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| **Role and therapeutic manipulation of iron metabolism in asthma and influenza-A virus infection associated disease** |
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| **Introduction/Aim:** Dysregulated iron metabolism is associated with asthma and influenza-A infection (IAV). The iron uptake protein, transferrin receptor-1 (*TFR1*) gene expression is increased in asthmatic sputum and murine lung tissue from experimental asthma and cellular iron loading within the lung and airways is associated with asthma pathophysiology. Respiratory viral infections are well-documented exacerbators of asthma and contribute to the development of asthma itself. We hypothesised that dysregulated iron metabolism in airway mucosal cells and tissues, drives the pathogenesis of asthma and IAV infection-induced disease. We aimed to determine the role and therapeutic potential in targeting TFR1 in both cases.  **Methods:** Asthma was modelled by house dust mite (HDM)-induced allergic airways disease and by culturing murine bone marrow derived-macrophages with IL-13 and HDM. Iron overload was modelled by culturing human airway epithelial cells (AECs) with ferric and ferrous iron, and *ad libitum* consumption of 2% carbonyl iron in mice. TFR1 and IL13 blocking antibodies (αTFR1, αIL13) were administered intranasally in our asthma model and αTFR1 was administered in our IAV-infection model (7.5PFU; A/PR8/H1N1).  **Results**: αTFR1 reduced TFR1hi granulocytes, airways inflammation, airways mucus hypersecretion, airways fibrosis and lung Matrix-Metalloproteinase-9 *(Mmp9)* gene expression, and improved lung function in our asthma model. Murine bone marrow derived macrophages (BMDM) stimulated with *Il-13,* had increased *Tfr1,* and *Il13+HDM* exposureincreased *Mmp9* geneexpression. αIL13 reduced lung *Tfr1hi* granulocytes *in vivo.*  Increased iron in AECs and murine lung was associated with increased viral titre and IAV-induced disease severity. *TFR1* gene expression was decreased in IAV-infected AECs and murine lung tissue. aTFR1improved IAV-induced disease outcomes *in vivo* (weight loss, airways inflammation, lung function and anti-viral and pro-inflammatory responses).  **Conclusion:** This study demonstrates therapeutic potential for manipulation of TFR1 in asthma and respiratory IAV infection. |