Seminar's informations Anya Jones and Kyle Mincham

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Biopolymères Interactions Assemblages

Asthma as a Systemic Disease - Activation of inflammatory cells during asthma exacerbations is initiated prior to their migration to the lung

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Abstract

Introduction:

Underlying acute asthma are recruitment of immune cells into the airways and ensuing activation of complex inflammatory gene networks. However, the precise location of tissue compartment(s) where activation of inflammatory cells is initiated, and the full range of gene networks involved, are incompletely understood.

Aim:

To characterise the cellular and molecular mechanisms underlying severe exacerbations of asthma and identify molecular drivers of these mechanisms.

Methods: Comparative cellular (Flow Cytometry) and molecular (RNA-Seq) profiling was employed of PBMC, obtained from atopic asthmatic children (n=19) presenting to the emergency department during an asthma exacerbation and following recovery. Network and upstream regulator analysis was employed to identify coexpression networks and infer the drivers of these networks.

Results:

Circulating PBMC exhibited reduced cell numbers (lymphocytes, dendritic cells) consistent with trafficking from blood to infection sites, in contrast, monocyte numbers were elevated. Network analysis identified coexpression networks associated with myeloid migration and activation, and the principal chemokine receptor CCR2 was upregulated, associated with lung homing. Upstream regulator analysis identified TGFB1 as the dominant molecular driver of the myeloid-associated modules.

Conclusion:

Components of the inflammatory cell activation process associated with acute asthma are triggered prior to their recruitment into the lung. Hence, novel therapies may benefit if targeted at relevant precursor populations in their tissues of origin as opposed to only after their recruitment to the airways.