New bioengineering approach to fix fetal membranes

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New research led by Queen Mary University of London and UCL has shown that small bioengineered molecules can be used to repair defects in the fetal membranes that surround and protect babies developing in the womb.

The study, published in the journal *Prenatal Diagnosis*, found that these molecules, known as peptide amphiphiles (PAs) self-assemble to form a 'plug' that seals holes within the fetal membranes, and could potentially help repair any damage.

The integrity of the fetal membranes during pregnancy is vital for normal development. The premature rupture of fetal membranes, known as preterm prelabour rupture of the membranes (PPROM), is a major cause of preterm birth accounting for around 40 per cent of early infant death.

Currently there are no clinical approaches available to repair or improve healing in the fetal membranes.

For the study, the researchers established a fetal membrane defect model, which mimics the creation of a defect site within the fetal membrane as a result of keyhole surgery. They assembled donated human fetal membrane tissue onto cell culture dishes and injected human amniotic fluid, the protective fluid which surrounds the developing fetus, underneath. The injection creates a small hole within the membrane to which the PAs were then added.

The research team found that PAs spontaneously assembled together seconds after coming into contact with the human amniotic fluid. Within two minutes, a dense mesh of fibres formed a plug, which sealed the hole created at the injection site after 24 hours.

When they combined this novel use of PAs with protein sequences known to promote adhesion and healing, the researchers observed an enhanced sealing and regenerative effect.

The findings follow on from previous work from the research team, which showed that reducing the levels of a protein called connexin 43 (Cx43) encouraged rebuilding of the fetal membranes, and enhances the processes of tissue healing and repair.

Whilst PPROM can occur spontaneously, it can also result from fetal surgery and prenatal diagnosis procedures such as amniocentesis that require doctors to make a hole in the fetal membrane sac.

Fetal medicine specialists are increasingly offering surgery to babies in the womb before birth, to treat abnormalities of the spine, diaphragm or placenta. PPROM complicates around one third of these cases, reducing the clinical effectiveness of fetal surgery.

Dr. Tina Chowdhury, Senior Lecturer in Regenerative Medicine at Queen Mary, said: "The next step in this research is to understand whether these molecular 'plugs' are able to withstand the mechanical forces such as tension or pressure induced by the developing fetus and the amniotic fluid. We also need to explore the wound healing mechanisms in more detail, and the safety of using the peptides for expectant mothers and babies during pregnancy."

Professor Anna David, Professor of Obstetrics and Fetal Medicine at UCL Elizabeth Garrett Anderson Institute for Women's Health and a co-author of the study, said: "Finding a method to heal the amniotic membranes and prevent preterm birth after PPROM is a vital step to improving the outcomes of babies where the membranes rupture. The sealing and regeneration that we saw is very encouraging for our bioengineering approach."

More information: David W. Barrett et al. Potential sealing and repair of human FM defects after trauma with peptide amphiphiles and Cx43 antisense, *Prenatal Diagnosis* (2020). DOI: 10.1002/pd.5826

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