Immunological profiles of COVID-19 patients reveal promising indicators and therapeutic targets for severe forms of the disease

SARS-CoV-2 infection causing coronavirus disease (COVID)-19 is characterized by pneumonia, respiratory and multiorgan failure in susceptible individuals. Severe COVID-19 is hallmarked by dysregulated immune response, cytokine storm and immune paralysis. However, key immunological mechanisms and indicators of this dysregulation are still largely unknown, which is hampering the development of efficient treatments. Extensive immune cells' and humoral markers profiling in peripheral blood of COVID-19 patients healthy donors enabled identification of several predictive markers of severe COVID-19, including proinflammatory cytokines and subsets of extracellular vesicles (EVs) in sera. In contrast to severe COVID-19, mild COVID-19 patients displayed an increased levels of CD24+ and HLA-ABC+ EVs, and proper activation of CD4+ T cells. Dysregulated T cell functions in severe COVID-19 were associated with lower expression of HLA-DR in different antigen-presenting cells, down-regulated autophagy genes and interferon-responsive factor 8 (IRF-8). Similar mechanisms lead to expansion of myeloid derived suppressor cells (MDSC) and regulatory T cell subsets, which drive immune paralysis in severe COVID-19. Therefore, therapies targeting the impaired antigen-presentation, expansion and functions of MDSCs might provide great clinical benefit for severe COVID-19 by restoring T cell functions and anti-viral response.