

DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

Coordination of innate immune response in infected cell population: experiment and mathematical modeling

Innate immune responses form the first line of defense against invading pathogens; it may eradicate pathogens or slow down progression of infection allowing adaptive immune responses to develop. We are used to think about immune response after getting sick, while the main task of innate immunity is to prevent development of infection, before we even notice it. Our lungs are in frequent contact with viruses, and potential infections can start from a very few infected cells. These cells may attempt to resist viral multiplication themselves, but more importantly they should try to inform other cells about the threat. Cell-to-cell communication is enabled by various cytokines, that is, proteins that are secreted by cells and activate specific programs in neighboring cells in the tissue. Cytokine-alarmed cells increase levels of numerous antiviral proteins and become more resistant to infection, but to have their protective effect the cytokines have to reach these cells hours before the replicating virus.

The competition between immune response and viral spread gives rise to temporal subpopulations of cells: infected/uninfected, cytokine-secreting or not, suppressing multiplication of virus or “allowing” virus to replicate. The aim of our study is to characterize these subpopulations, their communication by cytokines and their role in limiting the spread of the virus. In order to enable cytokine communication, cells have to allow for protein synthesis; however, to suppress multiplication of virus cells should inhibit protein synthesis and degrade viral genetic material. The specific question we aim to answer is how the cell population is able to reconcile these two contradictory functional programs.

We will work with two respiratory viruses: influenza virus and respiratory syncytial virus. Both viruses are responsible for life-threatening conditions such as bronchiolitis and pneumonia, and are a major cause of death among young children and the elderly. Unsurprisingly, both viruses have been intensively studied. Most studies however were performed either in animals (which makes the analysis of intracellular processes difficult) or at non-physiologically high levels of infecting viruses when majority of cells are infected and thus the immune responses cannot develop at the cell-population level. We expect that our studies will help to elucidate mechanisms of innate immune responses critical for preventing infections.