Linking Evolution, Ecology, and Health: TriCEM

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Ecological and evolutionary perspectives are essential for understanding human health. Consider, for example, the Ebola virus, which is thought to erupt from bat populations through contact among humans, bats, and other wildlife. In the ongoing outbreak in West Africa, the index case was a 2-year-old boy who may have played in and around a tree that was home to a colony of bats (Saéz et al. 2015). Thus, interactions between humans and wildlife in a highly disturbed ecological habitat probably served as the spark that ignited this epidemic that has killed more than 20,000 people (Baize et al. 2014). Every transmission of the Ebola virus to a new host represents an opportunity for natural selection and therefore for evolution of the virus. Some strains have longer chains of transmission, with more mutations, enabling viruses to discover more fit phenotypes. Phylogenetic analyses revealed the great extent of evolutionary change that occurred early in this latest epidemic, with 73 nonsynonymous substitutions among 78 infected individuals just from Sierra Leone (Gire et al. 2014).

The importance of ecology and evolution also applies to most other aspects of health, including autoimmune diseases, cancer, neurodegenerative disease, aging, obesity, mental health, and early life experiences. Cancer, for example, is a process of somatic evolution, with cells breaking the multicellular "covenant" of restrained replication and instead dividing excessively. This perspective enriches understanding and also leads to new treatment solutions (Aktipis and Nesse 2013). Many essential evolutionary concepts are relevant to understanding and controlling disease, and comparisons across species can provide insights into the causes of disease and how different species control disease.

With the appreciation that evolution is central to understanding and improving human health, enthusiasm is growing to nurture nascent communities of researchers who wish to investigate how evolutionary ideas can translate into practical medical outcomes. To meet this need, Arizona State University has launched the Center for Evolution and Medicine, directed by one of the pioneers in evolutionary medicine, Randolph Nesse, and Temple University recently launched the Institute for Genomics and Evolutionary Medicine. University of California, San Francisco, hosts a Center for Cancer and Evolution, and UCLA has an outstanding Program in Evolutionary Medicine that links their medical school with evolutionary biologists and ecologists. In Europe, the University of Zurich has the Center for Evolutionary Medicine, and University of Durham boasts a master's degree in evolutionary medicine. A new society has been launched—the International Society for Evolution, Medicine, and Public Health—and two new journals are focused on the links between evolution and medicine: *Evolution, Medicine, and Public Health* and the *Journal of Evolutionary Medicine*.

Here in the Research Triangle area of North Carolina, we are transforming the National Science Foundation–supported National Evolutionary Synthesis Center (NESCent) into the new Triangle Center for Evolutionary Medicine (TriCEM). The aim is to apply a synthetic approach, coupled with a successful model of research incubation (Rodrigo et al. 2013), to new questions in human, animal, and plant health posed explicitly in their ecological and evolutionary context. This focus on other animals and plants as well as on humans is a hallmark of TriCEM and is particularly timely as we monitor, understand, and predict how the ecological context is itself affected by human activities. TriCEM's focus represents a natural extension of NESCent's previous research, which included a focus on evolutionary medicine among its many supported projects.

Like NESCent, TriCEM is interdisciplinary. TriCEM teams unite doctors, veterinarians, microbiologists, mathematicians, evolutionary biologists, public health specialists, plant pathologists, ecologists, and social scientists. TriCEM also aims to bridge across institutions, bringing together scientists and students at Duke University, University of North Carolina (UNC), North Carolina State University (NC State), and North Carolina Central University (NC Central), along with other nearby universities, external collaborators of these teams, and members of other synthesis and evolutionary medicine centers. Indeed, the Triangle area is ideal for cross-institutional, cross-disciplinary collaboration, with two medical schools, a school of public health, a college of veterinary medicine, a school of the environment, a school of public policy, and a cadre of world-class ecologists and evolutionary biologists. We are in close proximity to the biomedical and computational research expertise in Research Triangle Park. TriCEM is also building strong connections to the North Carolina Museum of Natural Sciences, which already has an outstanding scientific outreach program, and to various other entities in the Triangle, such as the Canine Health Foundation.

TriCEM will support innovative working groups organized around four main tracks that capture central themes in evolutionary medicine. One track covers pathogenic and commensal organisms; research in this area will address topics such as the evolution of antibiotic resistance, emerging infectious diseases, the microbiome, and the

rise in autoimmune disease due to loss of symbiotic organisms. A second track covers cancer and evolution, including efforts to model the somatic evolution of cancer lineages in the body, antagonistic pleiotropy as a factor that explains genetic variants leading to higher cancer risk, and the evolution of chemotherapy resistance. A third track on brain sciences covers emerging evolutionary perspectives on neurodegenerative disease, mental health, and behavioral decisionmaking in relation to healthcare. The fourth track—on genetic, social, and developmental determinants of health—brings together biological and social scientists to address a wide range of topics, such as the effects of early life experience on long-term health and the genetics underlying disease.

A significant feature of TriCEM activities will be links to One Health, the concept that the health of humans, animals, and the environment are strongly connected. This idea is central to understanding the Ebola outbreak described above. The One Health concept also applies to developed nations, for example, in relation to forest fragmentation and Lyme disease in the United States or to the flow of antibiotic-resistant pathogens from animals to humans through industrial livestock production. This spring, TriCEM supported a "catalysis meeting" of more than 40 researchers to evaluate the links between habitat disturbance and infectious disease risk.

Along similar lines, TriCEM is also stimulating research in comparative medicine. As with the Ebola example, understanding patterns of disease in other animals can provide important insights for human health. For instance, placing human cancers in the context of cancers in other organisms may unlock new solutions for human treatments. Peto's paradox (Caulin and Maley 2011) stems from the expectation that larger animals undergo more cell divisions and therefore should have higher cancer rates. However, systematic comparative studies have failed to find this association. Several factors could explain this paradox, including the possibility that larger animals have more effective anticancer mechanisms. The goal is to learn from "evolution's solutions."

Discussions of One Health often note the insightful statement by the German physician, biologist, and anthropologist Rudolf Virchow, "Between animal and human medicine, there is no dividing line—nor should there be. The object is different, but the experience obtained constitutes the basis of all medicine." Keeping with this philosophy, TriCEM is actively engaging relevant communities in the Triangle and beyond to bridge the veterinary sciences with human medicine and public health—and always with rigorous evolutionary approaches. To achieve these aims, we are teaming with other centers and organizations, such as the Center for Comparative Medicine and Translational Research and the North Carolina One Health Collaborative. Recently, we worked with these groups to jointly sponsor a symposium to bring together veterinary, public health, and medical students to learn about comparative oncology. We aim to repeat this symposium multiple times in the coming year, covering different topics in One Health and developing new networks of students and faculty.

As with NESCent, education and outreach are important to TriCEM, including improving medical training and increasing students' exposure to evolutionary perspectives. Educating future doctors has been a goal for NESCent, which supported a working group with this aim. We continue to support this working group while also helping to initiate a medical student interest group that links medical students from UNC and Duke. Keeping with the importance of comparative medicine, the leaders of this group are connecting with veterinary students at NC State and with public health students at UNC, NC Central, and Duke. We appreciate that the medical school curriculum is already overcrowded. Therefore, an important aim of TriCEM is to enhance educational opportunities for undergraduates, the public, and medical professionals.

By engaging with diverse research communities in the Triangle and beyond, TriCEM is extending beyond NESCent's original reach with a mission that encompasses the incredible breadth of human and animal health issues that exist today, at a global scale. In these ways, TriCEM is expanding the role that interdisciplinary partnerships can play in addressing the wide array of challenges to human health—from understanding disease and its treatment to improving environmental sustainability, biodiversity conservation, and agricultural productivity.

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