Pre-eclampsia may be autoimmune disease

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Biochemists at The University of Texas Medical School at Houston say they are the first to provide pre-clinical evidence that pregnancy-induced high blood pressure or pre-eclampsia may be an autoimmune disease. Their research could provide novel diagnostic and therapeutic possibilities for this intractable disease. Findings appear online in *Nature Medicine* on July 27.

Scientists in the laboratory of Yang Xia, M.D., Ph.D., an assistant professor of biochemistry and molecular biology at the UT Medical School at Houston, provided evidence of the connection by inducing symptoms similar to pre-eclampsia in pregnant mice that had been administered autoantibodies isolated from women with the condition. This proof-of-principle experiment is called adoptive transfer.

Pre-eclampsia typically occurs in the last trimester of pregnancy and is characterized by a sudden increase in blood pressure, excess protein in the urine and swelling of the hands, feet and face. It affects about one in 20 pregnancies and the only cure is delivery of the baby. Pre-eclampsia contributes to 15 percent of premature babies and is associated with a high incidence of mother and infant morbidity and mortality in the United States.

"There is no effective treatment for pre-eclampsia other than delivery, in part because of the lack of complete understanding of the disease," said Susan Ramin, M.D., study co-author, the Emma Sue Hightower Professor and Chair in the Department of Obstetrics, Gynecology and Reproductive Sciences at the UT Medical School at Houston and a

member of the medical staff of Memorial Hermann - Texas Medical Center. "This collaborative research is important because of its potential to lead to a possible cure of pre-eclampsia in pregnant women. Using the animal model we were able to prevent pre-eclampsia in pregnant mice. I don't want to overstate the implications, but this is clearly a very exciting time for all of us involved in the research. We plan to focus our efforts in expanding this research to pregnant women."

Unlike antibodies which attack foreign substances and clear diseases from the body, autoantibodies attack their own cells and cause conditions like lupus in which a person's immune system attacks the body's own organs and tissues, said Xia, the senior author. In the case of pre-eclampsia, autoantibodies are believed to bind and activate an angiotensin receptor that results in artery constriction.

Pre-eclampsia like symptoms were prevented when the pregnant mice were given agents designed to block the activation of the angiotensin receptor.

"The antibody injection model of pre-eclampsia described here provides strong experimental support for our working hypothesis that pre-eclampsia is an autoimmune disease in which angiotensin receptor–activating autoantibodies contribute to many features of the disease," Xia and her colleagues wrote in the paper.

If the research is confirmed in human trials, Xia believes this information could be used for both the earlier diagnosis and treatment of pre-eclampsia. By measuring autoantibody levels, clinicians could detect the disease weeks before symptoms appear. In addition, new drugs could be developed to inhibit the activation of the angiotensin receptor.

In the meantime, Xia said further research is needed to determine what triggers the production of the autoantibodies.

"Pre-eclampsia is one of the leading causes of prematurity and Small For Gestational Age (SGA) infants. Many of these babies are born with underdeveloped lungs or poor lung clearance of fluid, necessitating neonatal intensive care admission and various respiratory therapies to support their breathing. We continue to struggle to find a proven prevention or treatment solution for these problems," said Nehal A. Parikh, D.O., an assistant professor of neonatal-perinatal medicine at the UT Medical School at Houston and a member of the medical staff of Children's Memorial Hermann Hospital.

"If targeting the angiotensin receptor autoantibody is a useful strategy to treat pre-eclampsia, then it will also be a useful way to prevent and treat SGA associated with pre-eclampsia," Xia said.

The risk factors for pre-eclampsia include: having a history of pre-eclampsia; being obese; having twins, triplets or other multiples; and developing gestational diabetes.

Source: University of Texas