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Constructing virtual patient populations to understand immune responses in immunosuppressed and cancer patients with COVID-19

The COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has significantly affected the lives of billions of people, causing millions of deaths. It was recognized that particular groups of people, including the elderly, experienced more severe COVID-19. Additionally, patients with existing immunosuppression and those undergoing active cancer treatments are known to respond more poorly to the virus and the disease. However, clinical studies in those populations are difficult to perform, time and money consuming, and there is overall a lack clinical data to relate mechanisms of dysfunction to outcomes. Therefore, mathematical modelling, which enables studying complicated immune response mechanisms, can be a promising solution to the need for extensive longitudinal human data.

To study the immune dynamics after infection with SARS-CoV-2 in immunosuppressed and cancer patients, we adapted our existing mathematical model of the immune response in COVID-19. Using our established virtual patient cohort generation procedure, we used our model to generate virtual patient cohorts of cancer and immunosuppressed patients. Model predicts that both cancer and immunosuppressed virtual patients with severe COVID-19 have decreased CD8+ T cells and delayed IFN peaks. Additionally, our results show that cancer patients experience higher viral loads likely caused by decreased initial neutrophil counts (i.e. neutropenia), a frequent toxic side-effect of anti-cancer therapy. Together, our study suggests that immune dysregulation in COVID-19 is determined by dysfunction in IFN and CD8+ T cells, and that these may be considered as biomarkers of severity. Further, they represent potential treatment targets in susceptible patient groups.