4.02 P2 receptor expression profiles in circulating and airway cells in Idiopathic Pulmonary Fibrosis.

Luke Forde [1], Debananda Gogoi[1], Rory Baird[1], Cormac McCarthy[2,3], Emmet E McGrath[2,3], Emer P. Reeves[1]

1) Department of Medicine, Royal College of Surgeons Ireland, Dublin, Ireland 2) Saint Vincent's University Hospital, Dublin, Ireland 3) University College Dublin, Dublin, Ireland.

Background: Idiopathic pulmonary fibrosis (IPF) is a progressive fibrotic interstitial lung disease (ILD), of unknown aetiology with a poor prognosis (1,2). There has been recent interest in purinoceptor signalling with a role reported in almost all major lung diseases (1). The P2 receptor family is subdivided into G-protein–coupled receptors (P2Y1, P2Y2, P2Y4, and P2Y6 receptors) and ATP gated ion channels (P2X1, P2X2, P2X3, P2X4, P2X5, and P2X7 channels). Purinoceptors and activators have previously been reported upregulated in ILD, but remain poorly understood (1,3,4). The aim of this study was to explore the panel of purinoceptors present in IPF patients, and levels of extracellular activators (ATP), to improve our understanding and provide targets for intervention.

Methods: Clinical samples were collected including nasal cells, bronchoalveolar lavage (BAL) and blood for isolation of plasma and monocytes. ATP was detected using ATP bioluminescence assay on plasma and BAL. Gene expression was assessed following RNA extraction and RT-qPCR analysis.

Results: Increased ATP was recorded in BAL and plasma of ILD patients in comparison to healthy control. Increased expression of P2X1, P2X4, P2X7, P2Y6, P2Y11, P2Y12 and P2Y13 was observed in IPF monocytes. Moreover, in BAL and nasal cells P2X3, P2X7, P2Y6, P2Y12 and P2Y13 were highly expressed.

Conclusions: Our study demonstrates increased P2 receptor expression in IPF. Further studies are underway to understand their involvement in disease initiation and progression.

Disclosures:

Funding: StAR MD programme 2023, Royal College of Surgeons Ireland and Blackrock Clinic, Dublin. Ethics was approved by the St Vincent's Healthcare Group Ethics Committee.
Conflict of Interest*: The authors declare that they have no conflict of interest.*
References:

1) Purinergic Signalling in the Distal Lung in Health and Disease. PMID: 32674494

2) Idiopathic Pulmonary Fibrosis. PMID: 29742380

3) The purinergic receptor subtype P2Y2 mediates chemotaxis of neutrophils and fibroblasts in fibrotic lung disease. PMID: 28415591;

4) Extracellular ATP is a danger signal activating P2X7 receptor in lung inflammation and fibrosis. PMID: 20522787.

Corresponding Author: Luke Forde, lukeforde23@RCSI.com, ORCID ID 0000-0002-3738-6512