How SARS-CoV-2 tricks our immune system?

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In viral infectious disease, type I interferon signal transduction is important for the activation of both the innate and adaptive immune system, which is necessary for the successful elimination of the pathogen. Especially in SARS-CoV2 infections, genetic mutations in genes involved in the interferon signal transduction pathway and the presence of type I interferon neutralizing autoantibodies lead to fatal diseases in about 10% of patients suffering from severe COVID-19. Thus, delayed onset of type I interferon signal transduction was hypothesized to be associated with severe COVID-19 courses and high SARS-CoV2 viral loads. At the onset of the pandemic, it was largely unknown what other factors contributed to a delay in the type I interferon response in the remaining 90% of patients with severe disease. In order to identify such host factors, we enriched specific immune cells from peripheral blood and inflamed tissues of severe COVID-19 patients and analyzed their transcriptomes and immune receptor repertoires at the single cell level. In this way, by zooming in on specific cell populations, we were able to identify the role of the host cytokine TGF-β in the pathogenesis of severe COVID-19. TGF-β promotes a chronic inflammatory response that leads to sustained production of antibodies that are no longer directed against SARS-CoV2. Moreover, early after infection, elevated TGF-β levels, cause a defect in the cytotoxic function of cells necessary for viral clearance. This functional defect can be reversed by neutralizing TGF-β in the serum of COVID-19 patients. In conclusion, we were able to identify the host cytokine TGF-β actively induced by SARS-CoV2 in infected cells in order to evade the immune response presumably interfering with the type I interferon signal transduction. Furthermore, the levels of TGF-β in the serum are predictive for hospitalization and the early blockage of the cytokine can be potentially used to prevent severe COVID-19.