

Cell-autonomous immunity and the pathogen-mediated evolution of humans

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Although immune responses are generated by a complex, hierarchical arrangement of immune system organs, tissues, and components, the unit of the cell has a particularly large effect on disease progression and host

survival. These cell-level defense mechanisms, known as cell-autonomous immunity, are among the most important determinants of human survival, and are millions to billions of years old, inherited from our prokaryotic and single-celled ancestors.

The authors of a new paper published in the September 2020 issue of *The Quarterly Review of Biology* argue that understanding how cell-autonomous immunity has evolved in primates is crucial to understanding the human evolution, not only because infectious agents thought to have affected human genomic evolution are excellent manipulators of cell-autonomous immunity, but because these defenses are found in every cell in every body system.

In "Cell-Autonomous Immunity and the Pathogen-Mediated Evolution of Humans: Or How Our Prokaryotic and Single-Celled Origins Affect the Human Evolutionary Story," Jessica F. Brinkworth and Alexander S. Alvarado discuss how the ubiquity of cell-autonomous immunity highlights a biological reality not commonly addressed in [human evolutionary studies](#)—pathogens can mediate the evolution of all body cells, and therefore, all human body systems.

The article examines these ancient tactics in light of evolutionarily important human pathogens and illustrates inter-primate differences in their function. The authors posit that, often considered an independent physiological system in human evolutionary biology, the immune system is ubiquitous, integrated into every other aspect of human physiology. "We argue, therefore, that immunity and pathogen-mediated natural selection is a consideration in the examination of the evolution and function of any human physiological system or trait."

The authors show how human pathogens considered important in the evolution of the human genome manipulate cell-autonomous immunity and have shaped primate [evolution](#), including phagosomes like *Yersinia*

pestis (the causative bacteria of plague) and antimicrobial peptides like *Toxoplasma gondii*, the 1-2 million-year-old obligate intracellular feline-borne parasite.

"The ancient nature of these defenses is an important consideration in human evolutionary studies because their antiquity is both why cell-autonomous immunity exists in every cell, and the pathogens commonly considered the most pernicious and to have exerted the most stringent selective pressure on the human lineage tend to be organisms that bear microbiological innovations that manipulate these tactics," the authors write.

The paper also illustrates that these defenses are diverging in primate immune cells, and present evidence that they are also changing in "nonimmune" tissues. "For decades, it has been understood that microorganisms and cell-autonomous immune responses to them alter human behavior and vice versa. Incorporation of the same biological relationships between pathogens, cell-autonomous defenses, and body system X extended to other physiological systems or traits at the center of the classic questions of human evolutionary biology (e.g., why does skin color vary in humans, why do primate placentae vary in shape and size, how did human bipedal locomotion evolve, how does primate bone and dental microstructure vary) can enrich and improve our understanding of why such features evolved."

For this kind of information to contribute to a better understanding of the gross features of [human evolution](#), however, the authors say researchers in this area must increase integration of molecular and morphological methods or findings in human evolutionary studies. "Any examination of human evolutionary biology, regardless of physiological system and when possible, should consider autonomous immunity of the cells in that system and how microorganisms have shaped them."

More information: Jessica F. Brinkworth et al, Cell-Autonomous Immunity and The Pathogen-Mediated Evolution of Humans: Or How Our Prokaryotic and Single-Celled Origins Affect The Human Evolutionary Story, *The Quarterly Review of Biology* (2020). [DOI: 10.1086/710389](https://doi.org/10.1086/710389)

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