Solving a sticky problem with fetal surgery using a glue inspired by the sandcastle worm

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By creating a glue mimicking an adhesive that sandcastle worms use to make shelters, researchers may have solved a surgical problem causing premature births. Credit: Fred Hayes, University of Utah

In creating an adhesive patterned after glue produced by the lowly underwater sandcastle worm, researchers are reporting today that they may have solved the problem of premature births that sometimes result from fetal surgery. It also could open up numerous opportunities to safely perform more complex fetal surgeries in the future. Their report will be presented as part of the 248th National Meeting & Exposition of the American Chemical Society (ACS), the world's largest scientific society.

Ruptures of the fetal membranes, or the sac containing the developing baby, occur when surgeons operate on a fetus. It can also happen when they check the fetus for problems such as anatomical abnormalities with a fetoscope, a long, wand-like instrument with a tiny camera at the end. To make room for it, they first create a channel to the fetus using a device with a sharp tip. But this also punctures the fetal membranes. If this causes a leak or rupture, there is a good chance it will lead to a premature birth, the researchers say.

"There are currently no effective treatments for preventing fetal membrane rupture caused by in utero surgery," says study leader Russell J. Stewart, Ph.D. "Using glue in the fluid-filled uterus is challenging. Our water-borne, non-swelling, non-toxic adhesives that won't dissolve in water have ideal properties for this challenging environment. The evidence so far suggests we likely will be able to solve this problem."

The team, in its new research, turned to the sandcastle worm to help solve the problem of creating an adhesive that sticks in a wet environment like the uterus. These creatures routinely glue particles together into protective shelters while completely submerged in water. "The problem of gluing things together underwater has been solved over and over in nature, in many different ways," says Stewart, who is with University of Utah. "Understanding the composition, packaging and chemical mechanisms of natural adhesives is a good starting point for engineering practical and cost-effective synthetic underwater adhesives."

Stewart explains that the team made synthetic polymers that mimic the strong adhesive proteins that sandcastle worms produce. These polymers are charged and can spontaneously come together. They form a "water-immiscible fluid," which means that the polymer adhesive remains separate from water when placed in the body. Thus, it can do its job of repairing punctures.

The team focused on developing a synthetic glue because natural glue can't be harvested directly from the worms or produced from recombinant genes in hosts, he explains. Stewart says another advantage of these new polymers is that they are inexpensive. He adds that they also could be used for nonmedical purposes — in underwater glues and paints.

"Our adhesive is many times stronger than fibrin-based tissue sealants, which are already approved for clinical use, but are ineffective for sealing fetal membranes," according to Stewart. And, he says, since the synthetic glue doesn't mix with water, it doesn't swell. This is critical for a tissue adhesive inside the body.

He also will report on successful initial experiments with the adhesive in animal tests. This work was done in collaboration with Ken Moise, Jr., M.D., and Ramesh Papanna, M.D., of the Texas Fetal Center. Papanna says that the innovation opens up opportunities for surgeons to perform more complex fetal interventions that are just too risky to attempt currently, such as treating spina bifida.

More information: Title: Crosslinkable complex coacervates for tissue repair after in utero surgery

Abstract
There remains room for improvement in adhesives for bonding living tissues. In an approach copied from the marine sandcastle worm, water-

borne adhesives were formed by complex coacervation of synthetic copolyelectrolytes (co-PEs) that mimic polyphosphate and polyamine proteins of the natural sandcastle worm glue. The phase separated adhesive complex coacervates can be applied to and bond wet or fully-submerged tissues. The adhesives are cured by photo- or chemically initiated covalent crosslinking through methacryloyl sidechains. The stiffness and bond strength of the crosslinked adhesive complex coacervates can be modulated by creating additional polymer networks within the coacervated co-PE network. Polymerization of polyethylene glycol diacrylate (PEG-dA) macromers entrapped during complex coacervate formation increased the modulus and bond strength of the crosslinked adhesives. The crosslinked complex coacervate adhesives with PEG networks swelled less than 1% over 30 days in physiological saline. Pre-clinical testing of the adhesive complex coacervates is in progress for applications during fetoscopic surgeries.

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