

Timothy P. Sheahan, Ph.D.

Exploring the host pathogen interface to develop new methods for viral control

Contact

email sheahan@email.unc.edu

twitter @timothysheahan

phone 919-966-3809

Education

2003-2008 **Ph.D. Microbiology and Immunology.** *University of North Carolina, Department of Microbiology and Immunology, Chapel Hill, NC.*

Dissertation: "SARS-CoV Pathogenesis and Therapeutic Treatment Design"

1994-1999 **B.S. Microbiology/Water Resources.** *University of New Hampshire, Department of Microbiology, Department of Natural Resources, Durham, NH.*

Professional Experience

2015-Present **Research Assistant Professor.** *Department of Epidemiology, University of North Carolina, Chapel Hill, NC.*

2014-2015 **Investigator.** *Antiviral Discovery Performance Unit. GlaxoSmithKline (GSK). RTP, NC.*

- o Project design, management and execution of studies to assess antiviral efficacy.
- o Created in vivo imaging platform to monitor virus replication and pulmonary inflammation in live animals through a three way public-private collaboration (U. Wisconsin, Perkin Elmer, GSK).

2009-2014 **Postdoctoral Fellow.** *Laboratory of Charles M. Rice. Laboratory of Virology and Infectious Disease. The Rockefeller University, NY.*

- o Developed laser capture microdissection driven systems biology approach chronicling the host response to hepatitis C virus (HCV) in primary human hepatocytes approaching single cell resolution.
- o Hepatitis E, Hepatitis A, and Yellow Fever virus molecular virology and pathogenesis.

2008-2009 **Postdoctoral Associate.** *Laboratory of Ralph Baric. Department of Epidemiology, University of North Carolina, Chapel Hill, NC.*

2003-2008 **Graduate Student.** *Laboratory of Ralph Baric. Department of Epidemiology, University of North Carolina, Chapel Hill, NC.*

- o Dissertation: SARS Coronavirus Pathogenesis and Therapeutic Treatment Design.
- o Trained in biosafety level 3 techniques.

2001-2003 **Research Associate.** *Tissue Engineering Laboratory of Joseph Vacanti. Department of Pediatric Surgery, Massachusetts General Hospital, Boston, MA.*

- o Developed bioabsorbable nerve grafts for nerve repair.

1999-2001 **Research Associate.** *Laboratory of Richard Mulligan. The Harvard Gene Therapy Initiative, Harvard Medical School, Boston, MA.*

- o Process development and GMP production viral vectors.

Honors

- 2015 Second Place Global GSK Beautiful Biology Award. *"In vivo imaging: A new platform to accelerate drug discovery at the host/pathogen interface"*.
- 2015 Third Place Regional GSK Beautiful Biology Award. *"In vivo imaging: A new platform to accelerate drug discovery at the host/pathogen interface"*.
- 2009-2012 Ruth L. Kirschstein National Research Service Award (Postdoctoral Fellowship).
- 2001-2002 Partners in Excellence Award, Massachusetts General Hospital.
- 1998 Gordon Byers Scholarship for an Outstanding Water Resources Student.

Memberships

- 2019-Present International Society for Antiviral Research member.
- 2007-Present American Society for Virology member.
- 2002-2020 American Society for Microbiology member.

Bibliography and Products of Scholarship

Dissertation:

Sheahan TP. *SARS Coronavirus Pathogenesis and Therapeutic Treatment Design.* 2008. University of North Carolina at Chapel Hill. Ph.D. Advisor Dr. Ralph S. Baric.

Books and Chapters:

Sheahan T, Baric R. SARS-CoV Pathogenesis and Therapeutic Treatment Design. 2010. **Molecular Biology of the SARS-Coronavirus.** Lal, Sunil K. (Ed.)

Sheahan T, Deming D, Donaldson E, Pickles R, Baric R. Resurrection of an "extinct" SARS-CoV isolate GD03 from late 2003. **Adv Exp Med Biol.** 2006;581:547-50.

Baric RS, **Sheahan T,** Deming D, Donaldson E, Yount B, Sims AC, Roberts RS, Frieman M, Rockx B. SARS coronavirus vaccine development. **Adv Exp Med Biol.** 2006;581:553-60.

Peer Reviewed Papers and Articles:

Sheahan TP, Sims AC, Leist SR, Schäfer A, Won J, Brown AJ, Montgomery SA, Hogg A, Babusis D, Clarke MO, Spahn JE, Bauer L, Sellers S, Porter D, Feng JY, Cihlar T, Jordan R, Denison MR, Baric RS. Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. *Nat Commun.* 2020 Jan 10;11(1):222. doi: 10.1038/s41467-019-13940-6.

Agostini ML, Pruijssers AJ, Chappell JD, Gribble J, Lu X, Andres EL, Bluemling GR, Lockwood MA, **Sheahan TP,** Sims AC, Natchus MG, Saindane M, Kolykhalov AA, Painter GR, Baric RS and Denison MR. Small molecule antiviral β -D-N⁴-hydroxycytidine inhibits a proofreading-intact coronavirus with a high genetic barrier to resistance. *J Virol.* 2019 Oct 2. pii: JVI.01348-19. doi: 10.1128/JVI.01348-19.

- Leist SR, Jensen KL, Baric RS, **Sheahan TP**. Increasing the translation of mouse models of MERS coronavirus pathogenesis through kinetic hematological analysis. *PLoS One*. 2019 Jul 24;14(7):e0220126. doi: 10.1371/journal.pone.0220126. eCollection 2019. PMID: 31339932
- Brown AJ, Won JJ, Graham RL, Dinnon KH 3rd, Sims AC, Feng JY, Cihlar T, Denison MR, Baric RS, **Sheahan TP**. Broad spectrum antiviral remdesivir inhibits human endemic and zoonotic deltacoronaviruses with a highly divergent RNA dependent RNA polymerase. *Antiviral Res*. 2019 Jun 21;169:104541. doi: 10.1016/j.antiviral.2019.104541. PMID: 31233808
- Gralinski LE, **Sheahan TP**, Morrison TE, Menachery VD, Jensen K, Whitmore A, Heise MT, Baric RS. Complement activation contributes to SARS-Coronavirus pathogenesis. *mBio*. *MBio*. 2018 Oct 9;9(5). pii: e01753-18. doi: 10.1128/mBio.01753-18. PMID: 30301856
- Agostini ML, Andres EL, Sims A, Graham R, **Sheahan TP**, Lu X, Smith EC, Case JB, Feng JY, Jordan R, Ray AS, Cihlar T, Siegel D, Mackman RL, Clarke MO, Baric RS, Denison MR. Coronavirus susceptibility to the antiviral remdesivir (GS-5734) is mediated by the viral polymerase and the proofreading exoribonuclease. *MBio*. 2018 Mar 6;9(2). PMID: 29511076
- Lindesmith LC, Mallory ML, Debbink K, Donaldson EF, Brewer-Jensen PD, Swann EW, **Sheahan TP**, Graham RL, Beltramello M, Corti D, Lanzavecchia A, Baric RS. Conformational Occlusion of Blockade Antibody Epitopes, a Novel Mechanism of GII.4 Human Norovirus Immune Evasion. *mSphere*. 2018 Feb 7;3(1). pii: e00518-17. doi: 10.1128/mSphere.00518-17. eCollection 2018 Jan-Feb. PMID: 29435493
- Sheahan TP**, Sims AC, Graham RL, Menachery VD, Gralinski LE, Case JB, Leist SR, Pyrc K, Feng JY, Trantcheva I, Bannister R, Park Y, Babusis D, Clarke MO, Mackman RL, Spahn JE, Palmiotti CA, Siegel D, Ray AS, Cihlar T, Jordan R, Denison MR, Baric RS. Broad-spectrum antiviral GS-5734 inhibits both epidemic and zoonotic coronaviruses. *Sci Transl Med*. 2017 Jun 28;9(396). pii: eaal3653. doi: 10.1126/scitranslmed.aal3653.
- Ramanan V, Trehan K, Ong ML, Luna JM, Hoffmann HH, Espiritu C, **Sheahan TP**, Chandrasekar H, Schwartz RE, Christine KS, Rice CM, van Oudenaarden A, Bhatia SN. Viral genome imaging of hepatitis C virus to probe heterogeneous viral infection and responses to antiviral therapies. *Virology*. 2016 Apr 26;494:236-247. doi: 10.1016/j.virol.2016.04.020. PMID: 27128351
- Menachery VD, Yount BL Jr, Sims AC, Debbink K, Agnihothram SS, Gralinski LE, Graham RL, Scobey T, Plante JA, Royal SR, Swanstrom J, **Sheahan TP**, Pickles RJ, Corti D, Randell SH, Lanzavecchia A, Marasco WA, Baric RS. SARS-like WIV1-CoV poised for human emergence. *Proc Natl Acad Sci U S A*. 2016 Mar 14. pii: 201517719.
- Tran V, Poole DS, Jeffery JJ, **Sheahan TP**, Creech D, Yevtodiyyenko A, Peat AJ, Francis KP, You S, Mehle A. Multi-Modal Imaging with a Toolbox of Influenza A Reporter Viruses. *Viruses*. 2015 Oct 13;7(10):5319-27.
- Wood ER, Bledsoe R, Chai J, Daka P, Deng H, Ding Y, Harris-Gurley S, Kryn LH, Nartey E, Nichols J, Nolte RT, Prabhu N, Rise C, **Sheahan T**, Shotwell JB, Smith D, Tai V, Taylor JD, Tomberlin G, Wang L, Wisely B, You S, Xia B, Dickson H. The Role of Phosphodiesterase 12 (PDE12) as a Negative Regulator of the Innate Immune Response and the Discovery of Antiviral Inhibitors. *Journal of Biological Chemistry*. 2015 Jun 8.
- Ramanan V, Scull MA, **Sheahan TP**, Rice CM, and Bhatia S. New methods in tissue engineering: improved models for viral infection. *Annual Review of Virology*. 2014. 1:475-499.
- Sheahan TP**, Imanaka N, Marukian S, Dorner M, Liu P, Ploss A, Rice CM. Interferon Lambda Alleles Predict Innate Antiviral Immune Responses and Hepatitis C Virus Permissiveness. *Cell Host and Microbe*. 2014 Feb 12;15(2):190-202

Schwartz R, Trehan K, Andrus A, **Sheahan TP**, Ploss A, Duncan SA, Rice CM, Bhatia SN. Modeling Hepatitis C Virus Infection using Human Induced Pluripotent Stem Cells. *Proceedings of the National Academy of Sciences USA*. 2012 Feb 14;109(7):2544-8.

Meuleman P, Catanese MT, Verhoye L, Desombere I, Farhoudi A, Jones CT, **Sheahan T**, Grzyb K, Cortese R, Rice CM, Leroux-Roels G, Nicosia A. A human monoclonal antibody targeting SR-BI precludes hepatitis C virus infection and viral spread in vitro and in vivo. *Hepatology*. 2012 Feb;55(2):364-72

Andrus L, Marukian S, Jones CT, Catanese MT, **Sheahan TP**, Schoggins JW, Barry WT, Dustin LB, Trehan K, Ploss A, Bhatia SN and Rice CM. Expression of paramyxovirus V proteins promotes replication and spread of hepatitis C virus in cultures of primary human fetal liver cells. *Hepatology* 2011. Dec;54(6):1901-12.

Marukian S, Andrus L, **Sheahan TP**, Jones CT, Charles ED, Ploss A, Rice CM, Dustin LB. Hepatitis C virus induces interferon- λ and interferon-stimulated genes in primary liver cultures. *Hepatology*. 2011. Dec;54(6):1913-23.

Sheahan T, Whitmore A, Rogers K, Ferris M, Rockx B, Funkhouser W, Donaldson E, Gralinski L, Collier M, Heise M, Davis N, Johnston R, Baric R. Successful Vaccination Strategies that Protect Aged Mice from Lethal Influenza and Lethal Heterologous SARS-CoV Challenge. *Journal of Virology*. 2011 Jan;85(1):217-30.

Sheahan T, Jones C, Ploss A. Advances and challenges in studying hepatitis C virus in its native environment. *Expert Reviews in Gastroenterology and Hepatology*. 2010 Oct;4(5):541-50.

Rockx B, Donaldson E, Frieman M, **Sheahan T**, Corti D, Lanzavecchia A, Baric R. Escape from Human Monoclonal Antibody Neutralization Affects In Vitro and In Vivo Fitness of Severe Acute Respiratory Syndrome Coronavirus. *Journal of Infectious Disease*. 2010 Mar 15;201(6):946-55.

Rockx B, Baas T, Zornetzer GA, Haagmans B, **Sheahan T**, Frieman M, Dyer MD, Teal TH, Proll S, van den Brand J, Baric R, Katze MG. Early Upregulation of ARDS Associated Cytokines Promote Lethal Disease in an Aged Mouse Model of SARS-CoV Infection. *Journal of Virology*. 2009 Jul;83(14):7062-74.

Becker M, Graham R, Donaldson E, Rockx B, Sims A, **Sheahan T**, Pickles R, Corti D, Johnston R, Baric R, Denison M. Platforms for the Synthetic Reconstitution of Noncultivable Zoonotic Viruses. *Proceedings of the National Academy of Sciences USA*. 2008 Dec 16;105(50):19944-9.

Sheahan T, Morrison T, Funkhouser W, Akira S, Heise M, Baric R. MyD88 is required for protection from lethal infection with a mouse adapted SARS-CoV. *PLoS Pathogens*. 2008 Dec;4(12):e1000240.

Sheahan T, Rockx B, Donaldson E, Corti D, Baric R. Pathways of Cross Species Transmission of Synthetically Reconstructed Zoonotic SARS-CoV. *Journal of Virology*. 2008 Sep;82(17):8721-32.

Lamirande EW, Dediego ML, Roberts A, Jackson JP, Alvarez E, **Sheahan T**, Shieh WJ, Zaki SR, Baric R, Enjuanes L, Subbarao K. A live attenuated SARS coronavirus is immunogenic and efficacious in golden Syrian hamsters. *Journal of Virology*. 2008 Aug;82(15):7721-4.

Sheahan T, Rockx B, Donaldson E, Sims A, Pickles R, Corti D, Baric R. Mechanisms of Zoonotic SARS-CoV Host Range Expansion in Human Airway Epithelium. *Journal of Virology*. 2008 Mar;82(5):2274-85.

Rockx B, Corti D, Donaldson E, **Sheahan T**, Lanzavecchia A, Baric B. A Panel of Cross-Neutralizing Human Monoclonal Antibodies that Protect Against Lethal Human and Zoonotic SARS-CoV Challenge in Young and Aged Murine Models. *Journal of Virology*. 2008 Apr;82(7):3220-35.

Zhu Z, Chakraborti S, He Y, Roberts A, **Sheahan T**, Xiao X, Hensley LE, Prabakaran P, Rockx B, Sidorov IA, Corti D, Vogel L, Feng Y, Kim JO, Wang LF, Baric R, Lanzavecchia A, Curtis KM, Nabel GJ, Subbarao K, Jiang S, Dimitrov DS. Potent cross-reactive neutralization of SARS coronavirus isolates by human monoclonal antibodies. *Proceedings of the National Academy of Sciences USA*. 2007 Jul 17;104(29):12123-8.

Rockx B, **Sheahan T**, Donaldson E, Harkema J, Sims A, Heise M, Pickles R, Cameron M, Kelvin D, Baric R. Synthetic reconstruction of zoonotic and early human severe acute respiratory syndrome coronavirus isolates that produce fatal disease in aged mice. *Journal of Virology*. 2007 Jul;81(14):7410-23.

Roberts A, Lamirande EW, Vogel L, Jackson JP, Paddock CD, Guarner J, Zaki SR, **Sheahan T**, Baric R, Subbarao K. Animal models and vaccines for SARS-CoV infection. *Virus Research*. 2007 May 10.

Enjuanes L, Dediego ML, Alvarez E, Deming D, **Sheahan T**, Baric R. Vaccines to prevent severe acute respiratory syndrome coronavirus-induced disease. *Virus Research*. 2007 Apr 6.

Roberts A, Deming D, Paddock CD, Cheng A, Yount B, Vogel L, Herman BD, **Sheahan T**, Heise M, Genrich GL, Zaki SR, Baric R, Subbarao K. A mouse-adapted SARS-coronavirus causes disease and mortality in BALB/c mice. *PLoS Pathogens*. 2007 Jan;3(1):e5.

Deming D, **Sheahan T**, Heise M, Yount B, Davis N, Sims A, Suthar M, Harkema J, Whitmore A, Pickles R, West A, Donaldson E, Curtis K, Johnston R, Baric R. Vaccine efficacy in senescent mice challenged with recombinant SARS-CoV bearing epidemic and zoonotic spike variants. *PLoS Medicine*. 2006 Dec;3(12):e525.

Hadlock T, **Sheahan T**, Heaton J, Sundback C, Mackinnon S, Cheney M. Baiting the cross-face nerve graft with temporary hypoglossal hookup. *Archives of Facial Plastic Surgery*. 2004 Jul-Aug;6(4):228-33.

Hadlock TA, **Sheahan T**, Cheney ML, Vacanti JP, Sundback CA. Biologic activity of nerve growth factor slowly released from microspheres. *Journal of Reconstructive Microsurgery*. 2003 Apr;19(3):179-84; discussion 185-6.

Commentaries and Editorials:

Sheahan TP, Baric RS. Is regulation preventing the development of therapeutics that may prevent future coronavirus pandemics? *Future Virol*. 2018 Mar;13(3):143-146. doi: 10.2217/fvl-2017-0143. Epub 2018 Feb 21. PMID: 30546388

Sheahan TP, Rice CM. "Single cell analysis of HCV infected patient hepatocytes: the science is no longer science fiction." *Gastroenterology*. 2013 Dec;145(6):1199-202.

Invited Presentations

Sheahan TP. Broad-Spectrum Therapeutics to Protect Against Coronavirus Epidemic Disease. International Conference on Antiviral Research. Atlanta, Georgia. May 24, 2017.

Sheahan TP. Broad-Spectrum Therapeutics to Protect Against Coronavirus Epidemic Disease. Pizza lunch podcast hosted by American Scientist Magazine, Sigma Xi The Scientific Research Society and Science Communicators of North Carolina (SCONC). The Frontier, RTP, North Carolina. November 21st, 2017.

Oral Presentations and Abstracts:

Sheahan TP. Broad-spectrum antiviral remdesivir provides superior in vivo therapeutic efficacy against MERS-CoV compared to a combination of lopinavir/ritonavir plus interferon beta. International Conference on Antiviral Research. Baltimore, Maryland. May 14, 2019.

Sheahan TP. Broad-Spectrum Therapeutics to Protect Against Coronavirus Epidemic Disease. American Society for Virology. Madison, Wisconsin. June 22, 2017.

Sheahan TP. Broad-Spectrum Therapeutics to Protect Against Coronavirus Epidemic Disease. International Nidovirus Conference. Kansas City, Missouri. June 4, 2017.

Sheahan TP. In vivo imaging: A new platform to accelerate drug discovery. GSK Antiviral Discovery Performance Unit Science Day. RTP, NC. *Research talk.* 2014

Sheahan TP. Transcriptomic profiling of the inflammatory response in primary human hepatocytes infected with hepatitis C virus. 19th International Symposium on Hepatitis C Virus and Related Viruses. Venice, Italy. *Research talk.* 2012

Sheahan TP. "MyD88 is required for protection from lethal SARS-CoV infection." American Society for Virology, Ithaca, New York. *Research talk.* 2008

Sheahan TP. "In Vitro Evolution of Zoonotic SARS-CoV Bearing an SZ16 Civet S Glycoprotein." American Society for Virology, Corvallis, Oregon. *Research talk.* 2007

Sheahan TP. "Synthetic Reconstruction and Characterization of Civet-Like and Civet-Associated SARS Coronavirus." American Society for Virology, Madison, Wisconsin. *Research talk.* 2006

Sheahan TP. "Construction and Characterization of a Civet Cat like SARS Coronavirus." Xth International Nidovirus Symposium, Colorado Springs, Colorado. *Research poster.* 2005

Digital and Multimedia Scholarship:

Video abstract. Self produced for publication "Interferon Lambda Alleles Predict Innate Antiviral Immune Responses and Hepatitis C Virus Permissiveness". *Cell Host and Microbe.* 2014 Feb 12;15(2):190-202. <https://www.youtube.com/watch?v=zKkoZuPUCM0>

This Week in Virology Podcast. Cell Host and Microbe paper (2014 Feb 12;15(2):190-202) featured on Podcast Episode 174. <http://www.twiv.tv/2014/02/23/twiv-273-lambda-is-not-just-a-phage/>

Radio In Vivo "Your Link to the Triangle Science Community." Guest on the radio show/podcast with Dr. Amy Sims. <https://radioinvivo.org/2017/08/09/coronaviruses-drug/>

Products of Creativity - Performances and Exhibitions:

Lead singer and guitar in the rock band "New Jersey Fairplan". 50+ performances from 1996-1999 throughout Northeastern, Mid-Atlantic and Midwestern cities including Portland, Portsmouth, Manhattan, Washington DC, Cleveland and Detroit.

Teaching Experience and Mentorship

Teaching experience:

- 2018 Epid 799a Guest Lecturer “Introduction to Virology” and “Human Genetics in Infectious Disease.”
- 2017 EPID 751 Guest Lecturer “Fundamentals of Virology”, “Emerging Viral Diseases”, “Therapeutics for Emerging Viral Diseases.”
- 2016 EPID 751 Guest Lecturer “Fundamentals of Virology” and “Emerging Viral Diseases”
- 2006 UNC Department of Microbiology and Immunology. Undergraduate Microbiology laboratory lecturer/instructor. Dr. Loraine Cramer.
- 2005 UNC Department of Microbiology and Immunology. Teaching assistant for undergraduate Microbiology. Dr. Loraine Cramer.

Mentorship:

- 2015-Present Mentor to Microbiology Department Graduate Student, Kenneth Dinnon III.
- 2014 GSK. Supervisor of technician Donald Creech on influenza virus in vivo imaging program.
- 2014 GSK. Supervisor of technician Amy Wang on antiviral drug efficacy program.
- 2012-2013 The Rockefeller University. Mentor to Peng Liu a visiting Ph.D. student from Peking University. Graduation May 2015.
- 2011-2012 The Rockefeller University. Supervisor of technician Naoko Imanaka who was integral to the completion of the Cell Host and Microbe paper (2014).

Grants as Principle Investigator

- 2017-2022 Source: National Institute of Allergy and Infectious Disease
 Type: R01
 Grant Number: R01 AI132178
 Title: Broad-spectrum antiviral GS-5734 to treat MERS-CoV and related emerging CoV
 Role: Co-PI
 Duration: 6/1/17 to 6/1/2022
 Total Funding Amount = \$7,605,685.
- 2017-2021 Source: National Institute of Diabetes and Digestive and Kidney Diseases
 Type: R01
 Grant Number: R01 AI131688
 Title: Analysis of immunity, viral adaptation and pathogenesis in a new mouse model of HCV-related rodent hepacivirus infection
 Role: Sub-Contract PI
 Duration: 3/15/2017 to 3/15/2021
 Total Funding Amount = \$268, 585.
- 2009-2012 Source: National Institute of Allergy and Infectious Disease
 Type: Ruth L. Kirschstein National Research Service Award

Grant Number: F32 AI 084448
Title: Hepatitis C virus host interactions in micropatterned hepatocyte co-cultures.
Role: Principal Investigator
Score: 116 (scale 100-500, with 100 being a perfect score)
Duration: 9/1/2009 to 9/31/2012
Total funding amount = \$150,726

Professional and Volunteer Service

Journal Peer Review

- 2016 Ad Hoc Reviewer mSphere
- 2016 Ad Hoc Reviewer for Hepatology
- 2013 Ad Hoc Reviewer for The Journal of Experimental Medicine
- 2013 Ad Hoc Reviewer for Gastroenterology
- 2012 Ad Hoc Reviewer for Science
- 2010-2011 Ad Hoc Reviewer for Proceedings of the National Academy of Science, USA
- 2007-2008 Mentor in Chapel Hill Big Brothers and Big Sisters Program
- 2005-2006 UNC Microbiology and Immunology Bassford Memorial Lecture Steering Committee Member. Lecture given by Nobel Laureate Dr. Ralph Steinman.
- 2005-2006 Graduate Student Representative of UNC Microbiology and Immunology Admissions Committee.

Grant Study Section

- 2018 NIAID R13 Study Section Reviewer
- 2019 AAAS Research Competitiveness Program study section assisting Saudi Arabia's Ministry of Education and Research Development Reviewer