

Evidence of SARS-CoV-2 bacteriophage potential in human gut microbiota

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Abstract

Background: In previous studies we have shown that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) replicates *in vitro* in bacterial growth medium, that the viral replication follows bacterial growth, and it is influenced by the administration of specific antibiotics. These observations are compatible with a 'bacteriophage-like' behaviour of SARS-CoV-2.

Methods: We have further elaborated on these unusual findings and here we present the results of three different supplementary experiments: (1) an electron-microscope analysis of samples of bacteria obtained from a faecal sample of a subject positive to SARS-CoV-2; (2) mass spectrometric analysis of these cultures to assess the eventual *de novo* synthesis of SARS-CoV-2 spike protein; (3) sequencing of SARS-CoV-2 collected from plaques obtained from two different gut microbial bacteria inoculated with supernatant from faecal microbiota of an individual positive to SARS-CoV-2.

Results: Immuno-labelling with Anti-SARS-CoV-2 nucleocapsid protein antibody confirmed presence of SARS-CoV-2 both outside and inside bacteria. *De novo* synthesis of SARS-CoV-2 spike protein was observed, as evidence that SARS-CoV-2 RNA is translated in the bacterial cultures. In addition, phage-like plaques were spotted on faecal bacteria cultures after inoculation with supernatant from faecal microbiota of an individual positive to SARS-CoV-2. Bioinformatic analyses on the reads obtained by sequencing RNA extracted from the plaques revealed nucleic acid polymorphisms, suggesting different replication environment in the two bacterial cultures.

Conclusions: Based on these results we conclude that, in addition to its well-documented interactions with eukaryotic cells, SARS-CoV-2 may act as a bacteriophage when interacting with at least two bacterial species known to be present in the human microbiota. If the hypothesis proposed, i.e., that under certain conditions SARS-CoV-2 may multiply at the expense of human gut bacteria, is further substantiated, it would

drastically change the model of acting and infecting of SARS-CoV-2, and most likely that of other human pathogenic viruses.

Keywords: COVID-19; SARS-CoV-2; gut microbiota.

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