NUTRIMETABOLOMICS APPROACH TO UNDERSTAND PROTECTION FROM SARS-COV-2 INFECTION

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Introduction. Although the mass vaccination campaign has opened a new chapter in the battle against SARS-CoV-2, COVID-19 pandemic is still raging in most countries. The application of metabolomics in the nutrition sciences has been used not only to discover new food intake biomarkers but also to assess dietary compliance or dietary patterns. Foods and food ingredients play an important role in achieving or maintaining a state of wellbeing. In the current study, we used nutrimetabolomics to identify chemicals and variables associated with a high risk of developing COVID-19 infection.

Methods. Untargeted metabolomics analysis was performed on a first cohort of 51 serum samples collected from healthy healthcare professionals at the onset of the COVID-19 pandemic in Italy and who were later exposed to the same risk for contracting COVID-19. Of these subjects, half developed COVID-19 within three weeks of the blood collection. Small molecules were extracted from serum, derivatized and then analyzed using bi-dimensional gas chromatography/mass spectrometer (GCxGC-MS). The metabolomics profiling between the two groups were then compared. The levels of monolaurin, which resulted more concentrated in protected subjects from the discovery phase, were then quantified in a larger cohort o subjects.

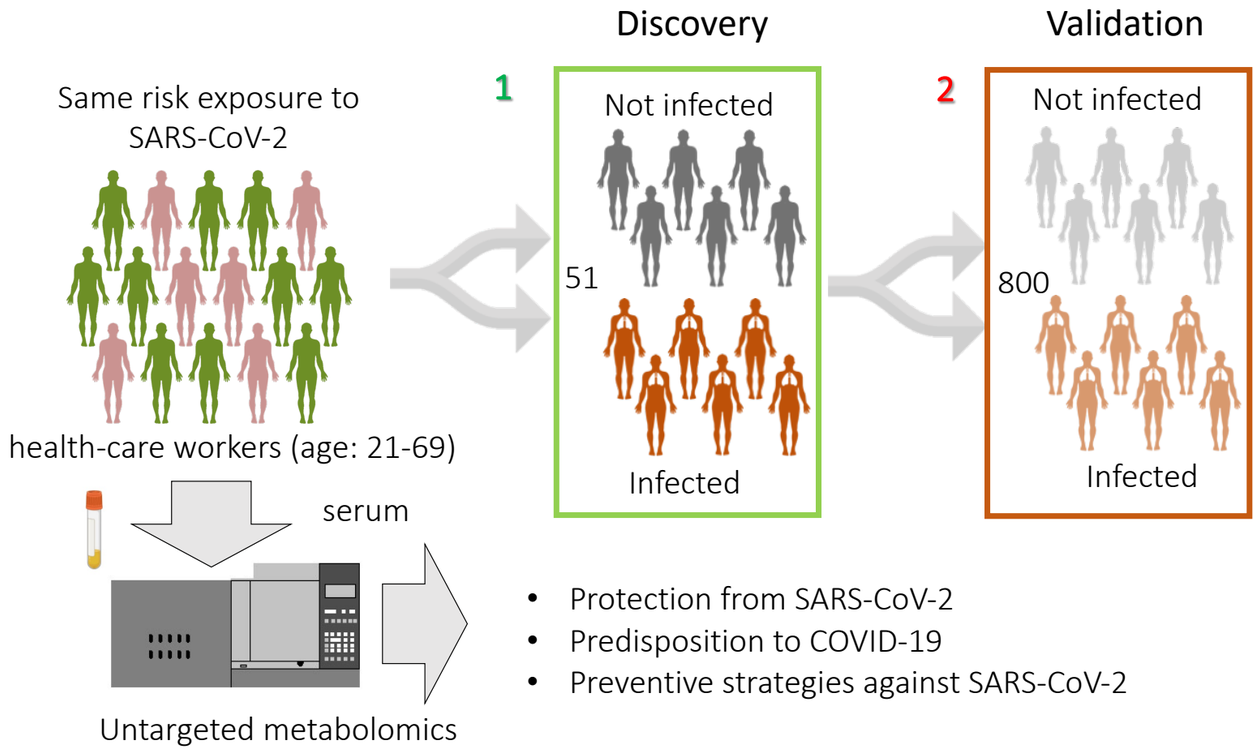


Fig 1: Experimental design of the study. Untargeted metabolomics was performed on 51 healthcare workers, 24 subjects developed COVID-19 in the weeks following the blood collection, while 27 subjects were more protected and did not develop the disease. The validation was performed using more than 800 subjects.

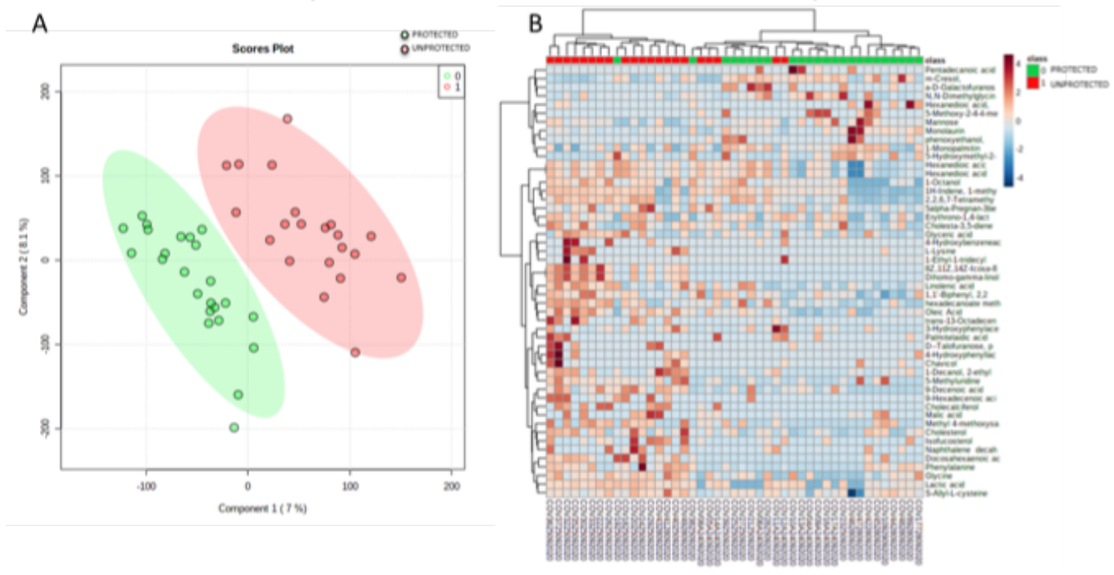


Fig 2: (A)Partial least square analysis (PLS-DA) showed two clusters of subjects (protected=green; unprotected=red), (B) Hierarchical heat maps of quantified small molecules highlighting the two groups of samples.

Results. We identified the presence of a metabolic phenotype associated with protection from SARS-CoV-2 infection and predisposition to COVID-19. Among molecules correlated to protection we identified several fatty acids and amino acids that could be used as dietary supplements. In particular, we identified an important role of **monolaurin**, which has well-known **antiviral and antibacterial** properties. The molecule was higher in protected subjects, suggesting a potential defensive role against SARS-CoV-2 infection; thus, dietary supplements could boost the immune system against this infection. A recent trial showed that virgin coconut oil, which is mainly composed of monolaurin, was able to reduce inflammation in COVID-19 patients.

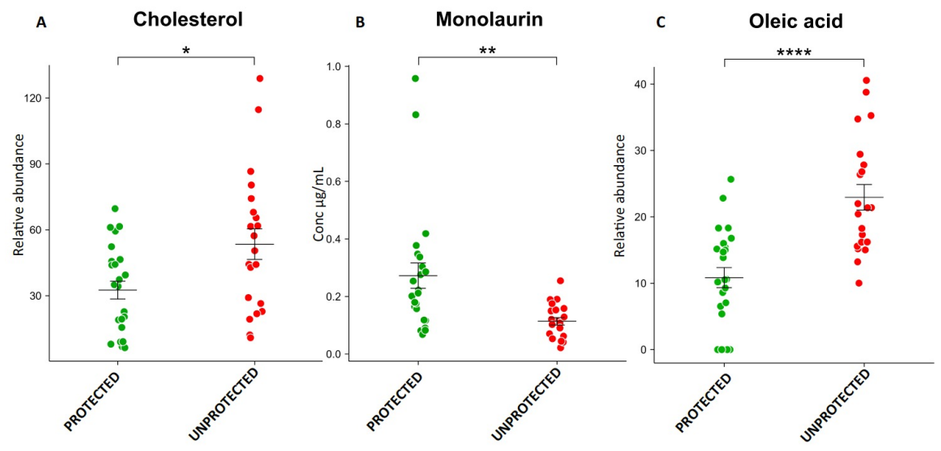


Figure 4: Molecules potentially involved in protecting individuals from SARS-CoV-2 infection or from COVID-19 development. Box-plot of monolaurin (A), cholesterol (B), and oleic acid (C) in protected and unprotected subjects.

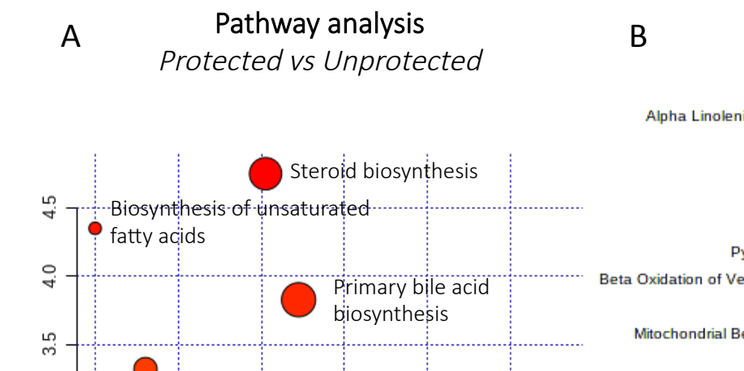
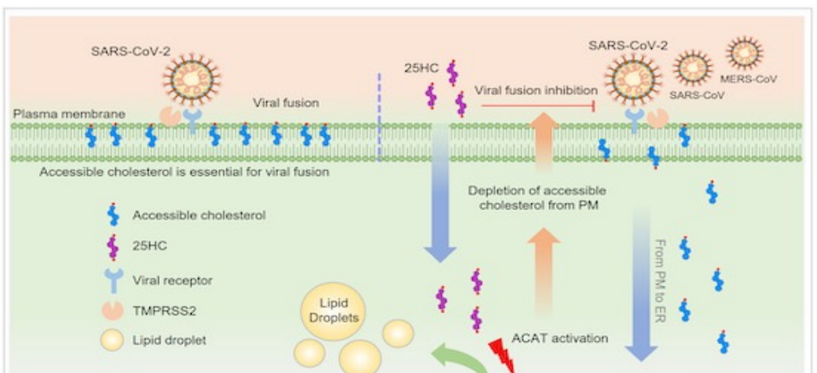
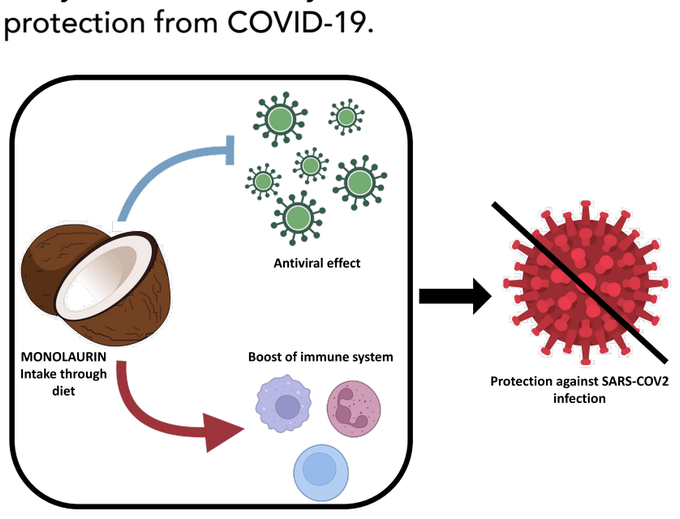


Fig 3: Pathways potentially involved in the protection from SARS-CoV-2. Metabolic pathway analysis performed on modulated metabolites (A) and metabolite sets enrichment (B). Steroid biosynthesis and biosynthesis of unsaturated fatty acids and amino acids may be involved in protection from COVID-19.



The presence of cholesterol in the cell membrane and viral envelope contributes to coronavirus replication. It is involved in binding and altering the oligomeric status of the N-terminal fusion peptide of SARS-CoV2, which is crucial for virus entry.



Role of Monolaurin in the protection against COVID-19: immunomodulator and antiviral activity.

The quantification of monolaurin on a larger cohort of healthy subjects is ongoing. We will then correlate the levels of this molecule with the time to infection with SARS-CoV-2.

Conclusion. This study shows that metabolomics can be of great help for developing personalized medicine and for supporting public healthcare strategies.

1. Barberis, E., Amede, E., Tavecchia, M. et al. Understanding protection from SARS-CoV-2 using metabolomics. Sci Rep 11, 13796 (2021).