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By 13 weeks of gestation, human fetuses have developed a much more unusual immune system than previously thought.

HUMAN DEVELOPMENT

Fetal immune system revs up in the womb

Human fetuses have an immune system that functions differently from the adult version.

BY HEIDI LEDFORD

A human fetus in its second trimester is extraordinarily busy. It is developing skin and bones, the ability to hear and swallow, and working on its first bowel movement. Now, a study published on 14 June in *Nature* finds that fetuses are also acquiring a functioning immune system — one that can recognize foreign proteins, but is less inclined than a mature immune system to go on the attack (N. McGovern *et al.* *Nature* <http://dx.doi.org/10.1038/nature22795>; 2017).

The results add to a growing body of literature showing that the fetal immune system

is more active than previously appreciated. “In general textbooks, you see this concept of a non-responsive fetus is still prevailing,” says immunologist Jakob Michaelsson at the Karolinska Institute in Stockholm. But the fetal immune system is unique, he says. “It’s not just immature, it’s special.”

A developing fetus is constantly exposed to foreign proteins and cells, which are transferred from the mother through the placenta. In humans, this exposure is more extensive than in many other mammals, says immunologist Mike McCune at the University of California, San Francisco. As a result, laboratory mice have proved a poor model for studying the

developing human fetal immune system.

But fully understanding that development could reveal the reasons for some miscarriages, as well as explain conditions such as pre-eclampsia, which is associated with abnormal immune responses to pregnancy and causes up to 40% of premature births. And organ-transplant surgeons have long been interested in how a developing fetus and its mother tolerate one another without either of them launching an immune attack — the hope is to find ways to suppress the immune system’s response to transplanted organs.

For Jerry Chan, an obstetrician and gynaecologist at the KK Women’s ▶

► and Children's Hospital in Singapore, understanding the fetal immune system was important for his goal of developing stem-cell treatments and gene therapies for genetic disorders in developing fetuses. Chan and his colleagues wanted to know whether there was a developmental stage at which such treatments could be given without the risk of the therapies themselves being attacked by the immune system.

To do this, Chan teamed up with immunologist Florent Ginhoux at the Agency for Science, Technology and Research in Singapore to study dendritic cells, immune cells that break down foreign material and present fragments of it to other immune cells called T cells. Some T cells are then activated to target the foreign material for destruction.

The team found that human fetuses have functional dendritic cells by 13 weeks of gestation. But although the cells behave much like the adult versions, their response to foreign human proteins differs: rather than mark the foreign material for annihilation, fetal dendritic cells are more likely to activate a special category of T cell called regulatory T cells, which suppress immune responses.

This could reflect a need to avoid a catastrophic immune response against a mother's cells. "You don't want too much immune response in a developing fetus," says Ginhoux. "It is very dangerous — this is a critical point in development."

Previous studies had found specialized immune cells — including T cells and natural killer cells — in fetuses as young as nine weeks, says Ginhoux.

But the dendritic-cell findings are particularly important because these cells orchestrate immune responses, says Michaelsson. Without them, he says, the body can't target specific foreign material for destruction.

The results highlight the fact that the fetal immune system is not merely an immature, less-active version of its adult counterpart, but one that has its own distinct function, says transplant immunologist William Burlingham at the University of Wisconsin in Madison.

Burlingham's laboratory had been studying fetal immune responses as a means of finding ways to help organ-transplant recipients tolerate their new organs without relying on immunosuppressive drugs. But a political uproar in the United States during the past few years over research using fetal tissue has made him shift much of his work to studying the newborn immune system, which tends to act more like the adult system.

The *Nature* study highlights how this shift could come at a price for many areas of research, says McCune. "It's important for us to understand the function of the human fetal immune system so that we can treat fetuses that are not doing well," he says. "And the analysis of adult and newborn cells is, as we now know, irrelevant. The fetal immune system is different." ■



TOBY MELVILLE/REUTERS

Theresa May's plan to increase her party's majority ahead of Brexit negotiations has backfired.

POLITICS

UK election raises hope of soft Brexit

Scientists hope for benefits in shock result.

BY ELIZABETH GIBNEY

The UK general election on 8 June has thrown the country's politics into disarray — but scientists trying to divine meaning from the chaos hope that the result will ultimately benefit their nation's research ties with the European Union.

The Conservative government had called the election in an effort to stretch its slim majority, which would have given it a firmer mandate to negotiate Brexit, the United Kingdom's split from the EU. The party, under the leadership of Theresa May, was aiming for a 'hard' Brexit — placing priorities on ending

the free movement of EU citizens to the United Kingdom, cutting immigration and taking the country out of the EU's single market. That stance alarmed scientists: it seemed likely also to cut the United Kingdom out of EU research programmes and dent the easy movement of scientists to and from the EU.

But the party actually lost seats — ending up eight short of an overall majority, although still the largest single bloc in the British parliament. After the result, which is termed a 'hung' parliament because no party has an outright majority, May said that she would form a government anyway, relying on the support of Northern Ireland's Democratic Unionist

UNEASY PARTNERS

The Democratic Unionist Party's controversial views

The Conservative Party is relying on an informal agreement with Northern Ireland's Democratic Unionist Party (DUP) to form the next government — which has put a spotlight on some DUP views. The party has a policy to block women's access to abortion; a Member of Parliament who has called the Paris climate pact "totally flawed and pointless"; and a sizeable minority membership who think that

creationism should be taught in science classes. But researchers needn't worry that such stances will affect UK laws: other politicians would veto them, says Kieron Flanagan, a science-policy researcher at Alliance Manchester Business School, UK. The DUP does advocate for a softer Brexit, however: it wants to maintain an open border with the Republic of Ireland after Britain leaves the European Union.