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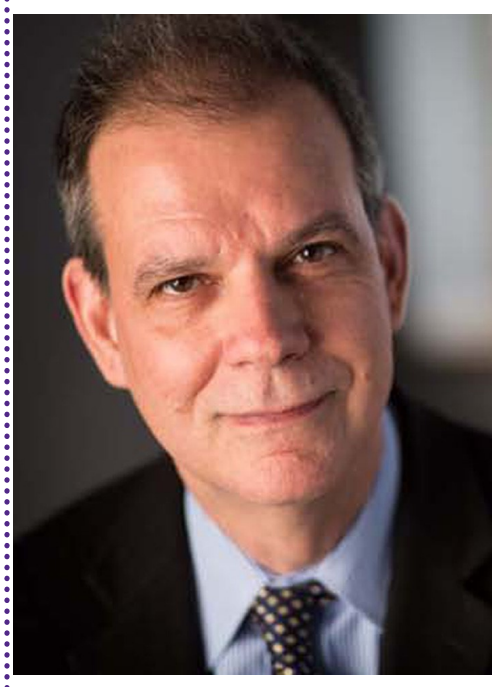

Insights into the Origin of Virulence from Model Organisms

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The germ theory of disease was a landmark moment in human progress because it catalyzed progress that greatly reduced mortality from infectious diseases. However, the germ theory left unanswered two major questions that have preoccupied scientists for the past century: 1) why are some microbes pathogenic and others not? 2) why are some hosts susceptible and others not? To these questions can be added the deeper question: how does the capacity for virulence emerge in some microbes? For microbes acquired from other hosts virulence, which includes many common pathogenic microbes, disease often results from host-microbe interactions that perturb host homeostasis. However, for the set of pathogenic microbes that are acquired directly from the environment, the origin of virulence is less clear, since those microbes have no need for animal virulence for their survival. Among the best candidates to study these problems are pathogenic fungi, which provide clear example of pathogenic microbes acquired from other hosts and directly from the environment. Studies with the fungus *Cryptococcus neoformans* have provided insight in how virulence can emerge in the environment through pressures that have no relation to the final host. *C. neoformans* is often found in the same environmental niches as amoeba, and fungal-amoeba interactions have been proposed to select for traits that also allow it to survive in mammalian hosts, in a process that has been called accidental virulence. A comparison of the interaction between amoeba and mammalian phagocytic cells reveals remarkable similarities in intracellular survival strategy despite the enormous phylogenetic distances for these two cellular hosts. Many of the virulence factors that are needed for *C. neoformans* virulence in mammals are also needed for survival against amoeba predation. The experience with *C. neoformans* has now been corroborated for several other pathogenic fungi. The environmental predatory selection hypothesis can also explain the non-specific nature of environmental fungal pathogens. Furthermore consideration of host susceptibility to fungal pathogens provides a fertile ground for re-thinking evolutionary processes including great mammalian radiation and the end of the age of reptiles after the events at the Cretaceous-Tertiary boundary.

Dr. Casadevall is a globally known expert in humoral immunity, molecular biology, virulence and cryptococcosis. The goal of his research is to protect people from harm caused by new pathogens and resistant organisms, and by compromised immune systems resulting from HIV, cancer therapy treatments and other causes. His laboratory focuses on how microbes cause disease and how the human immune system defends itself.

9:30 a.m., Friday, April 21, 2017
Lecture Hall, Biosecurity Research Institute
Pat Roberts Hall, 1900 Denison

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