SARS-CoV-2 infection triggers paracrine senescence and leads to a sustained senescence-associated inflammatory response.

Reports of "post-acute COVID-19 syndrome," in which the inflammatory response persists even after SARS-CoV-2 has disappeared, are increasing but the underlying mechanisms of post-acute COVID-19 syndrome remain unknown. The research group of Eiji Hara (IFReC/RIMD/CiDER, Osaka University) show that SARS-CoV-2 infected cells trigger senescence-like cell-cycle arrest in neighboring uninfected cells in a paracrine manner via virus-induced cytokine production. In cultured human cells or bronchial organoids, these SASR-CoV-2 infection-induced senescent cells express high levels of a series of inflammatory factors known as senescence-associated secretory phenotypes (SASPs), in a sustained manner, even after SARS-CoV-2 is no longer detectable. They show that the expression of the senescence marker CDKN2A and various SASP factor genes is increased in the pulmonary cells of patients with severe post-acute COVID-19 syndrome. Furthermore, they find that mice exposed to a mouse-adapted strain of SARS-CoV-2 exhibit prolonged signs of cellular senescence and SASP in the lung at 14 days post-infection when the virus was undetectable, which could be substantially reduced by the administration of senolytic drugs. The sustained infection-induced paracrine senescence described here may be involved in the long-term inflammation caused by SARS-CoV-2 infection.

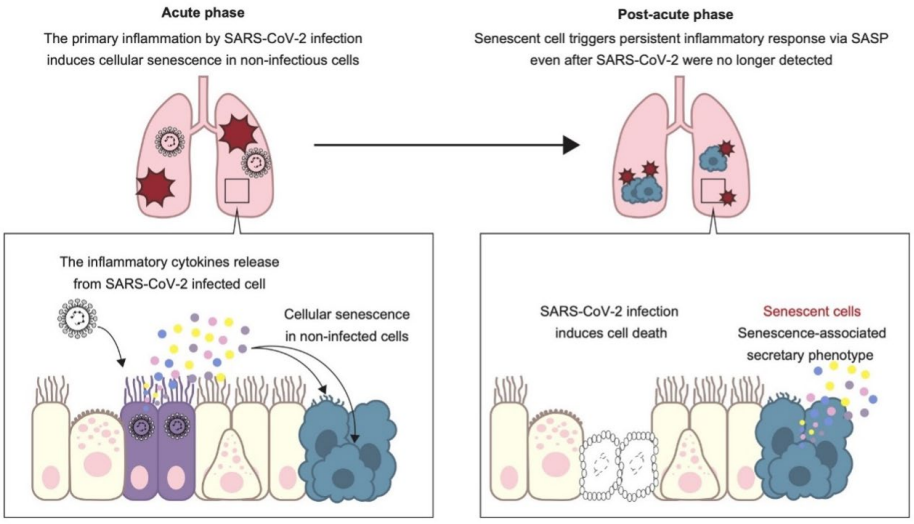

Figure: Induction of cellular senescence and persistence of inflammatory response by SARS-CoV-2

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