Immunology of Flu Infection: The Pociask Lab

During flu infection, the virus itself does not cause morbidity and mortality. Instead, it is the immune response to the virus and the virus' ability to skew the immune system toward certain response pathways. As a result, the immune system itself can damage the lung, and further shift the immune response in such a way that the body in ill-equipped to deal with subsequent infection. This is why mortality from flu is usually associated with bacterial pneumonia. The lab of **Derek Pociask** studies both how one immune signaling molecule, IL22, is important to the immune response to flu as a cause of lung injury, and more broadly examines how it impacts lung injury outside of infection.

IL22 in Influenza: Signaling Repair

IL22 belongs to the IL10 family of immune cytokines. While it is made by T-cells, IL22 receptors are only expressed on mucosal epithelial cells, *e.g.* the cells of the lung. This means that, unusually for a cytokine, its communicative capabilities are "one-way". This molecule is important in its ability to control the proliferation and expansion of progenitor cells. The Pociask Lab is interested in this molecule's ability to control lung tissue repair. In murine models, knock out of the IL22 gene leads to less epithelial repair following lung injury. Additionally, giving exogenous IL22 following lung injury encourages repair. The Lab is currently employing a strategy where they target endogenous inhibitors of IL22 to increase IL22 signaling and repair processes, with the ultimate goal of finding ways to therapeutically intervene during flu infection.

Immunology

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IL22 Binding Protein: A Target for Therapy

The IL22 molecule is endogenously inhibited by the IL22 Binding Protein (IL22BD). IL22B acts like a sponge, sopping up IL22 and rendering it unable to initiate its signaling cascade. The Lab has observed that mice lacking the IL22BP gene recover following flu infection, while it is normally lethal to wild-type mice with the IL22BP gene.

Targeted inhibition of IL22BP, because of the restorative and proliferative effects of IL22, can be helpful to lung injury beyond that caused by flu infection. Currently, the lab is collaborating with AI drug discovery company Atomwise to identify and screen potential small molecule inhibitors of IL22BP. It is hoped that these molecules could be developed into a viable treatment option for flu. In flu, while vaccination is quite effective, treatment options once you are infected are limited and can have low efficacy.

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