Role of cholesterol in COVID-19 disease and in the SARS-CoV-2 spike interaction

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Facing SARS-CoV-2 requires rapid development of effective diagnostic and antiviral therapeutic agents. Changes in lipid metabolism have been previously reported during viral infections (e.g. HBV, HCV, HIV), where a specific lipid profile of the host could serve as a biomarker. Besides being a fundamental lipid component of vertebrate cell membranes and participating in numerous physiological processes, cholesterol is being recognized as a molecule involved in regulating SARS-CoV-2 entry. Generally, higher membrane cholesterol coincides with higher efficiency of coronavirus entry, while disruption of cholesterol-enriched lipid rafts by lipid-lowering treatment affects their infectivity. Moreover, studies on COVID-19 patients show decreased levels of serum total cholesterol, HDL- and LDL-cholesterol, but the role of cellular cholesterol synthesis has not yet been thoroughly investigated. Herein we focus on serum cholesterol and its intermediates in patients hospitalized due to COVID-19. Samples were taken at three-time points during hospitalization, to contrast the disease severity in individual patient. We aim to evaluate whether the sterol-related biomarkers can be used for the prediction of the disease progression or outcome and whether the cholesterol and its sterol intermediates affect the entry of SARS-CoV-2. Initial results indicate that cholesterol precursors (*i.e.* lathosterol) correlate with COVID-19 severity in the Slovenian cohort. The analysis of the targeted cholesterol-related RNAs from patients' serum is in progress. The role of cholesterol and other sterols in SARS-CoV-2 spike protein interaction is studied in immortal cell lines with impaired cholesterol synthesis. Uncovering to which extend the blood and membrane-bound cholesterol imbalance relates to COVID-19 pathology will give valuable insight also regarding the suitability of treatment of patients with lipid-lowering drugs.