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# Embryo implantation offers insight into infertility

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(PhysOrg.com) -- A process that governs embryo implantation in the womb in humans has been identified for the first time. The Oxford University research, published in the journal PNAS, could shed light on what goes wrong when embryos fail to implant in the lining of the womb, a leading cause of infertility.

'In many women, attachment and implantation doesn't happen and this is a major cause of infertility,' says Professor Helen J. Mardon of the Nuffield Department of Obstetrics and Gynaecology and St Catherine's College, University of Oxford, who led the study. 'By understanding how this process works, we may be able to inform the development of drugs to help embryos implant properly.'

Implantation relies on a set of closely coordinated events occurring between a very early stage embryo and the lining of the womb. The embryo must initially attach to and form a contact with the lining. Then cells from the embryo begin to invade the womb lining, eventually connecting with the mother's blood vessels and forming the placenta.

'The embryo and womb lining talk to each other, molecularly speaking, which allows them to interact,' explains Professor Mardon. 'When the embryo lands on the surface of the uterus wall, it triggers a cascade of signals in both the embryo and uterus. The resulting changes allow the embryo to invade the lining.'

'This invasion process has to be tightly regulated for a placenta to form

correctly and hook up with the maternal blood supply,' she adds.

The Oxford team, along with Professor Anne J. Ridley at King's College, London, have now identified molecules that are responsible for controlling the invasion of human embryo cells into the womb lining. Their research, funded by the Wellcome Trust and Medical Research Council, showed two proteins belonging to a family called Rho GTPases are involved. These proteins ensure cells in a small area of the womb lining move out of the way to allow cells from the embryo to invade.

'We have shown that two proteins, called Rac1 and RhoA, control the invasion,' says Professor Mardon. 'The first stimulates cells in the womb lining to move and allow the embryo to invade and implant properly while the second inhibits this. We believe this controlled balance of the two proteins is critical for successful implantation of the embryo.'

'If the balance of the Rho GTPases is altered, the cells of the womb lining don't migrate and the embryo doesn't implant.'

The researchers had to develop a way to investigate the molecular process of human implantation in the lab. Embryos were added to a layer of cells from the womb lining in a culture dish. The research team were then able to video embryos implant themselves in the cell layer.

'Essentially what we've done is to capture a particular stage of implantation going on in a petri dish,' says Professor Mardon. 'The experiment mimics the stage in which an early-stage human embryo invades the lining of the womb, and allows us to dissect the molecular processes that control this critical stage of implantation.'

Provided by Oxford University