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Title: LSC 2012 abstract – The protective role of Pim1 in cigarette smoke induced damage of airway epithelium

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Body: Rationale The main risk factor of developing COPD is exposure to cigarette smoke. CS exposure induces airway epithelial cell damage, release of DAMPs and an innate inflammatory response. We previously observed increased expression of Pim1 in vivo after sub-chronic CS exposure in mice. Pim1 is a serine/threonine kinase involved in cell growth and survival by preventing apoptosis induction through the mitochondrial pathway. We hypothesize that Pim1 plays a protective role in the airway epithelium after CS exposure by phosphorylating BAD and enhancing cell survival. Methods Pim1-KO mice were exposed to CS twice a day for 4 days. Inflammatory cells and KC levels in BAL were determined. Beas-2b cells were treated with CS extract (CSE) for 4 hours with(out) Pim-inhibitor. Mitochondrial membrane potential (ΨM) and apoptosis/necrosis induction were measured by flowcytometry. BAD phosphorylation was determined by Western Blotting. Results CS exposure induces neutrophilic airway inflammation and increases KC levels in Pim1-KO mice, but not in WT controls. CSE induces a dose-dependent loss of BAD phosphorylation, loss of ΨM and necrotic cell death in Beas-2b cells. All of these CSE-induced effects are aggravated by inhibition of Pim1. Conclusion Pim1 protects airway epithelial cells from CS-induced damage and cell death by phosphorylating BAD and increasing the threshold for apoptosis. In vivo, this protective effect suffices to prevent CS-induced neutrophilic airway inflammation.