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Curriculum vitae

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Master of Medicine	2015 - 2018

Key publications

Declercq J, et al. Repeated COVID-19 mRNA-based vaccination contributes to SARS-CoV-2 neutralizing antibody responses in the mucosa.
Science Translational Medicine 2024

Declercq J*, et al. Effect of anti-interleukin drugs in patients with COVID-19 and signs of cytokine release syndrome (COV-AID): a factorial, randomised, controlled trial.
Lancet Respiratory Medicine 2021 *Shared first authorship

Declercq J, et al. Chitin is a potent inducer of type 2 airway inflammation independent of endogenous chitinolytic activity.
Under revision

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FACULTY OF MEDICINE AND HEALTH SCIENCES

Respiratory immunity at the intersection of infection, vaccination and allergy

Mechanisms and modulation of type 1 and type 2 inflammation in the upper and lower airways

Jozefien Declercq

Dissertation submitted to obtain the degree 'Doctor in Health Sciences'

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Summary

With every breath we take, our airways are exposed to countless inhaled particles, including viruses, bacteria and allergens. To keep us healthy, the airways rely on several defense mechanisms. Among the most important are local immune responses, both in the upper airways (the nose) and the lower airways (the lungs). These immune responses must be carefully balanced: if too weak, serious infections can occur; if too strong, they can damage the airways and cause breathing difficulties. In this thesis, we studied two conditions in which this balance of respiratory immunity is disturbed: COVID-19 and allergic asthma.

Severe COVID-19 is characterized by an overactive immune response in the lungs, which can lead to serious breathing problems. During the pandemic, several existing medicines that block certain immune signals were tested to help severe COVID-19 patients recover. In the first part of this thesis, we carried out a clinical trial to test drugs that block two immune messengers called interleukin-6 and interleukin-1. Unexpectedly, we did not find that patients given these drugs recovered faster compared to those who did not, neither did they prevent mortality.

Vaccines have been very successful at preventing COVID-19. However, to stop infection altogether, the immune system needs to act right at the virus's entry point: the nose and upper airways. In the second part of this thesis, we investigated whether COVID-19 mRNA vaccines can induce such local immunity. We found that repeated vaccination can lead to virus-blocking antibodies in the nose, but these responses are rather short-lived. Using a mouse model, we discovered that the majority of these antibodies originate in the blood and then move into the respiratory tissues.

Allergic asthma is caused by the immune system overreacting to harmless environmental substances, such as house dust mites, grass and tree pollen, leading to airway inflammation, mucus plugging and breathing difficulties.

In the third part of this thesis, we investigated chitin, a natural substance that is found in many allergens, including house dust mites, cockroaches, and crustaceans, to see if it could play a role in asthma. We showed that inhaled chitin promotes allergic asthma. Interestingly, while humans and mice do not synthesize chitin themselves, they do express enzymes, called chitinases, that break it down. To test whether these chitinases could influence chitin-driven asthma, we used genetically modified mice that lack chitinases.

In the final part of this thesis, we describe two new mouse models that will help researchers study allergic adaptive immune responses in much more detail. We generated the Derby mouse strain, in which most B cells recognize Der p 2, a major allergen found in house dust mite. The other strain, the 2der mouse strain, expresses T cells that are reactive to Der p 2. Together, these tools allow for a detailed study of adaptive immune responses mounted by natural allergens.

Overall, this thesis advances our understanding of how the respiratory immune system responds to infections, vaccines, and allergens. The described findings contribute to ongoing efforts to develop targeted strategies that prevent or cure respiratory diseases.