Understanding the evolutionary dynamics of host and pathogen through comparative transcriptomics

Dafna Tussia-Cohen
Supervisor: Dr. Tzachi Hagai

Abstract

Pathogens' ability to infect their host, the disease progression and its severity in the host body, are all affected by the genetics of the infected individual. Different host species often differ in their ability to resist pathogen infection, including viruses and bacteria, and this can range from unsuccessful or asymptomatic infection to a deadly outcome. For example, some reptiles are thought to be relatively more resistant to various infections in comparison with mammals (Zimmerman, Vogel and Bowden, 2010). Another example is various species of bats that are natural reservoirs of viruses that are often lethal to humans and other primates but lead to no significant disease in bats. In my research I aim to characterize evolutionary differences between hosts in their response to and interaction with pathogens. Using single-cell transcriptomics, I characterize conserved and divergent elements of the innate immune response to pathogens across vertebrates in evolutionary and biomedically important species, including mammals (bat, mouse and human), and reptile and avian species (chicken, crocodile, Komodo dragon, turtle). By looking at the cellular response to dsRNA and LPS, I have identified a conserved regulatory principle in mammalian PBMCs, where only a subset of highly-responsive monocytes is induced in the initial response. This may be related to regulatory constraints imposed on host cells to avoid excessive immune reaction. Currently, I am testing similarities and differences from these observations at both the cellular- and gene-level in the poorly understood reptilian immune response.

3 major points:

- Establishing computational protocols to process, annotate and compare single-cell transcriptomics data between species
- How do humans differ from other species in their response/resistance to infection?
- Estimating divergence and conservation of cell types and genes across species