Redefining our immune response

Our immune system is at war with the microorganisms attempting to invade our body and cause us harm. However, the fight is not quite black and white, with our own "good guys" able to do us ill. **Jamie McCarthy** is a PhD student in the Department of Infection, Immunity and Inflammation and will talk through both sides of the story for one particular immune cell type.

Setting the scene

Our scientific understanding is constantly evolving over time; manifested in this article by observing the immune system. The vast majority of the cells which characterise our immune response have been identified within the last 50 years, making this a relatively young subject–in scientific terms! Cultivated by research, the way we describe immune cell interactions is constantly progressing.

Several research groups will often have the same focus; this results in a rush to publish the best data in the most prestigious journals. This competitive landscape results in a fast paced rewriting of once central dogma.

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New kid on the block

In 2002 it was known that messenger proteins such as Interleukin-13, were required to combat parasitic worms. Current theory placed the source of these proteins as white blood cells called T cells. These are well characterised white blood cells responsible for many aspects of our immune response. One of the first studies to test this was conducted on mice genetically modified to be unable to produce both T and B cells. Unexpectedly however, Interleukin-13; the messenger protein utilised by the body to fight against parasitic worms was still produced in an infection indicating that messenger proteins were also produced elsewhere.

The cells responsible were identified and characterised in 2010 as a new type of immune cell. Different research groups assigned various names to this cell and it wasn't until 2013 that the current name, Group 2 Innate Lymphoid Cells (ILC2s), and the characteristics used to define these cells were widely agreed upon.

Knowing their place

It is worth noting that in this instance it does not appear to be the ILC2s who are getting their hands dirty and directly dealing with the parasite. The ILC2s appear to be aiding the recruitment of other cells, acting as a "conductor" of the immune response; shown by these cells taking in information from the surrounding environment and producing signals to tailor the correct response from the body. These signals are proteins that would act to recruit specific immune cells to the scene. In this way it would appear they are part of our rapid response team of immune cells, whereas other lymphoid cells will come in afterwards to cover this role long term.

> "The ILC2s appear to be aiding the recruitment of other cells, acting as a "conductor" of the immune response"

The messenger proteins produced by ILC2s are certainly not unique. They are produced by a wide range of cells within the body, often cells which are much more populous and whose biology is more widely understood. Deciphering whether ILC2s are indeed the source of high concentrations of messenger proteins in a particular scenario is one of the barriers for wide acceptance for this cell's role. Researchers must justify why such a rare cell has such a significant effect within the body; much in the same way a small vocal group of people may have their opinions heard over a silent majority.

They've got a dark side too…

So far ILC2s appear to be a force for good within our immune response. But our immune system is not that simple. ILC2s have also been implicated in several instances of allergic disease, namely those of the lung, the skin and within our digestive tract. This is when an over active immune response actually starts to cause damage to our own body.

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ILC2s have been shown as a cell that produces messenger proteins. ILC2s are a very rare cell type. This is perhaps why they remained undiscovered for so many years. Despite this they are messenger protein factories producing a larger amount of protein when compared to other similar cell types. This fact is one of the key reasons they are implicated in allergic disease; the over production of messenger proteins can cause inappropriate activation of our immune system. To this end, ILC2 derived proteins have been implicated in the diseases: asthma, atopic dermatitis (a skin condition similar to eczema) and ulcerative colitis (an inflammatory disease of the intestines).

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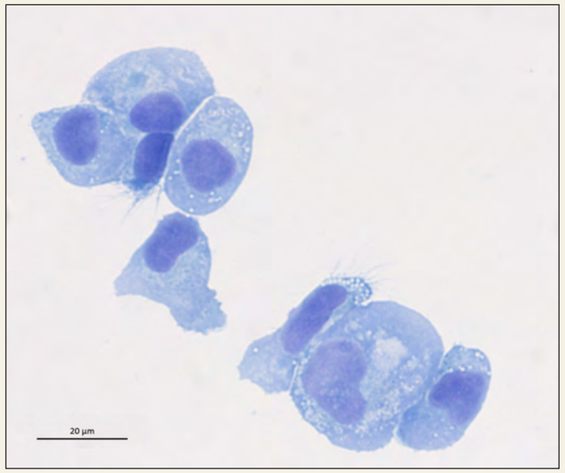
A therapeutic target?

Understanding the role of ILC2s in Asthma is of particular interest, as they may hold the answer to long-standing mystery within the disease. Asthma exacerbations can be very serious and lead to severe illness and hospitalisation. The most common cause of an exacerbation is through a viral infection. How the virus causes such an impact is not fully understood. It is possible that ILC2s are responding inappropriately to one of the many damage signals put out following an infection (such as interleukin-25 or interleukin-33) resulting in an imbalance of messenger proteins, which can cause damage to the body.

Once the biology of asthma exacerbations is fully understood it may provide opportunities for therapeutic targets and potential new treatments could be trialled. Specifically, nullifying the effects of various messenger proteins has already been the subject of several pharmaceutical clinical trials, resulting in several licensed drugs available for use.



Light Microscope image of isolated ILC2s

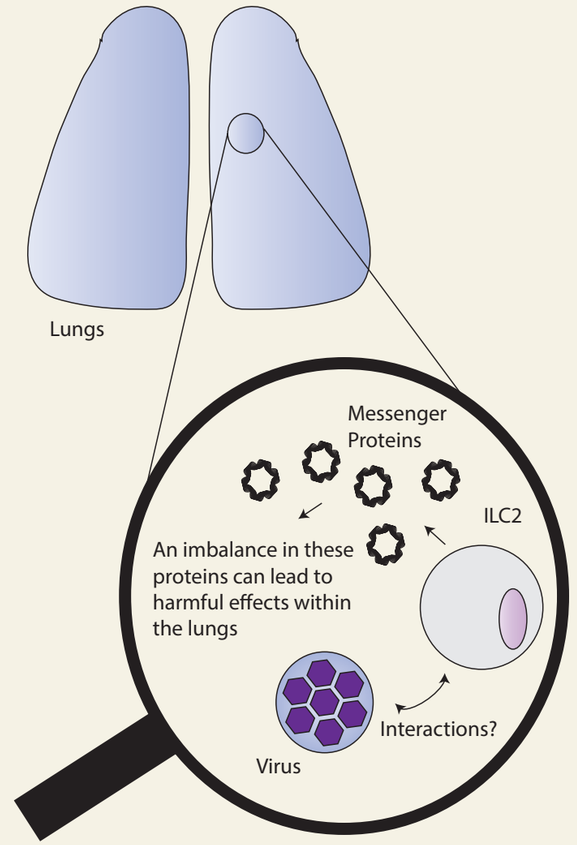


Illustration to represent potential interactions between ILC2s and viruses and the consequences.

My research focuses on adding to our understanding of ILC2s within the context of Asthma. I am studying the interactions between a virus and the cells within our lungs, focusing on the environment within our body which occurs during an Asthma exacerbation. If it is found that ILC2s provide a mechanistic link between the virus and the symptoms of exacerbations it will illuminate potential avenues for treatments. Most likely to be the messenger proteins to which ILC2s respond (interleukin-25 and interleukin-33). It remains to be seen whether ILC2s play a crucial role in facilitating the suffering an individual experiences within an exacerbation and the subsequent burden on the healthcare system this results in.

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