INFECTIOUS INTERACTIONS: HOW EPITHELIAL CELLS DETERMINE THE OUTCOME OF RESPIRATORY VIRAL INFECTIONS IN CONCERT WITH ACTIVATED MONOCYTE-MACROPHAGE RESPONSES

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Abstract text

Text: Background:

Respiratory viral infections caused by SARS-CoV-2 and Influenza virus pose significant public health concerns, with severe outcomes for at-risk and even healthy patients. While disease severity is often associated with dysregulated monocyte-macrophage activities in patients, emerging evidence highlights the active role of infected epithelial cells in early viral defense with subsequent implications on disease severity.

Methods and Results:

We assessed the contribution of monocytes to host defense against respiratory viral infections and discovered that mice deficient in the C-C chemokine receptor type 2 (*Ccr2*$^{-/-}$ mice) exhibited a markedly worsened outcome, increased viral load and more severe lung damage following SARS-CoV-2 infection, whereas we found similar disease severity upon Influenza A virus (IAV) infection. Both viral infections prompted early monocyte infiltration in wild-type mice, and longitudinal RNA sequencing of sorted lung monocytes and monocyte-derived macrophages in SARS-CoV-2 and IAV infection revealed transcriptionally similar yet temporally distinct gene expression patterns, including an induction of Interferon (IFN) type I and type II dependent genes. Interestingly, transcriptional responses in epithelial cells differed significantly between SARS-CoV-2 and IAV infection. This, and the fact that WT bone marrow transplanted in *Ccr2*$^{-/-}$ mice could not mitigate disease severity upon SARS-CoV-2 infection, supports the critical role of epithelial cell responses in the context of CCR2 deficiency.

Conclusions:

Our findings emphasize the significant role of epithelial cells in shaping the immune response during respiratory viral infections. The distinct interactions between epithelial cells, monocytes, and macrophages can lead to varying antiviral immune outcomes, as observed in SARS-CoV-2 and IAV infections, warranting further investigation.

Conflict of Interest statement

Do you have any conflict of interest to declare?: No

Affirmation

1. Consent to participate and present onsite: Yes

2. Consent to publication publication: Yes

3. Consent on treatment of contact details saved in this system: Yes