

Press information

A new therapeutic target in allergic asthma

Vincent Sauzeau, Inserm researcher and his team located at the Nantes Thorax Institute¹ (Inserm, CNRS, University of Nantes, Nantes University Hospital) have recently discovered the major role played by the Rac1 protein in the development of bronchial hyperresponsiveness associated with allergic asthma. Researchers will use this new therapeutic target to reduce bronchoconstriction and pulmonary inflammation in patients. This article has been published in [The Journal of Allergy and Clinical Immunology](#).

Allergic asthma is a major public health problem, which currently affects 8 to 10% of the global population. It represents 70% of the various types of asthma, and is responsible for more than 250,000 deaths per year. Asthma attacks are triggered by an allergen, which induces excessive contraction of muscle cells in the bronchial wall (bronchial hyperresponsiveness). This reduces the diameter of the bronchi and causes breathing difficulties in the patient (sense of suffocation, shortness of breath, cough, wheezing, etc.).

Vincent Sauzeau, Inserm researcher and his team have recently evidenced the essential role played by the Rac1 protein in bronchial muscle contraction and bronchial hyperresponsiveness associated with allergic asthma, making Rac1 a new therapeutic target in allergic asthma.

A promising avenue for treating patients

The researchers used a dust-mite sensitized asthmatic mouse model to imitate the human disease, in order to determine the role of Rac1 in bronchial hyperresponsiveness. They noted that inhalation of a Rac1 inhibitor prevents bronchial hyperresponsiveness in this allergic asthmatic mouse model. Furthermore, bronchial inflammation and the infiltration of certain white blood cells into the lungs (which promote bronchial hyperresponsiveness in allergic asthma) are also reduced by long-term administration of the Rac1 inhibitor. The research team observed a 70 to 80% reduction in bronchial contraction due to Rac1 inhibition, on bronchial samples taken from lung transplant patients.

"Blocking the activity of Rac1 made it possible to both limit bronchial contraction during an asthma attack, and also to reduce local inflammation during maintenance therapy," clarifies Vincent Sauzeau, Inserm researcher leading these studies. The inhibitors used in these studies are research instruments, which can only be used in a laboratory setting. Hence, the researchers are currently developing new molecules for clinical applications.

This research team, in partnership with the Pulmonology Department at the *Thorax Institute* based at Nantes University Hospital has recently obtained funding to verify the relationship between bronchial hyperresponsiveness and abnormal Rac1 activation in the bronchi in patients suffering from allergic asthma. *"If this relationship is confirmed, this will validate the significance of developing a new Rac1 inhibitor for therapeutic purposes in humans. It would then be administered by inhalation, for a targeted action in the bronchi,"* concludes Vincent Sauzeau. At present, 5 to 10% of patients suffering from allergic asthma do not gain any relief

¹ (<http://www.umr1087.univ-nantes.fr/>)

from standard anti-inflammatory and bronchodilator treatments. Rac1 inhibitors could offer new therapeutic solutions.

Sources

Targeting of Rac1 prevents bronchoconstriction and airway hyperresponsiveness

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