Asthma : good and bad eosinophils

8/23/16

The eosinophils that contribute to inflammation and exacerbation of the asthmatic response had been known to scientists for some time. But another type of eosinophil has been discovered that, to the great surprise of Researchers at the University of Liege's GIGA research centre, has been shown to play a protective and beneficial role. Their astonishing discovery is published in *The Journal of Clinical Investigation* (1).

During allergic reactions such as asthma, our immune system does not work correctly and responds in an abnormal way to harmless allergens present in the environment (pollen, dust mites etc.). In an asthmatic individual, the eosinophil cells - granulocytes that are produced in the bone marrow and which circulate in the body via the blood - are recruited to the lungs where they participate to the pathological manifestations associated with an asthmatic reaction. In an article published in *The Journal of Clinical Investigation*, researchers at the University of Liege have, for the first time, identified the existence of a sub-group of eosinophils called resident eosinophils which are present in the lungs of healthy individuals and which, unlike inflammatory eosinophils, play a regulatory and protective role while maintaining the balance of the immune system and preventing it from responding in an abnormal way such as observed during an asthma attack. The discovery of these specific eosinophils offers promising therapeutic and prophylactic opportunities for the treatment and prevention of asthma.

A team of scientists directed by Professor Fabrice Bureau and Dr, researchers at ULg's GIGA research centre, discovered this sub-type of eosinophil in mice and subsequently in humans. In mice, the nucleus of these resident eosinophils appears as a ring shape (or doughnut shape), which make them easily...
distinguishable from the other inflammatory eosinophils. In humans, all eosinophils have the same morphology, which could explain why the sub-types have only just been discovered. The researchers have also demonstrated, in both mice and humans, that the resident eosinophils carry an identical marker on their surface, the protein CD62L, which means that they are easily distinguishable from inflammatory eosinophils.

By pursuing their investigations, the researchers observed that, in mice that are deficient in lung-resident eosinophils, the "allergic" immune response was greatly exacerbated after inhalation of small doses of allergens, suggesting that these specific eosinophils play a role in the prevention of asthma sensitization and therefore in the regulation of pulmonary immune homeostasis. Specifically, resident eosinophils act upstream of the inflammatory cascade by inhibiting the activation of dendritic cells. In the case of asthma as in the case of other inflammatory diseases characterised by an abnormal response of the immune system, the dendritic cells - veritable sentinels of the immune - surveillance system - are activated and trigger a chain of events which ultimately results in exaggerated inflammation and clinical manifestations of the disease, which is partly due to the activation of inflammatory eosinophils.

"For the first time, this study identifies a distinct sub-type of non-inflammatory pulmonary eosinophils in mice and humans which seem to be able to prevent the development of abnormal immune responses. Because these disorders of the immune system are involved in many disease conditions such as asthma, food allergies, Crohn's intestinal disease or autoimmune diseases, this fundamental discovery is of outstanding interest to identify a way to prevent the development of these diseases", explains Dr. Thomas Marichal.

"Recent anti-asthmatic treatments by injection of interleukin-5 monoclonal antibodies have proven to be clinically effective, but it was not understood why they did not totally eradicate the eosinophils, whose survival and function depend on interleukine-5. In light of our study, we now understand that, in fact, they spared the "good" regulating lung-resident eosinophils that are not so dependent on Interleukin-5 and that is a very good thing !", explains Professor Fabrice Bureau.
"In the future, the question is to know how to facilitate the production of resident eosinophils, rather than inflammatory eosinophils, in the bone marrow. Indeed, by acting at the top of the cascade, we will have new weapons for the prevention of inflammatory diseases such as allergies or autoimmune diseases", concludes Professor Fabrice Bureau.

(1) "Lung-resident eosinophils represent a distinct regulatory eosinophil subset. Claire Mesnil et al. The Journal of Clinical Investigation."