Testosterone explains why women more prone to asthma

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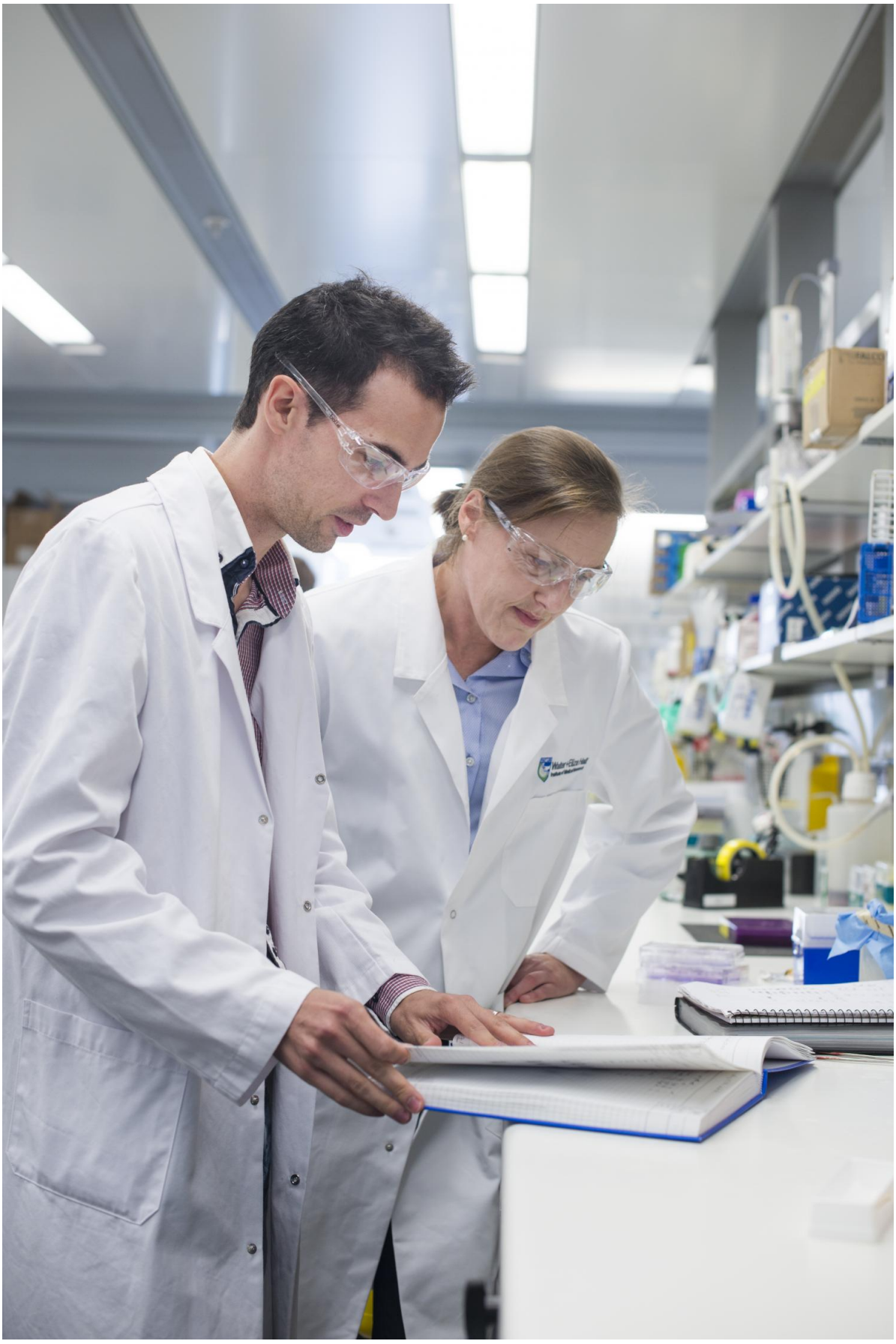

An international research team has revealed why women are twice as likely to develop asthma after puberty.Dr Cyril Seillet (left) and Professor Gabrielle Belz were part of an international research team that discovered testosterone protected males against developing asthma by suppressing immune cells that initiate the condition. Credit: Walter and Eliza Hall Institute

An international research team has revealed for the first time that testosterone protects males against developing asthma, helping to explain why females are two times more likely to develop asthma than males after puberty.

The study showed that testosterone suppresses the production of a type of immune cell that triggers allergic asthma. The finding may lead to new, more targeted asthma treatments.

One in nine Australians (2.5 million people) and around one in 12 Americans (25 million) have asthma, an inflammatory airway condition. During an asthma attack, the airways swell and narrow, making it difficult to breathe. In adults asthma is two times more prevalent and more severe in women than men, despite more being more common in boys than girls before puberty.

In 2016, the city of Melbourne, Australia, experienced a 'thunderstorm asthma' event that was unprecedented internationally in its scale and severity of consequences, with almost 10,000 people visiting hospitals over a two-day period. Thunderstorm asthma refers to allergic asthma thought to be initiated by an allergy to grass pollen. Many people with no history of asthma experienced severe asthma attacks.

Dr Cyril Seillet and Professor Gabrielle Belz from Melbourne's Walter and Eliza Hall Institute, with Dr Jean-Charles Guéry and his team at the Physiopathology Center of Toulouse-Purpan, France, led the study, published today in the *Journal of Experimental Medicine*.

Dr Seillet said hormones were speculated to play a significant role in the incidence and severity of asthma in women. "There is a very interesting clinical observation that women are more affected and develop more severe asthma than men, and so we tried to understand why this was happening," Dr Seillet said.

"Our research shows that high levels of testosterone in males protect them against the development of allergic asthma. We identified that testosterone is a potent inhibitor of innate lymphoid cells, a newly-described immune cell that has been associated with the initiation of asthma."

The research team found that innate lymphoid cells - or ILC2s - 'sensed' testosterone and responded by halting production of the cells.

"Testosterone directly acts on ILC2s by inhibiting their proliferation," Dr Seillet said. "So in males, you have less ILC2s in the lungs and this directly correlates with the reduced severity of asthma."

ILC2s are found in the lungs, skin and other organs. These cells produce inflammatory proteins that can cause lung inflammation and damage in response to common triggers for allergic asthma, such as pollen, dust mites, cigarette smoke and pet hair.

Professor Belz said understanding the mechanism that drives the sex differences in allergic asthma could lead to new treatments for the disease.

"Current treatments for severe asthma, such as steroids, are very broad based and can have significant side effects," Professor Belz said.

"This discovery provides us with a potential new way of treating asthma, by targeting the cells that are directly contributing to the development of allergic asthma. While more research needs to be done, it does open up the possibility of mimicking this hormonal regulation of ILC2 populations as a way of treating or preventing asthma. Similar tactics for targeting hormonal pathways have successfully been used for treating other diseases, such as breast cancer."

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