The impact of COVID-19 on rare diseases: Incontinentia pigменти (IP) as a model to improve the knowledge on both COVID-19 and IP

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- The emergence of severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) disease (COVID-19) has caused a large global outbreak. COVID-19 affected people with mild or severe symptoms that leads to pulmonary inflammation and cause the lung failure (Acute Respiratory Distress Syndrome) especially in patients with older age and comorbidities (diabetes mellitus, hypertension, and heart failure). The SARS-CoV-2 infection invokes a hyperinflammatory state driven by multiple cells and mediators. Recently we reported in an international collaborative study that at least 10% patients with life-threatening COVID-19 pneumonia have neutralizing auto-Abs against type I IFNs or in 3-4% of cases inborn errors of type I IFNs.

Interestingly, this study revealed that a young patient affected by a rare disease, Incontinentia pigменти (IP, OMIM308300), developed very severe form of COVID-19 including respiratory limiting and showed neutralizing auto-Abs against type I IFNs. Moreover, the presence of auto-Abs was pre-existing to SARS-CoV-2 infection in the 25% of IP patients without COVID-19, a percentage higher respect the general population (25% vs 3%). IP is an X-linked dominant disease caused by NF-κB Essential MODulator (NEMO/IKBKG) mutations. Its pathogenesis is strictly related to a critical inflammatory response that results in the abnormal production of inflammatory cytokines and chemokines, IL-6, and TNFα, although IP has not been previously associated auto-Abs against type I IFNs.

We are evaluating the impact SARS-CoV2 infection in IP patients to investigate the genetic background in our cohort of IP patients belonging to our BBMRI-IPGB biobank (INCONTINENTIA PIGMENTI GENETIK BIOBANK, http://www.igb.cnr.it/ipgb/) to reveal the genetic alterations that regulate the production of auto-Abs. This project is done in collaboration with the research group of Prof JL Casanovà in France and with the help of the Italian Association of IP patients (IPASSI ONLUS). We are collecting clinical information related to COVID-19 disease by characterizing a specific COVID-19 clinical profile trough a survey (project approved by COMITATO ETICO SPALLANZANI Parere #170_2020_IP Covid) on the CNR platform (https://survey.cnr.it). In the main time, we are investigating the presence of Auto-Ab in the plasma of the in IP patients participating to the survey and/or belonging to our IPGB biobank. Moreover, we will search for genetic factors shared in the severe forms to identify the candidate variations/genes/pathways in IP involved in clinical variability of COVID-19 disease.

The expect output will permit to identify putative cellular/molecular target for novel drugs and an early treatment in COVID-19 and in IP diseases.

References:
Auto-antibodies against type I IFNs in patients with life-threatening COVID-19.

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