

## Miguel Soares

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### Why do we survive or die from infectious diseases?

Why do some individuals develop severe infectious disease and eventually go on to succumb from those while others develop only mild forms of the same disease and survive. The accepted answer is: Those that succumb fail to clear invading pathogens, while survivors do so efficiently. Yet, there are “exceptions to this rule”, with major consequences to global human morbidity and mortality. Sepsis, a life-threatening organ dysfunction caused by a dysregulated host response to infection, develops under pathogen burdens in the range of non-septic patients. The same is true for severe and often-lethal outcomes of malaria, caused by *Plasmodium* infection. More recently we well became aware of this same phenomenon in the COVID-19 pandemic, caused by SARS-CoV-2 infection. These “exceptions” can be explained, in part, by host genetic variations that pertain to disease tolerance to infection, an evolutionary conserved defense strategy that does not target pathogens directly. In this seminar I will discuss experimental evidence for an evolutionary conserved genetic program that promotes disease tolerance to malaria while also targeting and killing *Plasmodium*, in humans and in mice.