Abstract: P378

Circulating B cell phenotypes in chronic thromboembolic pulmonary hypertension

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Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare consequence of venous thromboembolism. Mechanisms underlying thrombus persistence are unclear. Since splenectomy is a risk factor for CTEPH and the spleen is important for B cell maturation, we hypothesised that CTEPH patients might be characterised by alterations in circulating B cell phenotypes.

Purpose

In this study, we aimed to characterise circulating B cells of CTEPH patients with regard to total B cell numbers, B cell subpopulations, cytokine production and B cell receptor signalling.

Methods

We analysed peripheral B cells of 9 CTEPH patients by mass cytometry and compared them with cells from 9 idiopathic pulmonary arterial hypertension (IPAH) patients and 11 healthy control subjects. We stained peripheral blood mononuclear cells (PBMCs) with a panel of metal-conjugated antibodies recognising 21 surface antigens to define different B cell subsets. These extracellular markers were combined with two different sets of antibodies detecting intracellular targets, analysing phosphosignalling as well as cytokine production both at baseline and after cell stimulation. Data was collected on a CyTOF2 mass cytometer.

Results

Mass cytometry of CTEPH, IPAH and control PBMCs revealed a decrease in total B cell numbers in CTEPH compared to IPAH and controls. Importantly, this decrease did not affect the subpopulation of B-1 cells, resulting in an increase of B-1 cell frequency relative to total B cells in CTEPH. Interestingly, CTEPH B cells shared functional characteristics with IPAH B cells, with increased production of IL-6 and increased phosphorylation of Stat1 at baseline. In CTEPH, but not IPAH B cells, we also found increased Stat5 phosphorylation at baseline. Upon B cell receptor activation, both CTEPH and IPAH B cells displayed greater induction of phosphorylated p38 MAP kinase and ribosomal protein S6.

Conclusions

Our data suggest an important role for B-lymphocytes in CTEPH. Individuals with CTEPH were characterized by decreased number of circulating B cells accompanied by a relative increase of the B-1 cell subset.
Interestingly, B cells of CTEPH patients, despite being reduced in number, had an activated phenotype similar to IPAH B cells, which may reflect spontaneous germinal centre formation and increased (auto-)antibody production. Further studies will be necessary to better describe the role of B cells in CTEPH and to discern changes in B cell function related to thrombus persistence from those related to pulmonary hypertension.