Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Reply to the Letter to the Editor: Regional differences in dietary use of immune-modulating catechins should be investigated regarding COVID-19

We appreciate Dr. Desoto's commentary on our paper, "The impact of nutrition on COVID-19 susceptibility and long-term consequences." We agree this conversation should be extended to include a discussion of how specific nutrients may dampen the cytokine storm associated with severe COVID-19 pathology. The role of tristetraprolin (TTP), increased by green tea consumption, in regulating tumor necrosis factor (TNF) levels is an interesting avenue to explore regarding the resolution of the cytokine storm. As Dr. Desoto suggests, regional differences in green tea consumption, and thus TTP synthesis, could account for discrepancies in mortality rate. While Japan, Indonesia, and China have an increased green tea consumption relative to Western countries, it should also be noted that these same regions also have a higher intake of omega 3 fatty acids (n-3 FAs) due to their high consumption of fish and other seafood (Hosomi et al., 2012).

The polyunsaturated n-3 FAs, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), are critical regulators of the immune response. Upon an inflammatory event, such as that caused by a viral infection, DHA and EPA are cleaved from the phospholipid membrane and metabolized by cyclooxygenase, lipoxygenase, or cytochrome P450 enzymes to produce specialized pro-resolving mediators (SPMs), including protectins, D-series resolvins (from DHA), and E-series resolvins (from EPA). These bioactive metabolites bind to receptors on multiple types of immune cells and resolve the inflammatory response (Gutiérrez et al., 2019).

One of the most prominent effects of n-3 FAs is their ability to reduce inflammation by modulating macrophage activity. Both *in vivo* and *in vitro* studies reveal that pretreatment with DHA or EPA reduce cytokine release in macrophages following an immune challenge (Gutiérrez et al., 2019). Much like the role of TTP, it will be important to establish a causal role of n-3 FAs in resolving the cytokine storm observed in COVID-19 patients. While not related to COVID-19, the results of a recent randomized, controlled trial showed n-3 supplementation reduced plasma levels of interleukin 6 (IL-6) and interleukin 1β (IL-1 β) in aging adults (Tan et al., 2018). This, along with the n-3 effect on macrophage activity, is relevant to the current pandemic because chronic macrophage activation and elevated levels of IL-6 and IL-1 β have been observed in patients with severe COVID-19 (McGonagle et al., 2020).

As alluded to by Dr. Desoto, the typical diet of Western countries is lacking in nutrients that could be beneficial for immune function. In addition to low green tea consumption, the Western diet is extremely deficient in n-3 FAs. This, coupled with declining DHA levels associated with natural aging (Weiser et al., 2016), could put Europe and the United States at a disadvantage regarding COVID-19 severity and mortality. Thus, researchers should investigate direct connections of specific nutrients to COVID-19 pathology. Furthermore, in addition to social distancing behaviors and use of facial coverings, public health officials should stress the importance of specific nutrients and their involvement in an appropriate immune response as a strategy to mitigate the impact of COVID-19.

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