

Pathogen interactions with host resources and immunity result in bimodal infection outcomes

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Abstract

Death or survival are the two outcomes of an infection. Pathogen infections perturb the resource and energy balance of hosts and in response hosts adjust metabolism and resource assimilation. Host resistance against infection relies on the allocation of resources, in particular to mount sufficient immune responses. We hypothesize that interactions between host resources, host immune responses and pathogens determine host homeostasis and result in contrasting infection outcomes. In this study, we mathematically formulate these interactions and find that the temporal dynamics lead to two distinct trajectories of disease progression. The pathogen load responds in a bistable manner by either proliferating or persisting, if not being eliminated, which corresponds to the death or survival of the host. We identified two key negative feedbacks causing bistability: 1) host resources are either directly consumed or indirectly inhibited by pathogens; 2) pathogen elimination by the host immune response. The dynamics is also sensitive to “initial conditions”, such as resource availability, immunocompetence, and pathogen load at the onset of infection. Our result provides a mechanistic intuitive explanation for the bistable outcome of pathogen infection based on resource reallocation. It also provides a quantitative framework to monitor disease trajectories and forecast the physiological tipping point of death and survival.

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