4.19 Investigation of the role of the toll-like receptor 3 (TLR3) Leu412Phe (*TLR3* L412F) single nucleotide polymorphism in the pathogenesis of long COVID.

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Background: the role of the *TLR3* L412F (rs3775291) single nucleotide polymorphism in the pathogenesis of long COVID has not been reported to date. TLR3 is central to the innate immune response against a number of viruses, including SARS-CoV-2. *TLR3* L412F has previously been shown to reduce cellular TLR3 activity and has been implicated in acute COVID-19 disease severity.

Methods: we carried out a case-control study to investigate the frequency of *TLR3* L412F in long COVID patients (n=183) and healthy controls (n=263). In addition, we investigated the effect of *TLR3* L412F on pulmonary function (% predicted FVC, DLCO, MIP and MEP), serum ACE and vitamin D levels, and olfactory function (SNIFF score) in long COVID patients.

Results: our case-control study observed no significant association between *TLR3* L412F and the development of long COVID. Furthermore, *TLR3* L412F had no significant effect on pulmonary function, serum ACE and vitamin D levels, or olfactory function in long COVID patients.

Conclusions: This is the first study to report the effect of *TLR3* L412F in long COVID patients. This study suggests that *TLR3* L412F does not significantly contribute to long COVID pathogenesis.

Keywords: long COVID, viral response, toll-like receptor 3, *TLR3* L412F polymorphism.

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