# Study shows potential disease treatment in newborns via drug delivery to amniotic fluid

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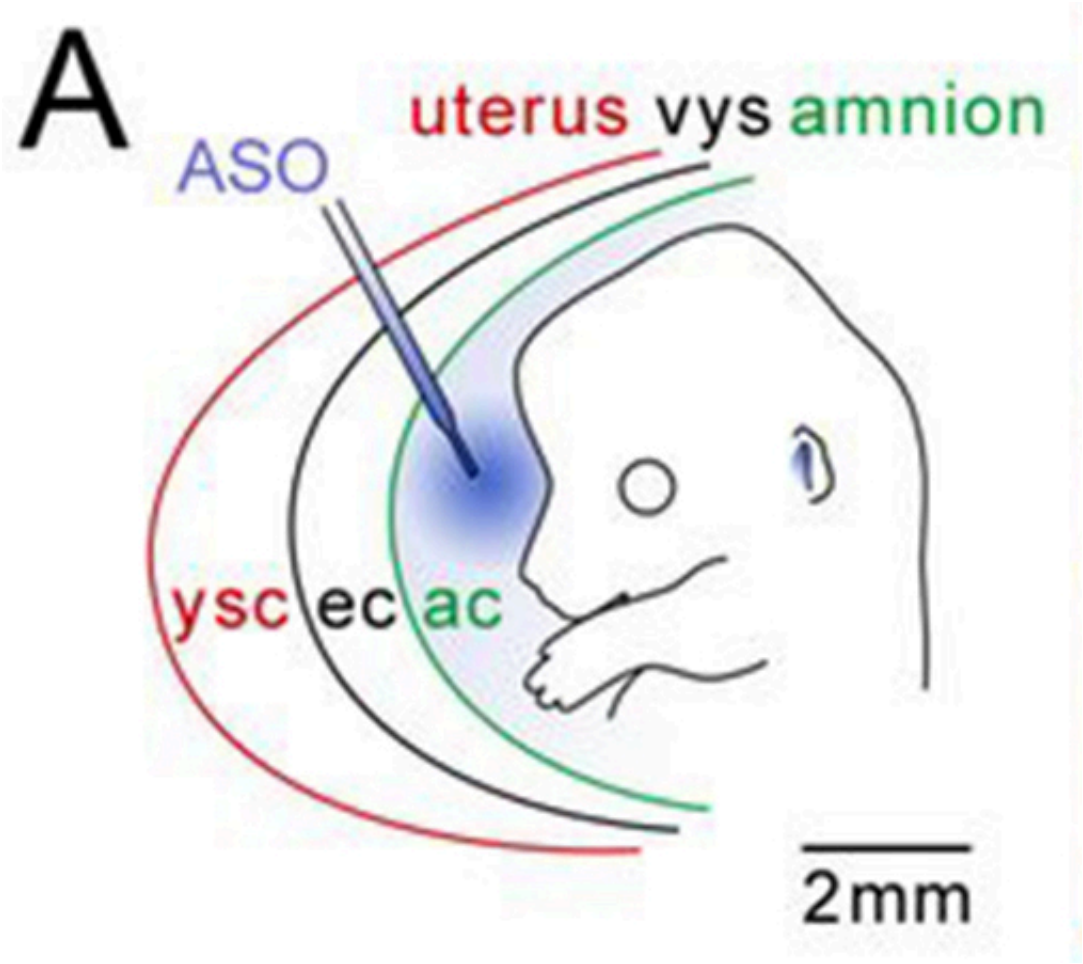


This is a schematic representation of transuterine microinjection into the amniotic cavity surrounding the E13 embryo. The microinjection pipette (blue) traverses the uterus (red), the yolk sac cavity (ysc), the visceral yolk sac (vys, black), the exocoelomic cavity (ec) and finally the amnion (green) en route to the amniotic cavity (ac). Credit: Rosalind Franklin University

A breakthrough study by research teams at Rosalind Franklin University of Medicine and Science and Oregon Health & Science University offers promise for therapeutic management of congenital diseases in utero using designer nucleotide sequences that can simply be injected into the fluid surrounding the developing fetus to potentially treat disabling-to-lethal genetic defects.

Recently published in the journal *Nucleic Acids Research*, the study shows that antisense oligonucleotides (ASOs), short strands of engineered nucleic acid that are designed to bind to a specific gene-derived sequence, can be safely injected into the amniotic cavity—the fluid-filled sac that holds the embryo. The procedure, performed in mice, resulted in targeted alteration in gene expression for up to a month after birth in some tissue.

"A major barrier to the development of treatments for congenital disorders is the risk to the developing fetus that interventions may pose," said Michelle Hastings, PhD, associate professor of cell biology and anatomy, who led the RFU team. "Our demonstration that this promising type of therapeutic can be delivered to the amniotic cavity is an important advance for fetal treatment of disease."

The study is the first demonstration of ASO embryonic transfer with amniotic fluid administration, or non-surgical insertion of ASOs into the developing fetus—a key step toward broad application of this powerful gene therapy approach in humans.

"This could be really useful in the future to treat all types of genetic diseases," said study co-author Lingyan Wang, Ph.D., a researcher with the Oregon Hearing Research Center at OHSU.

Congenital disease, estimated to cause the death of ~300,000 infants within the first month of life each year across the globe also causes

childhood illness and long-term disability. Prenatal screening techniques now make early diagnosis possible, presenting the opportunity to intervene in disease processes before birth.

"The best way to treat a disease that we know will emerge at birth is to deliver a therapy in utero to the developing fetus before irreparable damage occurs," said co-author John Brigande, Ph.D., a principal investigator in the Oregon Hearing Research Center.

The combination of a potentially low-risk delivery approach with the promising antisense drug platform, which, in theory, can alter any disease-associated aberrant gene expression by simply designing the sequence of the injectable molecule to match the target gene, is an exciting breakthrough, though more work needs to be done to improve the efficiency of drug uptake and distribution to specific tissues.

"We predict that fetal ASO pharmacotherapy has the potential to safely enable therapeutic strategies for the treatment of fetal and congenital genetic disease," the authors wrote.

**More information:** Frederic F. Depreux et al, Antisense oligonucleotides delivered to the amniotic cavitymodulate gene expression in the postnatal mouse, *Nucleic Acids Research* (2016). DOI: 10.1093/nar/gkw867

Provided by Rosalind Franklin University of Medicine and Science