Dependence of HIV Cure on Immune System Shaped by Microbiota

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Evidence is mounting that it is possible to control the virus that causes AIDS with early treatment so that further therapy is not immediately needed—a condition called “functional cure” of the infection. Recent studies have been reported that 15 patients with HIV, who received antiretroviral treatment within months of infection, had their viral loads durably decreased so much that we could consider that they are "functionally cured". It has previously been shown that provision of therapy even sooner after infection (Post Exposure Prophylaxis or PEP) can also prevent HIV infection. PEP has a small window of opportunity, being less effective beyond 24-36 hours after exposure and probably ineffective beyond 48-72 hours. Many host factors may determine the length of time available for cure. In a previous study, we found that infant rhesus macaque with different diets (breast- and bottle-fed) showed different microbial composition in their gut and had also developed very different immune systems, particularly in development of cell types that have been shown already to control HIV infection. We suggest that these differences in development of immune cells could also generate different probabilities to achieve cure. Therefore, we hypothesize that individuals with higher amount of Th17 cells will have a larger window to achieve functional cure.

To test our hypothesis, we will perform two experiments. In the first, we aim to establish a model defining the time period during which functional cure might be achieved in individuals having favorable development of the immune system. When treatment is started within hours of infection we know already that individuals can be cured, but also that if treatment is started later (up to 48-72 hours) the probability of cure is less. We will initiate treatment at a variety of times after SIV infection. We expect that when therapy is initiated at 24 hours no individuals will be infected, while at 48 and 72 hours some will be durably infected and experience high viral load while others may be cured.

In the second experiment we will test if having a higher amount of Th17 cells, or their functional opposite, T-reg cells, could favor the achievement of functional cure. We will screen blood samples to find individuals having a higher number of Th17 cells or of T-reg cells. These two groups will then be infected with SIV and treated at the time point that was shown in the first experiment to allow occasional but not uniform cure of the infection. We will determine the proportion of achieving cure in each group.

The goal of this project is to determine if variable development of the immune system, which we have shown is fundamentally shaped by the gut microbes that are present in infancy, has an important influence on establishment of the virus in immune cells, and thereby on the likelihood of “functional cure”.