Set up of experimental models for the study of virus host interactions and discovery of novel host-targeted approaches against respiratory viruses

Among the human pathogens, respiratory viruses, such as influenza virus and coronaviruses (CoVs), have the highest potential to create epidemics and global severe pandemics, since they transmit efficiently between humans by contact with suspended droplets or fomite, have an asymptomatic infectious period that facilitate virus dissemination from infected persons, and are associated with a plethora of symptoms thus hampering an accurate early diagnosis. Although there has been significant progress in understanding the mechanisms involved in their infectivity and pathogenicity, the complex virus-host interactions underlying severe infections, e.g. SARS-CoV-2 induced disease (COVID19), have yet to be fully understood. To go insight this issue, this project, in strict collaboration with the Public Health Dept. of Sapienza University, is firstly aimed at the establishment of suitable in vitro experimental models that may recapitulate the natural setting of the infection. Specifically, experiments are ongoing to set up experimental infection models in nasal epithelium cell line and primary human small airway epithelial cells with different respiratory viruses, such as human influenza (H1N1 strain), NL-63 coronavirus, and SARS-CoV-2 (in collaboration with BSL-3 labs). These models will allow to investigate viral replication and the inflammatory response in different airway epithelial districts. Furthermore, to study the potential damaging effects of respiratory viruses on brain cells, experimental models of infection are setting up in human neuronal or glial cell lines as well as primary culture of neurons and glia cells form rodents. Overall, these models will be exploited for the identification of host factors that could be a potential target of therapeutic strategies. Along this line, we started focusing on ACE2, the SARS-CoV2 receptor, which is a member of the renin-angiotensin system (RAS) that hydrolyzes Ang-II to form Ang eliciting anti-inflammatory pathways and modulating intracellular redox state. Despite its role in viral entry, the protective role of ACE2 in the pathogenesis of respiratory lung infections, including SARS-CoV and influenza virus, was demonstrated in many in vitro and in vivo studies. Indeed, during respiratory viral infection the down-regulation of ACE2 has been related to the induction of Acute Respiratory Distress Syndrome (ARDS). This finding suggests that the use of compounds that modulate ACE2 expression could decrease the severity of infection and ameliorate its outcomes. RAS interfering compounds such as Stilbenes has been also reported to impair the replication of several viruses, suggesting that ACE2 modulation could affect viral life-cycle. We are currently evaluating the effect of Resveratrol analogue compounds on ACE2 modulation and their efficacy against respiratory virus infections.

Keywords: respiratory viruses; influenza virus, coronaviruses; SARS-CoV.2; experimental models of infection; ACE2 modulators

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Others: abstract: “ACE2-modulating compounds for the treatment of respiratory viral infections” by DE ANGELIS, PROTTO, PACIFICI, DI MARTINO, DE CHIARA, STEFANELLI, GARACI, DELLA MORTE, PALAMARA, NENCIONI presented at SIM 2020 (n°76 book of abstract)