Letter

The Burden of Memory: Response to Ortega

Ger Rijkers1,2,*

At the time of writing a response to the letter from Enrique Ortega in this issue of Trends in Immunology [1], on 15 July 2020, PubMed returned 31 963 results for the search term ‘COVID-19’ and the preprint server MedRxiv, another 5175 manuscripts1. Despite this overwhelming amount of data, it is still unclear what constitutes a protective immune response, while such a protective response of the immune system is key to survival of coronavirus disease 2019 (COVID-19). In my TrendsTalk, I stated that ‘in times of COVID-19, it would seem as if loss of memory is the key to survival’ [2]. Dr Ortega stresses the importance of immunological memory, and I agree. Indeed, having survived a primary infection with a given pathogen does not guarantee a favorable outcome of a subsequent infection with that same pathogen. During the primary response of the immune system, effector cells and molecules are generated, as well as (T and B) memory cells. Upon re-exposure to the same pathogen, the memory cells are activated, generating a faster, higher, and better response, in many cases as effective that the infection is cleared before any clinical symptoms occur. The progressive decrease in frequency and severity of lower respiratory infections during early childhood is the best example of development of immunological memory in practice [3].

In times of COVID-19, the situation is completely different. The global population, young and old, is exposed to a novel virus, requiring an effective primary immune response for survival. For this strain of coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the existing memory against circulating coronaviruses does not appear to offer clinical protection. It can even be argued that the major reason why SARS-CoV-2 could rise to pandemic proportions is the lack of cross-reactivity of existing memory against other circulating coronaviruses, although this remains unknown.

From an evolutionary perspective, it is vital for the survival of populations that the young build up immunological memory against prevalent pathogens. The accumulation and persistence of long-lived memory cells offers protection during childhood, into adulthood, and well above the reproductive age.

The current pandemic has taught us that a risk factor for severe COVID-19 includes age: hospital mortality is <5% among patients younger than 40 years, but increases to 35–60% for patients aged 70 years and older [4]. A marked difference between infants and older individuals is a progressive shift from an immune system comprising many naïve lymphocytes (both T and B cells) and few memory cells to one that contains mostly memory cells and a smaller pool of naïve cells [5]. The price to be paid might be that, at advanced age, an immune system comprising mainly memory cells precludes the generation of a robust and effective primary response against a newly emerging pathogen.

Resources
1https://pubmed.ncbi.nlm.nih.gov/?term=COVID-19&sort=date&size=200
2www.medrxiv.org/search/COVID-19

Forum

Modeling Potential Autophagy Pathways in COVID-19 and Sarcoïdosis

Alain Calender,1,* Dominique Israel-Biet,2 Dominique Valeyre,3,4,5 and Yves Pacheco1

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and mainly affects the lungs. Sarcoïdosis is an auto-inflammatory disease characterized by the diffusion of granulomas in the lungs and other organs. Here, we discuss how the two diseases might involve some common mechanistic cellular pathways around the regulation of autophagy.

From COVID-19 to Sarcoïdosis

The pandemic induced by SARS-CoV-2 (COVID-19) raises vital questions regarding the most beneficial putative therapeutic procedures that could prevent fatal aspects of acute respiratory distress syndrome