Scientists find key to miscarriages in blood clotting disorder

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Prof Harshal Nandurkar and Dr Anushka Samudra are respectively last and first authors on the paper on APS and miscarriage. Credit: Monash University

Monash University researchers have potentially shed light on why women with the rare autoimmune disorder Antiphospholipid syndrome (APS) are prone to successive pregnancy losses.

APS causes abnormal blood clots in the arteries or veins along with the risks that go with clotting, including stroke and Deep Vein Thrombosis. For pregnant women the effects of the disorder can be devastating, causing about half of them to be at risk of sequential miscarriages, spontaneous abortions or premature births.

Now researchers in Monash's Australian Centre for Blood Diseases have identified a protein that may protect against APS miscarriages. The researchers used purpose-bred mice injected with the antibodies that cause the condition to test the effects of the proteins CD39 and CD73, which work together to produce a molecule known as adenosine. Adenosine has anti-inflammatory, anti-oxidant and anti-clotting properties.

APS occurs when there is an increased level of circulating antibodies – the proteins designed to attack invading pathogens in the system but which, in the case of autoimmune diseases such as APS, attack the body's own cells. It was known that these antibodies were linked to clotting but not all patients with them go on to have APS; a "second hit" was suspected in triggering the disease.

Dr Maithili Sashindranath, a senior researcher on the paper, which appeared in the *Journal of Autoimmunity*, said the researchers went in search of this second hit.

"We set out specifically to investigate APS-induced miscarriages," Dr Sashindranath said.

The rates of miscarriages were compared in mice that lacked CD39 and CD73, in normal mice, and in mice with large amounts of the two proteins in their blood. The study found, as hypothesised, that mice that lacked CD39 and CD73 both had increased rates of miscarriages. Those with no CD39 lost 20% of fetuses. That is a six-fold increase compared

with normal mice which lost 3.67% of foetuses. The mice with no CD73 had a three-fold increase.

Mice with large amounts of CD39 had reduced miscarriage rates compared to those without it.

"Effectively what we were able to show is that the loss of CD39 or CD73 is likely to be the second hit – nothing like this has been shown before," Dr Sashindranath said.

The study lays the foundation for investigations looking at blood samples in women with APS to see if they have reduced levels of CD39/CD73 or antibodies which remove the activities of these proteins, she said.

"Down the track we can look at whether we can deliver CD39 to the affected foetuses using new drugs that we have developed and reduce the rate of miscarriages for these patients. We will also find out if we would be able to predict why some women with APS go on to develop devastating pregnancy complications and some don't."

Provided by Monash University