# Newly discovered cell type plays a crucial role in the immune response to respiratory infections

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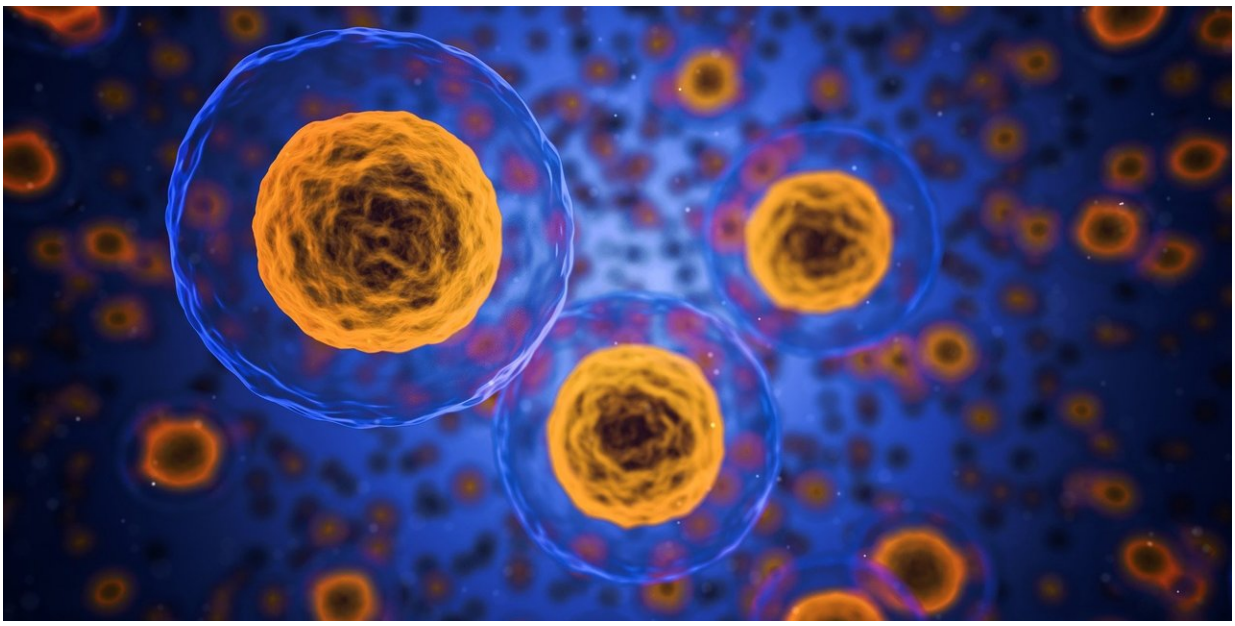

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With a discovery that could rewrite the immunology textbooks, an international group of scientists, including the teams of Bart Lambrecht, Martin Guilliams, Hamida Hammad, and Charlotte Scott (all from the VIB-UGent Center for Inflammation Research) identified a new type of antigen-presenting immune cell. These cells, that are part of an expanding family of dendritic cells, play a crucial role presenting

antigens to other immune cells during respiratory virus infections, and could explain how convalescent plasma helps to boost immune responses in virus-infected patients.

## Inflammation and immunity

When our body faces an infection, it responds with inflammation and fever. This is a sign that the immune system does its work, and leads to the activation of many cells, like soldiers in an army. Dendritic cells (DCs) are the generals of that army. They can precisely activate and instruct the soldiers to kill infected cells by presenting antigens derived from the 'invaders' to cells of the immune system.

## Mistaken identity

There are several types of DCs that perform antigen-presenting functions in the body. A first type of conventional DCs continuously scan the body for dangerous invaders, even when there is no infection. When there is inflammation triggered by infection, another subset of DCs emerges from inflammatory monocytes. Because monocyte-derived DCs are easily prepared in vitro from monocytes isolated form human blood, it was always assumed these cells were very important antigen-presenting cells. Clinical trials using monocyte-derived DCs in cancer therapy have however been
disappointing.

A study by the teams of Bart Lambrecht, Martin Guilliams, Hamida Hammad, and Charlotte Scott (all from the VIB-UGent Center for Inflammation Research) and international colleagues, shows that monocyte-derived DCs are poor antigen-presenting cells, but have wrongly been assumed to have these functions because of a case of mistaken identity.

The scientists studied mice with a viral respiratory infection (pneumonia virus of mice and influenza virus) with single-cell technologies. This single-cell resolution allowed them to finely separate the monocyte-derived cells from other DCs during their response to the infection. They found that monocyte-derived DCs do exist, but actually do not present antigens. The reason for all the confusion in the past is that a look-alike new DC emerges—called inflammatory type 2 conventional DC, or inf-cDC2—that combines some of the best characteristics of monocytes, macrophages, and conventional DCs, to induce the best form of immunity.

Bart Lambrecht: "This was a big surprise for us. We've all been taught that monocyte-derived cells are excellent antigen presenting cells, certainly when there's inflammation. Now, we show that it's actually a new hybrid DC type that's doing all the work. This really changes what we know about the immune system and is very important knowledge for understanding respiratory viral infections and other inflammatory diseases."

Martin Guilliams: "It took a massive team effort but the strength of single-cell sequencing has finally cracked the complex DC code. Many contradicting findings from the last two decades now make much more sense. This also opens tremendous therapeutic opportunities, since vaccination strategies can now be designed to trigger formation of inf-cDC2s and thus generate a stronger antiviral immune response."

Charlotte Scott: "Through the use of single cell technologies we have been able to align all the findings from the past few years and identify the distinct cell types involved. Moving forward it will be very interesting to see under what other inflammatory conditions these inf-cDC2s are generated and how they can potentially be targeted therapeutically."

## Convalescent plasma and COVID-19

The findings of the researchers also have a direct relevance for the current COVID-19 pandemic, caused by another respiratory virus. An emergency treatment that is currently being explored is the use of convalescent plasma, or the blood plasma of recovered patients.

Cedric Bosteels, lead author of the new paper: "One of the unique features of the new DCs is that they express functional Fc receptors for antibodies that are found in the plasma of patients who have recovered from COVID-19"

This study is the first to show that one of the mechanisms through which convalescent plasma and the virus-specific antibodies in it work, is via boosting of inf-cDC2. Since boosted DCs induce a much stronger immune response, this study reveals a new target for therapeutic intervention for viral infections and other inflammatory diseases.

**More information:** Inflammatory Type 2 cDCs Acquire Features of cDC1s and Macrophages to Orchestrate Immunity to Respiratory Virus Infection. *Immunity*. 2020

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