ImmunoTools *special* Award 2021

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T Cell Lymphopenia in Respiratory Viral Infections

Respiratory viruses have the greatest potential to cause wide-spread epidemics, such as SARS-CoV-2 and Respiratory Syncytial virus (RSV). In COVID-19 disease, prolonged lymphopenia is a very common finding in both the most severe and moderate cases, but the cause for it is unknown. More importantly, lymphopenia predicts worse outcomes and mortality. The lymphopenia is more pronounced in a specific T cell population called Mucosal Associated Invariant T (MAIT) cells. Similar, but only transient, global T cell lymphopenia is common in infants that suffer from bronchiolitis caused by the RSV. Also in RSV bronchiolitis the lymphopenia is associated with increased morbidity. However, there is no knowledge of MAITs kinetics in RSV infection.

MAITs are a relatively recently identified innate-like T cell population. They are defined based on the expression of their invariant T cell receptor and many innate receptors (such as CD161) mostly expressed by innate lymphocytes such as natural killer cells. MAITs recognize and are activated by bacterial and fungal metabolites presented in an evolutionary conserved, and non-variable major histocompatibility complex-like molecule MR1 that is expressed on many different cell types. Therefore, they are believed to have a significant role in mucosal early responses to bacterial and fungal pathogens. MAITs are activated in some viral infections, mostly through indirect cytokine-mediated activation, but their relative significance in acute viral infections is still mostly unknown. T cells generally do not express the SARS-CoV-2 receptor ACE2 and productive infection of lymphocytes with the virus have not been convincingly shown. Interestingly, MAITs do express low levels of ACE2. It is thus possible that the SARS-CoV-2 virus has a direct effect on MAITs or MAITs could be even infected with the virus. Also RSV have been shown to directly infect T cells but generally the cause for T cell lymphopenia in RSV bronchiolitis is unknown. In addition, thymic involution which leads to insufficient production of naïve T cells is suggested to be the main reason for failure of older individuals to raise efficient immune responses to new pathogens or vaccines. This phenomenon has been proposed to contribute to COVID-

19 severity in the elderly, but thymic output has not been studied in prospective patient cohorts yet.

By identifying the risk factors and pathophysiology of severe respiratory viral infections, we can prepare for the next pandemic and develop treatments targeting the dysregulated immune response rather than the virus. We hypothesize that the lack of T cells could exacerbate immune dysregulation in severe viral infections. Lower thymic output and lower number of MAITs could be predisposing risk factors for severe COVID-19. Similarly, a physiologically low number of MAITs in neonates could lead to a more severe RSV bronchiolitis.

Thus, our focus is to study the mechanism that causes the T and more specifically MAITs lymphopenia and recent thymic emigrants (RTEs) during acute disease in respiratory viruses infection. In longitudinal samples we aim to study how well the immune system recovers from it. Here, T cells, B cells and monocytes will be distinguished with CD3, CD14 and CD19 antibodies. MAITs will be classified with CD161 and Va7.2 antibodies. CD4, CD8, CD45RA and CD31 antibodies will be used as markers of Näive T cells and RTEs. CD69, CD25 and HLA-DR antibodies will be used to identify activated cells after viral challenge. ImmunoTools fluorescently labelled antibodies would provide a good opportunity for target cells status study after viral challenge and longitude target cell kinetics study in viral infections.

ImmunoTools *special* AWARD for **Xiaobo Huang** includes 10 reagents

FITC - conjugated anti-human: CD14, CD19

PE - conjugated anti-human: CD4, CD31

PerCP - conjugated anti-human: CD8, CD45RA, HLA-DR

APC - conjugated anti-human: CD3, CD19, CD69

DETAILS more AWARDS