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| **Peripheral Blood T cell signatures during acute exacerbation of four common lung diseases: chronic obstructive pulmonary disease, asthma, cystic fibrosis and non-cystic fibrosis bronchiectasis** |
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| **Introduction/Aim:**  Pulmonary exacerbations are a common feature of chronic obstructive pulmonary disease (COPD), asthma, cystic fibrosis (CF) and non-cystic fibrosis bronchiectasis (NCFB). Individuals hospitalised with these chronic airway diseases usually have severe disease and experience repeated exacerbations, but the impact on the host immune response and in particular, T cell responses and potential for exhaustion and thus loss of immune function is poorly characterised.  As a first step towards understanding the role of T cell immunity across these airway diseases, we characterised and compared Tcell phenotypes during acute exacerbations of COPD, asthma, CF and NCFB. We compared both activation and exhaustion markers and investigated expression of these immune checkpoint markers over the course of an exacerbation through to clinical resolution.  **Methods:**  Peripheral blood mononuclear cells were isolated from people with COPD, asthma, CF and NCFB and analysed using flow cytometry to examine the activation status of conventional CD4, CD8, regulatory T cells and mucosa associated invariant T cells. Blood was collected at the time of admission with an acute exacerbation and followed through to clinical resolution.  **Results:**  Our analysis found that asthma and NCFB were the most alike with both diseases characterised by an exhausted phenotype observed across multiple T cell lineages. In contrast, people with COPD had distinct features characterised by up-regulation of immune checkpoint inhibitors CTLA4 and PD-1. In contrast, people with CF were characterised by upregulation of inhibitory TIM3. Interestingly, despite these major differences at time of presentation, in all four diseases there was little change in the comparative levels of each immune check point marker or overall significant change in expression apparent during treatment despite clinical improvement experienced in all subjects.  **Conclusion:**  This is the first observational study of its kind to directly compare immune inhibitory and activation markers across four major respiratory diseases during an acute exacerbation. Our analysis highlighted evidence of global dysfunction across multiple T cell populations, which will facilitate the discovery of new novel therapeutic targets in in these devastating diseases.  **Grant Support:**  QIMR-Berghofer Clinician Research Collaboration Grant award 2015.  TPCH Research Foundation Murray New investigator award (Abella Murray). |