SCIENCE & SCILIFELAB PRIZE

From Persistence to Cross-Species Emergence of a Viral Zoonosis

Interdisciplinary research on zoonotic pathogens illuminates ecology and evolution, while guiding disease prevention and control.

Daniel G. Streicker

Emerging infectious diseases threaten all forms of life on Earth. Many pathogens of great historical and contemporary significance have originated from other species, triggering pandemics, disrupting agriculture, and challenging efforts to conserve endangered wildlife. Despite decades of research on species-jumping pathogens, the most central questions in the field remain major stumbling blocks for societies that seek to mitigate their impacts. These questions include which pathogens are most likely to emerge, which hosts are most likely to share pathogens, and what will be the long-term fate of newly emerged pathogens? Part of the challenge is that emergence, by nature, transcends scientific disciplines, occurring as the product of human behavior, environmental change, population, cellular and molecular biology, and evolution. Solutions therefore demand innovative pairing of theory and fundamental science with applied research and evidence-based policy-making.

Science and SciLifeLab are pleased to present the grand prize–winning essay on the topic of Environmental Life Science by Daniel G. Streicker, the 2013 winner of the *Science* & SciLifeLab Prize for Young Scientists.

My doctoral research used viral infections of bats to answer fundamental questions about pathogen emergence and to help guide control of a major zoonosis in the developing world. Working on bats was partly pragmatic—natural populations can easily be sampled in large numbers, and existing surveillance systems for reportable diseases, such as rabies, provide rich data sets. This choice was also driven by the fact that bats are a major source of highly pathogenic viruses, including severe acute respiratory syndrome (SARS), Nipah, Hendra, and Ebola viruses, which often emerge in the context of anthropogenic change with devastating outcomes for humans and animals (*1*). From an ecological and evolutionary perspective, the high species diversity of bats also presents a unique and fascinating system to test hypotheses on cross-species emergence in complex host communities.

Working with bat tissue samples from public health laboratories across the United States, I first constructed a data set of hundreds of rabies virus sequences from more than 20 bat species. Using ecological and molecular sequence data from both bats and viruses, I developed a novel population genetic framework to quantify transmission rates between species. This analysis (*2*) showed that, counter to the popular notion that rapid evolution in RNA viruses should make ecological overlap the best predictor of which host species share viruses, the genetic similarity of hosts constituted the strongest barrier to both initial infection and viral establishment in new species. The strong phylogenetic constraints on cross-species transmission move us closer to predicting the species origins of viral emergence.

Despite recurrent cross-species transmission in many natural systems, sustained pathogen transmission in newly infected species is rare. This outcome, although fortunate for agricultural, veterinary, and public health interests, represents an obstacle to identifying the mechanistic underpinnings of emergence, because many independent introduction events must be tracked to deduce the predictors of successful emergence. Dozens of historical host shifts among American bat species make rabies an ideal system to explore the epidemiological and evolutionary repeatability of viral emergence. Genomic and demographic inference showed that rabies followed distinct evolutionary pathways to become established in different host species. Further, viruses for which greater adaptive evolutionary changes occurred took longer to establish endemic transmission in new hosts. This work (*3*), addressed the outstanding question of how much evolution happens during host shifts, which may help anticipate the speed and likelihood of viral establishment in new host species. A related study explored the interactions between host ecology and viral evolution by quantifying the rate of molecular evolution across 21 bat-associated rabies viruses. The tempo of viral evolution was surprisingly variable and profoundly dependent on host ecology. Viruses in temperate bats evolved more slowly (by a factor of up to 22) than those in tropical and subtropical species, a likely consequence of seasonal interruption of transmission during hibernation. These results (*4*) imply that bat rabies risk for humans and domestic animals in the tropics will be less predictable than in the temperate zone and demonstrated how host biology can shape the speed of viral evolution.

These studies highlight the power of integrated ecological and evolutionary analyses to reveal general patterns in the frequency, origins, and dynamical outcomes of cross-species transmission. However, they offer no easy solutions for policy-makers seeking to prevent disease. Efforts to control wildlife zoonoses often rely on interventions such as culling; a method perceived to offer the possibility of

Bats as a model and a source of emerging viruses. Cross-cutting research across ecology, phylogenetics, mathematical modeling, and public health on species such as the common vampire bat can illuminate basic principles of disease biology and provide crucial tools to mitigate the impacts of emerging viruses on health, agriculture, and conservation.

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pathogen elimination, thereby providing a cost-efficient alternative to mass vaccination of humans or domestic animals. Yet, interventions in reservoirs are notoriously challenging and controversial because of limited understanding of pathogen persistence in complex wildlife systems (*5*, *6*). The only bat that is culled to manage zoonotic disease is the common vampire bat *Desmodus rotundus*, found throughout the neotropics (see the photo). Despite control campaigns since the 1960s, lethal human rabies outbreaks transmitted by this species are common, and annual livestock deaths number in the thousands (*7*). In 2007, I launched a collaborative research program aimed at reducing this burden through enhanced understanding of rabies ecology in vampire bats. Findings from this project question the core assumptions underlying culling bats for disease control. By monitoring more than 1000 bats across a network of colonies in Peru for nearly 4 years, I showed that rabies exposure in vampire bats was unrelated to colony size. This work (*8*) further showed that culled colonies had either equivalent or higher rates of viral exposure compared with those that were not. Exploration of these data with mechanistic mathematical models suggested that high rates of bat dispersal drive viral persistence and may inherently limit the efficacy of culling, especially if culling increases bat dispersal (*9*). These results challenge the conventional wisdom that fewer bats equals less disease and provide a view toward more effective rabies control in Latin America through spatially synchronized interventions.

My thesis work at the interface between ecology, evolution, and anthopogenic change underscores emerging diseases as one of the most fascinating, challenging, and important topics in the environmental life sciences. Together, these studies provide salient examples of how transdisciplinary collaboration can illuminate fundamental concepts in disease biology, while advocating a science-guided path to anticipate and prevent future disease emergence.

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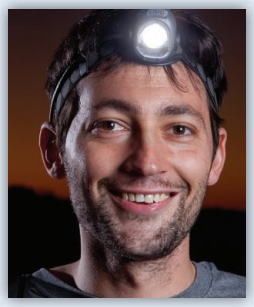
2013 Grand Prize Winner



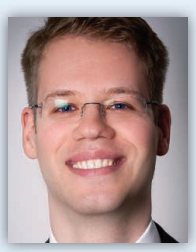
The author of the grand prize–winning essay in the category of Environmental Life Science, **Daniel G. Streicker**, is a Sir Henry Dale Research Fellow at the Institute of Biodiversity, Animal Health and Comparative Medicine at the University of Glasgow. His research applies longitudinal field studies, phylogenetics, and epidemiological modeling to understand the process by which infectious diseases emerge and establish in new host species. He received his Ph.D. from the Odum School of Ecology at the University of Georgia in 2011 and worked previously as an Emerging Infectious Diseases Fellow at the U.S. Centers for Disease Control and Prevention. He received the 2013 Robert C. Anderson Award for Best Dissertation in Life Science from the University of Georgia and has received funding from the National Science Foundation, the Wellcome Trust, the Royal Society, the American Philosophical Society, and National Geographic.

2013 First Runner-Up

Gabriel D. Victora for his essay in the category of Molecular and Cellular Biology, "Stop, Go, and Evolve," is the first runner-up. Dr. Victora is a Whitehead Fellow at the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, where he heads the Laboratory of Lymphocyte Dynamics. He received his Ph.D. from New York University School of Medicine for work done jointly at this institution and at the Rockefeller University. His work combines mouse genetics with intravital microscopy to study the development of high-affinity antibodies in the germinal center. He is a recipient of the 2011 Weintraub Award for Graduate Research, the 2012 March of Dimes Foundation Basil O'Connor Scholar Award, and the 2012 National Institutes of Health director's Early Independence Award. http://scim.ag/SciLifeLab_Victora

2013 Second Runner-Up

Weizhe Hong for his essay in the category of Developmental Biology, "Assembly of a Neural Circuit," is a second runner-up. Dr. Hong is a Helen Hay Whitney Fellow at California Institute of Technology, working on neural mechanisms underlying social and emotional behaviors in David Anderson's laboratory. Dr. Hong received a B.Sc. degree in biological sciences at Tsinghua University and a Ph.D. degree from Stanford University, where he worked in Liqun Luo's laboratory and studied the cellular and molecular mechanisms of wiring specificity in olfactory system development. Dr. Hong received the Genetics Society of America's Larry Sandler Memorial Award for the best Ph.D. dissertation on *Drosophila*-related research and presented the Larry Katz Memorial Lecture at the Cold Spring Harbor Conference for the best Ph.D. dissertation on neural circuit research. http://scim.ag/SciLifeLab_Hong



Dominic Schmidt for his essay in the category of Genomics/Proteomics/Systems Biology, "Dynamics and Evolution of Vertebrate Transcriptional Regulator Binding," is a second runner-up. Dr. Schmidt is a Strategy Consultant at L.E.K. Consulting in London where he works as a strategic adviser to the biopharma and life sciences industry. He received his Ph.D. in Oncology from the University of Cambridge where he combined experimental and computational approaches across multiple species to study how gene-regulation and genomes are evolving. Before getting his Ph.D., he received his German diploma degree in biochemistry at the Max Planck Institute for Molecular Genetics and the Free University of Berlin. http://scim.ag/SciLifeLab_Schmidt

For the full text of all winning essays and further information, see the *Science* site at http://scim.ag/SciLifeLab.

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