AAIR Charity
ASTHMA, ALLERGY & INFLAMMATION RESEARCH

Research Award:
The role of pericytes in ADAM33 induced airway remodelling in asthma.

Awarded to: Hans Michael Haitchi Amount: £11,762

Lay summary

AAIR Anuj Panchmatia Award 2014/2015 "The role of pericytes in ADAM33 induced airway remodelling in asthma" – "Understanding the role of the asthma gene, ADAM33, in the airways in asthma", awarded to Associate Professor Dr Hans Michael Haitchi in support of postdoctoral research fellow Elizabeth R Davies.

Asthma is a common lung disease in the UK and is commonly triggered by exposure to allergens, viruses and pollutants. Asthma tends to run in families, which suggests an underlying genetic contribution. The aim of our work is to understand the how an asthma gene, known as 'ADAM33', contributes to the development of asthma.

We recently published our exciting new discovery that the asthma gene ADAM33 plays an important role in driving the structural changes (remodelling) that occur in the airways of asthmatic patients (University of Southampton press release). Of great interest and very novel is the fact that this takes place without inflammation of the airways, which is contrary to current beliefs that inflammation is the driver of the development of remodelling in asthma. "Pericytes" are cells found within the walls of blood vessels and have stem cell properties (ie. they can give rise to many other cell types). When stimulated pericytes can grow and become smooth muscle cells and fibroblasts, both cell types, which are known to contribute to remodelling of asthmatic airways.

To elucidate the role of pericytes in this remodelled airways we studied lungs from mice producing the 'faulty' ADAM33 protein and lung tissue from patients with asthma. We have shown that markers for pericytes are increased in the lungs from mice producing the 'faulty' ADAM33 protein. Furthermore, when we studied these markers in small pieces of human lung tissue from healthy subjects and asthmatic patients we could detect the pericytes, and they seem to be different in healthy and asthmatic samples.

The support for Lizzie Davies as part of this subproject of our ADAM33 work has resulted in a first author publication in The Journal of Clinical Investigation-Insight 2016 and she has presented her work at several local, national and international meetings.

Based on this work, we were successful in a grant application for a Medical Research.

Foundation/Asthma UK grant for 3 years in 2016, which allows us to further study the role of the 'faulty' ADAM33 protein in early life development of asthma.

Publications

- R. Davies, J.F.C. Kelly, P.H. Howarth, D.I Wilson, S.T. Holgate, D.E. Davies, J.A. Whitsett, H.M. Haitchi. Soluble ADAM33 initiates airway remodeling to promote susceptibility for allergic asthma in early life. JCI Insight. 2016 Jul 21;1(11). pii: e87632: https://insight.jci.org/articles/view/87632.
- The press release from the University of Southampton related to our research publication had been widely covered by most major national newspapers as well as national radio and many other international media: https://www.southampton.ac.uk/news/2016/07/adam-33-gene.page.

Presentations

- Elizabeth R. Davies, Joanne F.C. Kelly, Peter H. Howarth, Stephen T. Holgate, Donna E. Davies, Jeffrey A. Whitsett, Hans Michael Haitchi. Soluble Enzymatically Active ADAM33 Initiates Airway Remodelling and Promotes Allergic Asthma In Early Life. Annual Meeting of COST BM 1201: Early Origins of Chronic Lung Disease: "The end of the beginning". Athens, Greece, 3-4 November 2016.
- Elizabeth R. Davies, Joanne F.C. Kelly, Peter H. Howarth, Stephen T. Holgate, Donna E. Davies, Jeffrey A. Whitsett, Hans Michael Haitchi. Enzymatically Active sADAM33 Is Increased in Asthma and Causes Airway Remodelling Without Inflammation, 31st Symposium of the Collegium. International Allergologicum in Charleston, South Carolina, USA, 5 April 2016.
- Elizabeth R. Davies, Joanne F.C. Kelly, Peter H. Howarth, Stephen T. Holgate, Donna E. Davies, Jeffrey A. Whitsett, Hans Michael Haitchi. sADAM33 Causes Airway (P) Remodeling In Early Life and Enhances Eosinophilic Airway Inflammation and Bronchial Hyperresponsiveness, 31st Symposium of the Collegium International Allergologicum in Charleston, South Carolina, USA, 5 April 2016.
- ER Davies, JA Whitsett, DE Davies, HM Haitchi. Soluble ADAM33 causes airway remodelling to promote allergic airway inflammation. Thorax 2015;70(Suppl 3): S128, A73. British Thoracic Society (BTS) Winter meeting, London, December 2015.
- ER Davies, ST Holgate, DE Davies, JA Whitsett, HM Haitchi. The asthma susceptibility gene ADAM33 promotes structural remodelling to augment airway inflammation and bronchial hyperresponsiveness. Oral presentation at Faculty of Medicine Conference, 17 June 2015, Southampton, UK.

- ER Davies, ST Holgate, DE Davies, JA Whitsett, HM Haitchi. Asthma-Like Airway Remodelling Induced by ADAM33 Is Reversible. Oral presentation Breaking Boundaries Conference, Faculty of Medicine, University of Southampton, 24 September 2014, Southampton, UK.

External Grants

- Medical Research Foundation (MRF)/Asthma UK Research Grant (MRFAUK-2015-322): The impact of pre- and perinatal ADAM33 induced airway remodeling on sensitivity to environmental challenges and the early life development of asthma. PI: HM Haitchi, 2016 – 2019: £ 291,756.
