UTMB, Galveston, Texas

Selected Honors, Awards, and Fellowships

- 1989 Society for General Microbiology (President's Fund)
- 1992 Royal Entomological Society Fellowship
- 1999 American Society for Virology (Travel award)
- 2006 President, American Committee for Medical Entomology

B. Selected Publications (from 108)

1. Gould, E.A., Buckley, A., Cane, P.A., **Higgs, S.** & Cammack, N. 1989. Use of a monoclonal antibody specific for wild-type yellow fever virus to identify a wild-type antigenic variant in 17D vaccine pools. *J. Gen. Virol.* 70: 1889-1894.
2. Gould, E.A., Buckley, A., **Higgs, S.** & Gaidamovich, S. 1990. Antigenicity of flaviviruses. *Arch. Virol. Supplementum I*: 137-152
3. **Higgs, S.**, Powers, A.M., and Olson, K.E. 1993. Alphavirus expression systems: applications to mosquito vector studies. *Parasit. Today*, 9: 444-452.
4. Olson, K.E., **Higgs, S.**, Gaines, P.A., Powers, A.M., Davis, B.S., Kamrud, K.I., Carlson, J.O., Blair, C.D. & Beaty, B.J. 1996. Genetically engineered resistance in mosquitoes to dengue virus transmission. *Science*. 272: 884-886.
5. Edwards, J.F., **Higgs, S.** and Beaty, B.J. 1998. Mosquito feeding-induced potentiation of Cache Valley Virus (Bunyaviridae) in mice. *J. Med. Ent.* 35: 261-265.
6. Johnson, B.W., Olson, K.E., Allen-Muir, T., Rayms-Keller, A., Carlson, J.O., Coates, C.J., Jasinskiene, N.J., James, A.A., Beaty, B.J. & **Higgs, S.** 1999. Inhibition of luciferase expression in transgenic *Aedes aegypti* mosquitoes by Sindbis virus expression of antisense luciferase RNA. *PNAS*. 96: 13399 - 13403.
7. Limesand, K.H., **Higgs, S.**, Pearson, L.D., & Beaty, B.J. 2000. Potentiation of vesicular stomatitis New Jersey virus infection in mice by mosquito saliva. *Parasite Immunol.* 22: 461-467.
8. **Higgs, S.**, Snow, K. & Gould, E.A. 2004. The potential for West Nile virus to establish outside of its natural range: a consideration of potential mosquito vectors in the United Kingdom. *Trans. Roy. Soc. Trop. Med. Hyg.* 92: 82-87.
9. **Higgs, S.**, How do mosquito vectors live with their viruses? 2004. In: *Microbe-Vector Interactions in Vector-Borne Diseases*. Gillespie, S.H., Smith, G.L. & Osbourn, A. eds.). Cambridge University Press. pp 103-137

10. Vanlandingham, D.L., Schneider, B.S., Klingler, K., Fair, J., Beasley, D., Huang, J,H Hamilton, P., & **Higgs, S.** 2004. Real-time RT-PCR quantification of West Nile virus transmitted by *Culex pipiens quinquefasciatus*. *Am. J. Trop. Med. Hyg.* 71: 120-123
11. Girard, Y.A., Klingler, K.A. & **Higgs, S.** 2004. West Nile virus dissemination and tissue tropisms in orally-infected *Culex pipiens quinquefasciatus*. *Vector-borne & Zoonotic Diseases.* 4: 109-122.
12. Wanasen, N., Nussenzveig, R.H., Champagne, D.E., Soong, L. & **Higgs, S.** (2004). Differential modulation of murine host immune response by salivary gland extracts from the mosquitoes *Aedes aegypti* and *Culex quinquefasciatus* *J. Med. Vet. Entomol.* 18: 191-199.
13. Mutebi, J-P, Gianella, A., Travassos, A., Tesh, R.B., Barrett, A.D.T. & **Higgs, S.** 2004. Infectivity of yellow fever virus for Bolivian *Aedes aegypti* mosquitoes. *Emerging Inf. Dis.* 10: 1657-1660..
14. McElroy, K.L., Tsetsarkin, K.A., Vanlandingham, D.L. & **Higgs, S.** 2005.Characterization of yellow fever virus-mosquito interactions using an infectious clone of the wild-type Asibi virus. *J.G.Virol.* 86: 1747-1751.
15. Vanlandingham, D.L., Tsetsarkin, T., Hong, C., Klingler, K., Lehane, M.J. and **Higgs, S.** Development and characterization of a double subgenomic chikungunya virus infectious clone to express heterologous genes in *Aedes aegypti* mosquitoes. *Ins. Biochem. Mol. Biol.* 35: 1162-1170. 2005.
16. Schneider, BS, L Soong, NS Zeidner, Higgs, S.. *Aedes aegypti* Salivary Gland Extracts Modulate Anti-Viral and TH1/TH2 Cytokine Responses to Sindbis Virus Infection. *Vir. Immunol.* 17: 565-573. 2004.
17. **Higgs, S.**, Schneider, B.S., Vanlandingham, D.L., Klingler, K. & Gould, E.A. Non-viremic transmission of West Nile virus. *PNAS* 102: 8871-8874. 2005.
18. Schneider, B.S., Soong, Girard, Y.A., Campbell, G., Mason, P. and Higgs, S. Potentiation of West Nile Encephalitis by mosquito feeding. *Viral Immunology.* 19: 74-82. 2006.
19. Girard, Y.A., Popov, V., Wen, J., Ham, V. and **Higgs, S.** 2005. Ultrastructural study of West Nile virus pathogenesis in *Culex pipiens quinquefasciatus* (Diptera: Culicidae). *J. Med. Entomol.* 42: 429-444
20. McElroy, K.L., Tsetsarkin, K., Vanlandingham, D.L. and **Higgs, S.** Role of the Yellow Fever Virus Structural Protein Genes in Viral Dissemination from the *Aedes aegypti* Mosquito Midgut *J.Gen.Virol.* 87: 2993-3001 2006
21. **Higgs, S.**, Vanlandingham, D.L., Klingler, K.A., McElroy, K.L., McGee, C.E., Harrington, L., Lang, J., Monath, T.P. and Guirakhoo, F. Growth characteristics of ChimeriVax-DEN vaccine viruses in *Aedes aegypti* and *Aedes albopictus* from Thailand. *Am. J. Trop. Med. Hyg.* 75: 1158-1164 2006
22. Tsetsarkin, T., **Higgs, S.**, McGee, C.E., de Lamballerie, X., Charrel, R.N. & Vanlandingham, D.L. Infectious Clones of Chikungunya Virus (La Réunion Isolate) for Vector Competence Studies *Vector-Borne and Zoonotic Diseases* 6: 325-337 2006
23. McElroy, K.L., Tsetsarkin, K., Vanlandingham, D.L. and **Higgs, S.** Manipulation of the yellow fever virus non-structural genes 2A and 4B and the 3'non-coding region to evaluate genetic determinants of viral dissemination from the *Aedes aegypti* midgut. *Am. J. Trop. Med. Hyg.* 75, 1158-1164. 2006
24. Girard, Y., Schneider, B.S., McGee, C., Wen, J., Han, V., Popov, V., Mason, P., **Higgs, S.** Salivary gland morphology and virus transmission during long-term cytopathological West Nile virus infection in *Culex* mosquitoes. *Am. J. Trop. Med. Hyg.* 76. 118-128. 2007.
25. Schneider, B.S., McGee, C.E., Jordan, J.M., Stevenson, H.L., Soong, L. & **Higgs, S.** Prior exposure to uninfected mosquitoes enhances mortality in naturally-transmitted West Nile virus infection. *PLoS ONE* 2(11): e1171. doi:10.1371/journal.pone.0001171
26. Tsetsarkin, K.A., Vanlandingham, D.L., McGee., C.E. & **Higgs, S.** A single mutation in chikungunya virus affects vector specificity and epidemic potential. *PLoS PATHOGENS* 3(12): e201. doi:10.1371/journal.ppat.0030201
27. De-Lamballerie, X., Leroy, E., Charrel, R.N., Tsetsarkin, K., **Higgs, S.** & Gould, E.A. Chikungunya Virus Adapts to Tiger Mosquito via Evolutionary Convergence: a Sign of Things to Come ? *Virology Journal* 5:33doi:10.1186/1743-422X-5-33. 2008.
28. McGee, C.E.,Tsetsarkin, K., Vanlandingham, D.L., McElroy, K.L., Lang, J., Guy, B., Decelle, T. & **Higgs, S.** Substitution of wild-type yellow fever Asibi sequences for homologous 17D vaccine sequences in ChimeriVax™-Dengue 4 does not enhance infection of *Aedes aegypti* mosquitoes. *Journal of Infectious Diseases* 197: 686-692. 2008
30. McGee, C.E., Lewis, M.G., St. Claire, M., Wagner, W., Lang, J., Guy, B., Tsetsarkin, K., **Higgs, S.** & Decelle, T. Recombinant ChimeriVax™ dengue 4 with virulent yellow fever Asibi backbone sequences is dramatically attenuated in non-human primates. *J. Inf. Dis* 197: 693-697 2008
31. McGee, C.E., Shustov, A.V., Tsetsarkin, K., Frolov, I.V., Mason, P.W., Vanlandingham, D.L & **Higgs, S.**

Program Director/Principal Investigator (Last, First, Middle):

- Infection, Dissemination, and Transmission of a West Nile virus Green Fluorescent Protein Infectious Clone by *Culex pipiens quinquefasciatus* Mosquitoes. Vector- Borne and Zoonotic Diseases (in press).
32. Tsetsarkin, K., McGee, C., Volk, S., Vanlandingham, D., Weaver, S. & **Higgs, S.** Epistatic roles of E2 glycoprotein mutations in adaptation of chikungunya virus to *Aedes albopictus* and *Ae. aegypti* mosquitoes. PLoS.ONE (in press).
33. Sognat M., Gay B., **Higgs S.**, Briant L. & Devaux C. Replication cycle of Chikungunya: a reemerging arbovirus. Virology (in press).

C. Research Support During the Past Three Years

Current Support

National Institutes of Health: R21 AI073389 "Epidemic chikungunya virus: mosquito infection determinants"
PI: Stephen Higgs (20% effort)
08/05/07 – 08/04/10

Navigant Biotechnology

"Photochemical inactivation of chikungunya virus in Mirasol®- treated human plasma"
PI: Stephen Higgs (20% effort)
11/01/07 – 10/31/09

National Institutes of Health: RO1 AI067847 "West Nile Virus: Epidemiology and Mosquito Competence"

PI: Alan Barrett
Stephen Higgs (10% effort)
07/01/06-06/30/11

National Institutes of Health: U01 "Stable Micronized Vaccines Against Smallpox and Japanese Encephalitis"

PI: Stephen Higgs (15% effort) with Victor Bronshtein of Universal Stabilization Technologies.
To 8/31/09

Cerus Inc. "Chikungunya virus inactivation studies in platelet preparations"

PI: Stephen Higgs (10% effort)
2006-2009

"Developing coupled transgenic ribozymes and insecticide resistance approaches to establishing dengue virus refractoriness in natural *Aedes aegypti* populations"

Bill & Melinda Gates Foundation: Foundation for the National Institutes for Health
PI: Stephen Higgs (10% effort)
2006-2009

National Institutes of Health "GNL Insectaries Core E"

PI: Stephen Higgs (20% effort).
5/1/08-4/30/09.

Past/No Support

Centers for Disease Control and Prevention: "Fellowship Training in Vector-borne Infectious Diseases"

PI: Stephen Higgs (no salary)
06/15/03-09/29/07

Acambis Inc. "The production and evaluation of yellow fever vaccine viruses".

PI: Stephen Higgs (10% effort)
2005-2006

Program Director/Principal Investigator (Last, First, Middle):

Acambis Inc. "Evaluation of yellow fever vaccine viruses".
PI: Stephen Higgs (20% effort)
2004-2005

Sanofi-Pasteur. "Evaluation of wild type Asibi yellow fever virus sequences in vaccine viruses".
PI: Stephen Higgs (20% effort)
04/01/06-03-31/07

National Institutes of Health (R01 AI 47246): "Salivary potentiation of arboviral infections"
PI: Stephen Higgs (25% effort)
07/01/01 – 06/30/05

National Institutes of Health (R01 AI 47877): "Genetic determinants of epidemic alphavirus transmission"
PI: Stephen Higgs (15% effort)
08/01/00-07/31/03

Centers for Disease Control and Prevention: "Vector Competence for West Nile Virus of Mosquitoes Indigenous to East Texas"
PI: Stephen Higgs (15% effort)
09/29/01-09/30/04

National Institutes of Health: "Epidemiology of Yellow Fever in the Americas"
PI: Robert Tesh
06/01/01-05/31/06

NO1-AI 25489 (NIH/NIAID). "U.S. Based Collaboration in Emerging Viral and Prion Diseases".
R.B. Tesh, Program Director
Stephen Higgs supported from 2002-2005
09/30/02 – 09/29/09