Scientists pinpoint molecular signals that make some women prone to miscarriage

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(Medical Xpress)—Scientists have identified molecular signals that control whether embryos are accepted by the womb, and that appear to function abnormally in women who have suffered repeated miscarriages.

The research, carried out at Imperial College London and the University of Warwick, suggests these signals could be targets for drugs that would help prevent miscarriage in women who are particularly vulnerable.

At the start of pregnancy, the fertilised embryo must embed itself in the lining of the uterus. The uterus is only receptive to embryos for a few days in each menstrual cycle, ensuring that embryos can only implant at the right stage of development. Currently scientists know only a few

details about the biological processes that control when an embryo can be implanted.

In the latest study, published in the journal *PLOS ONE*, researchers studied chemical signals produced by human cells, taken from the lining of the uterus and grown in the lab. They identified a key role for a molecule called IL-33, which the cells secrete during the receptive phase and which influences the activity of nearby cells.

Normally, the effects of IL-33 and other chemical signals in the lining of the womb are short-lived, which helps to ensure that woman can only conceive during a narrow window. In cells from women who had suffered three or more miscarriages however, high levels of IL-33 continued to be secreted for 10 days, suggesting that the receptivity of the uterus was not being controlled properly in these women.

The study also looked at the effects of these molecular signals on fertility in mice. The researchers treated the uteruses of the mice with chemicals secreted by cells from the human womb lining. They found that chemicals produced by cells from women with repeated miscarriages extended the time during which mice could become pregnant, but also made miscarriages more likely. The researchers conclude that a prolonged window of fertility increases the risk of abnormal embryos implanting. In addition, it is associated with inflammation in the lining of the womb, which compromises the development of healthy embryos.

Dr Madhuri Salker, a study author from the Department of Surgery and Cancer at Imperial College London, said: "Our study suggests that in women who have had successive miscarriages, the mechanisms that control whether the womb can accept and support an embryo don't work properly. This might mean they can become pregnant with poor quality embryos or that the embryo implants in an unsupportive environment,

which would seriously compromise the chances of a successful pregnancy."

The senior author of the study, Professor Jan Brosens from the University of Warwick, said: "The molecular signals we identified are known to be involved in a range of diseases, including Alzheimer's, asthma and heart disease. Our findings suggest that targeting these molecules might also be a promising strategy for developing treatments that would prevent miscarriages in women who are especially vulnerable."

More information: M.S. Salker et al. (2012) 'Disordered IL-33/ST2 activation in decidualizing stromal cells prolongs uterine receptivity in women with recurrent pregnancy loss.' PLoS ONE 7(12): e52252. doi:10.1371/journal.pone.0052252. www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0052252

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