Offspring immunity is altered by maternal SARS-CoV-2 infection

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Maternal immune activation (MIA) has been linked to various offspring diseases, including neuropsychiatric disorders and asthma. Up to 20 million pregnant women are infected by SARS-CoV-2 annually, with millions of children exposed to a potential influence of the MIA effect. The implications of MIA on offspring immunity, however, are poorly understood as of today.

We therefore investigated the impact of SARS-CoV-2-induced MIA on postnatal lung immune development and susceptibility to infection in mice.

We induced MIA by infecting pregnant females at embryonic day 14.5 with SARS-CoV-2 and assessed the immune development in the offspring by analyzing lung, blood, and bone marrow cell composition through flow cytometry. In parallel, offspring were challenged with *Streptococcus pneumoniae*, where disease severity, bacterial clearance and immune response were evaluated.

In MIA-affected offspring, we observed an expansion of lung eosinophil and neutrophil populations during early lung immune development (0–4 weeks). Elevated pulmonary neutrophil numbers persisted into adulthood and were accompanied by increased expression of pro-inflammatory cytokine genes in the lung, including *Il1b* and *Tnfa*, suggesting a more inflammatory lung micro-environment. Accordingly, MIA provided protection against bacterial pneumonia caused by *Streptococcus pneumoniae*, leading to a significantly improved survival. This could be explained by enhanced early cytokine production and neutrophil recruitment to the lung upon infection in MIA offspring.

Our findings demonstrate that MIA alters postnatal lung immune development, highlighting the active engagement of neutrophils in both homeostasis and bacterial infection responses. This study offers new insights into the effects of MIA and the potential crosstalk between maternal immune status and fetal immune programming.