

## Project Title

## Understanding the pathobiology of asthma and allied disorders

## Researcher

Prof. Stephen T Holgate



Country	▶ United Kingdom
Field	▶ Immunopharmacology
Scientific Affiliation	▶ University of Southampton, Faculty of Medicine

## Abstract

Study of cellular and molecular basis of asthma identifies novel therapeutic targets for asthma. Motivated by the rising asthma death rate in the 1970-80s linked to overuse of  $\beta$ -agonist bronchodilators, Stephen Holgate pursued a research career focused on understanding the mechanisms of asthma and uncovering novel therapeutic approaches. Particular achievements:

- To definitively establish the direct involvement of mast cells in human asthma and establishing the link between mast cell activation and leukocyte (especially eosinophils and T helper 2 lymphocytes) recruitment into the airways.
- The first to place the epithelium at the centre of asthma pathobiology and to demonstrate its role in driving both acute and chronic inflammation and remodelling the airways in chronic disease.
- Defining a role for the bronchial epithelium and characterise it as a chronic wound response of the epithelium which not only contributed to increased inflammation, but also increased susceptibility to other asthmagens such as viral infection and air pollution. We introduced the concept of reactivation of the epithelial-mesenchymal trophic unit similar to that occurring in branching morphogenesis of the foetal lung to sustain chronic airway inflammation and remodelling.
- Uncovering reversibility of the remodelling response that identifies inhibition of ADAM33 as a novel therapeutic opportunity for altering the natural history of human asthma.
- Identifying the role of viruses especially rhinovirus in the causation of asthma exacerbations.
- The discovery of impaired production of interferon- $\beta$  by the asthmatic epithelium contributing to viral exacerbations of asthma leading to the first clinical development of inhaled IFN- $\beta$  in the treatment of viral asthma exacerbations.

## Biography

Prof. Holgate is Medical Research Council Clinical Professor of Immunopharmacology at the Faculty of Medicine in Southampton. After completing his medical training in London, he spent two years at Harvard Medical School to acquire skills in allergic disease mechanisms. On returning to Southampton in 1980, he set up a research group focused on the causative processes leading to asthma and allied diseases and produced over 1000 peer-reviewed publications achieving an h index of 165. He has received a number of honours and awards including the Paul Ehrlich Prize of the European Academy of Allergy Asthma and Clinical Immunology, the William Frankland award for Clinical Allergy and the British Thoracic Society Medal.

