European Respiratory Society
Annual Congress 2012

Abstract Number: 4633
Publication Number: 4541

Abstract Group: 3.2. Airway Cell Biology and Immunopathology
Keyword 1: Asthma - mechanism **Keyword 2:** Epigenetics **Keyword 3:** Cell biology

Title: miRNA-17 and -144 regulate cAMP-responsive element binding protein (CREB1) signaling in murine ovalbumin-induced asthma and in human bronchial epithelial cells

Ms. Sabine 28389 Bartel Sabine.Bartel@helmholtz-muenchen.de [1], Dr. Francesca 28390 Alessandrini franci@helmholtz-muenchen.de [2], Prof. Dr Oliver 28391 Eickelberg oliver.eickelberg@helmholtz-muenchen.de MD [1] and Dr. Susanne 28392 Krauss-Etschmann Susanne.Krauss-Etschmann@med.uni-muenchen.de MD [1]. [1] Comprehensive Pneumology Center, Helmholtz Zentrum München, Munich, Germany, 81377 and [2] Center for Allergy and Environment, Helmholtz Zentrum München, Munich, Germany, 81377 .

Body: Background: MicroRNAs (miRs) are small non-coding RNAs that are essential for immune function and lung development. They are influenced by environmental exposures such as smoke or nutrition, both of which are also known to affect asthma risk development. Previously, we reported increased pulmonary expression of miR-17 and -144 in mice with OVA-induced asthma. This correlated with decreased mRNA and protein levels of CREB1, a validated target of both miRs. In addition, the cAMP-regulated transcriptional co-activators, CRTC-1 and -3, have been described to enhance CREB1-mediated gene transcription (Altarejos et al., Nat Rev Mol Cell Biol., 2011, 12) and are also predicted targets of miR-17 and -144. Thus,we hypothesized that miR-17 and -144 regulate CREB1/CRTC-mediated gene transcription in experimental asthma and sought to elucidate this interdependency in vitro. Methods: Human bronchial epithelial cells (16HBE) were transfected with precursor miRs or antagomiRs for miR-17 and miR-144. The expression of miR and endogenous CREB1, CRTC-1, -2, and -3 was assessed by RT-qPCR and Western blot analysis. Results: The mRNA levels of CRTC-1 and -3, but not CRTC-2 in the lung were decreased in OVA-induced murine asthma. In 16HBE cells, the mRNA and protein levels of CREB1 and the mRNA levels of its co-activators CRTC-1,-2, and -3 were significantly decreased after transfection with precursor miR-17 and -144. Vice versa, their expression increased after inhibition of miRs by antagomiRs. Conclusion: These findings suggest a role for microRNA-17 and -144 in the regulation of CREB1/CRTC signaling of potential relevance in asthma.