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| **Role and therapeutic manipulation of iron metabolism in asthma and influenza-A virus infection associated disease** |
| **Amber Pillar 1,** Alexandra Brown 1, Katie Daly1, Alen Faiz2, Karosham Diren Reddy2,3, Jessica Barnes 1 , Ama-Tawiah Essilfie4 , Gabriela Hoefel1 , Md Khadem Ali 5 , Kristy Nichol1, Richard Kim6 , Chantal Donovan 6 , Henry Gomez 1 , Kanth Swaroop Vanka 1 , Kane Prebedon1, Hock Tay 1 , Nazanin Kermani8 , Yi-ke Guo8, Sharon Mumby9, Ian Adcock9 , Greg Anderson4 Alan Hsu1,10, David Fraser4, Daniel Johnstone 1 , Elizabeth Milward 1 , Philip Hansbro9 , Peter Wark 1 , David Reid6 , Paul Foster 1 , Jemma Mayall1, Jay Horvat 1 |
| 1. The University of Newcastle, Hunter Medical Research Institute, Newcastle, NSW, Australia
2. Respiratory bioinformatics and molecular biology group, School of Life Sciences, Faculty of Science, University of Technology Sydney, NSW, Australia
3. Respiratory cellular and molecular biology group, Woolcock Institute of Medical Research, Glebe, NSW, Australia
4. QIMR-Berghofer Institute of Medical Research, Brisbane, QLD, Australia
5. Division of Pulmonary and Critical Care Medicine, Stanford University, Stanford, California, USA
6. School of Life Sciences, Faculty of Science, University of Technology Sydney, Sydney, NSW, Australia
7. Center for Inflammation, Centenary Institute, University of Technology, Sydney, NSW, Australia
8. Department of Computing & Data Science Institute, Imperial College London, London, UK
9. Airways Disease, National Heart & Lung Institute, Imperial College London, London, UK
10. National University of Singapore (NUS) and Duke-NUS Medical School, Singapore.
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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.  |