Genetic link to preeclampsia

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Researchers have linked a gene to development of preeclampsia, a condition that causes high blood pressure, fluid retention and swelling in pregnant women. The discovery may lead to development of a screening test to identify pregnant women at risk of the dangerous condition.

The research that linked the gene, called COMT, to preeclampsia was led by Dr Raghu Kalluri of Harvard University in collaboration with MRC-funded researchers Professor Asif Ahmed and Dr Shakil Ahmad at the Department of Reproductive and Vascular Biology in the University of Birmingham and Birmingham Women's Hospital. The results are published online in Nature.

Using mice genetically engineered to lack the COMT gene the team found that when the COMT gene was absent the mice experienced preeclampsia-like symptoms. These included protein leakage in urine, high blood pressure and problems with blood vessels in the placenta caused by decreased oxygen levels. The symptoms were reversed when the mice were given a supplement of a steroid hormone called 2-methoxyestradiol (2-ME).

This molecule is formed when the product of the COMT gene, an enzyme called catechol-O-methyltransferase (COMT) breaks down oestrogen, a hormone essential to healthy pregnancy. The 2-ME formed then suppresses the activity of a protein called hypoxia inducible factor that can lead to an increase in another protein that in turn initiates some of the symptoms of preeclampsia. Examples include damage to the kidneys and raised blood pressure.

In the absence of COMT and 2-ME the normal regulation of blood pressure during pregnancy is lost. As part of this research, Dr Shakil Ahmad found that patients who have preeclampsia have lower than usual levels of COMT and 2-ME. Dr. Shakil Ahmad said: "I am excited about the potential for this work to lead to patient benefit and am grateful to Professor Ahmed for his mentorship and support."

Professor Ahmed explained the significance of this finding: ''The link between low levels of COMT and 2-ME in women who have preeclampsia suggests that screening for irregularities in the COMT gene in pregnant women could identify those at risk of developing preeclampsia. The 2-ME, metabolised from oestrogen, may serve as both a diagnostic marker and therapeutic supplement for the treatment of preeclampsia.''

He concluded: ''The research itself is an excellent example of translational work, it has combined genetic observations in mice with evidence of lower levels of important proteins in patients to highlight that defects in the COMT gene could be used as a marker of preeclampsia risk and that 2-ME might have a role in treatment of preeclampsia.''