



Rogue lung cells solve **asthma mysteries**

Dr John Faul is leading an Irish research project that shows there is a build up of a certain type of cells in the lungs of people who have asthma, writes Sheila O'Kelly

THERE IS a large number of a particular type of inflammatory cells in the lungs of people who have asthma, but not in people who don't. This has been discovered by Dr John Faul who is consultant physician in respiratory medicine at Connolly Hospital, Blancharstown. This cell is called the invariant Natural Killer-T cell (iNKT).

People with asthma have the same low levels of iNKT cells in the bloodstream as everyone else, but the difference is that someone who has asthma accumulates a high number of these cells in their lungs.

Dr Faul is leading a pioneering three-year research study to find out why these cells build up in the lungs of people with asthma. "Preventing iNKT cells from accumulating in the lung may be a new approach to treating asthma," said Dr Faul.

"We can only find very, very small numbers of iNKT cells in the lungs of people who do not have asthma. However, in people who have asthma, some 60% of the T cells are iNKT cells compared to 1% in the rest of the population.

"In people without asthma, iNKT cells do go into the lungs but they either migrate out again or they are being killed there – we don't know which," said Dr Faul.

Dr Faul has been working on this research for five years. He recently received a joint three-year research grant from the Asthma Society of Ireland and the Health Research Board to continue his work. Papers detailing his research into these iNKT cells have been published in the respected professional peer-reviewed journals *New England Journal of Medicine* and *Nature Medicine*.

Why are iNKT cells important?

Until now researchers have focused on cells called CD4 T cells. These are the cells that 'learn' to give you an allergic reaction to the protein in things like pollen and cause an asthma attack.

However, this recent discovery shows that the iNKT cells that build up in the lungs don't just react to the protein in allergens like pollen, but they also react to a substance called glycolipids. In addition, while CD4 T cells 'learn' to react over time, the iNKT cells will react the first time someone with asthma is exposed to a new substance that contains glycolipids.

"This helps to explain why people can meet an entirely new pollen or get an infection that they have never had before and it triggers their asthma," said Dr Faul.

"In the old days we would have said that you would have had to have seen that pollen, inhaled it, processed it, and that these CD4 T cells would take 10 days to produce the chemicals that give you asthma.

Then if you came into contact with that pollen again, it would give you an asthma attack. Now we would say that with these iNKT cells, any glycolipid you come in contact with could immediately cause an asthma attack.

"So this reaction by iNKT cells to glycolipids is not a conventional allergy. Conventional allergies are a 'learned' reaction to proteins, but iNKT cells trigger a reaction to glycolipids on first contact.

"Before we could never figure this out.



that if people with asthma take inhaled steroids, it gets rid of most of the cells that cause asthma. However, Dr Faul said this new research shows that the iNKT cells are left behind.

The iNKT cells were a big discovery because for the first time they explained:

- Why people could still get asthma attacks while taking inhaled steroids;
- Why people who were not allergic still got asthma attacks; and
- Why infections could cause asthma attacks.

For example, if someone with asthma told us they went to a field of corn on their holidays in Greece and got an asthma attack, we would have said that was unlikely. This was because they had never been there before and we did not understand how they could have developed the allergy. Now we understand that not the protein in the pollen, but the glycolipid in the pollen could have triggered the immediate reaction.

"It also helps to explain why so many viral and bacterial infections cause asthma – you can't be allergic to all of them," said Dr Faul. Some people have non-allergic asthma and Dr Faul's research may show if they are reacting to the glycolipids and not to protein.

The research project will:

- Compare the different levels of iNKT cells in people with and without asthma;
- Study why these cells build up in the lungs of people who have asthma;
- Examine what the cells are doing;
- Investigate how they cause asthma;
- Look at how they get to the lungs; and
- Try to find out why they accumulate there.

iNKT cells and asthma medication

Some 80% of people with asthma are allergic and produce large amounts of IgE antibodies. Both people who are allergic and those who are not, have a build up of iNKT cells in their lungs. The newest therapy for asthma is anti IgE therapy but it is only useful for allergic asthma.

Over the last 10 years research has shown

"If we want to get an overall cure for asthma, it won't be enough just to stop people's sensitisation to protein because people could still react to glycolipids. We would need to find a way to stop people reacting to both proteins and glycolipids."

Dr Faul is collaborating with two other studies that are examining other aspects of iNKT cells. At Harvard University, Prof Dale T. Umetsu is working on how animals get an accumulation of these cells in their lungs. And in France Professor Mariette Lisbonne is studying how iNKT cells work in children.

Dr Faul has also received funding for his research from the US National Institute of Health. The Department of Respiratory Medicine in Connolly Blanchardstown Hospital, lead by Dr Conor Burke, Professor Len Poulter and Dr Liam Cormican, is assisting him with this current research.

Volunteer co-operation

Dr Faul said that Irish people were very enthusiastic about taking part in the study and providing samples for research.



"Patients want to know why they have asthma and they want the field of asthma to go forward.

"This is a fantastic initiative by the Asthma Society and it helps to push the field of research forward. If you do nothing now, nothing will get better for patients and that's terrible. This is the only way to do it.

"Irish people are very aware of asthma but may be too accepting of it – but it should be curable. They have to think about how great life would be if kids did not have asthma. It is the leading cause of lost school days and the commonest chronic medical illness of children in Ireland. It is also the commonest occupational disease. It would be fantastic if they could cure it – and it is achievable but it takes time, money and effort." **A**