

Yeast as a model to study the effect of SARS-CoV-2 non-structural proteins on cell stress response and interactions with cell components

The project aims at studying the effects of the ectopic expression of SARS-CoV-2 non structural proteins nsp3, nsp4, nsp6 e nsp15 on cell viability and on programmed cell death, on cell stress response and on nucleus-cytoplasm-mitochondria communication. Moreover, the intracellular localization of the viral proteins will be identified, as well as the formation of replication organelles.

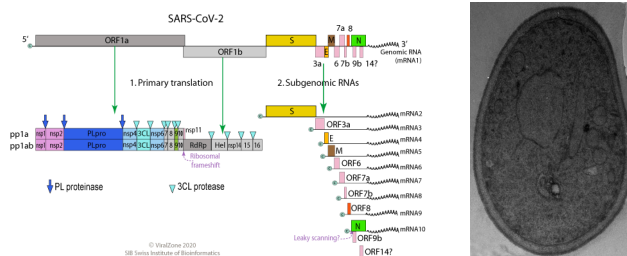
The budding yeast *Saccharomyces cerevisiae* will be used as a safe non-animal model, since this unicellular organism shares all the features with higher eukaryotes. Viral proteins are being cloned under the control of specific promoters in different strains of *Saccharomyces cerevisiae*. The biological activity of the ectopic expression of SARS-CoV-2 non structural proteins in yeast cells will be evaluated by bio-imaging, RNA-seq, pull-down assay, biochemistry assays, electron microscopy. The study of the interactions of the viral protein with cell membranes and of the effects on cell functions will shed light on virus-host cell interactions, and will allow the identification of new protein interactors and antiviral therapy targets.

Partners in this project are the Institute of Biomembranes and Bioenergetics (CNR-IBIOM) and the Institute for Sustainable Plant Protection (CNR-IPSP), Bari, with the following research staff:

IBIOM: Dott. Sergio Giannattasio, Dott. Antonella Bobba, Dott. Giuseppe Petrosillo, Dott. Alessandra Costanza;

IPSP: Dott. Luisa Rubino, Dott. Angelo De Stradis, Sig. ra Antonia Antonacci

The research staff has a long standing experience in the study of positive-strand RNA viruses and in the viral proteins expression in yeast and has all the know-how to carry out the experiments. A collaboration will be set with the University of Bari "Aldo Moro" and the European Research Infrastructures ELIXIR and EuroBioimaging.



Left: SARS-CoV-2 genome organization and expression (available at <https://viralzone.expasy.org/9076>)
 Right: electron microscope analysis of a *S. cerevisiae* cell

References Rubino et al. *Mech Ageing Dev* 161 (2017) 255–261; Rubino et al. *J Gen Virol* 81 (2000) 279-286; Navarro et al. *J Gen Virol* 87 (2006) 705-714; Rubino et al. *J Gen Virol* 88 (2007) 1634-1642; Guaragnella et al. *FEMS Yeast Research*, 18, 2018, foy088;

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