THE HARTWELL FOUNDATION

2017 Individual Biomedical Research Award

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Fetal Cure for Spina Bifida

Spina bifida is a birth defect that occurs when the spine and spinal cord don't form properly in the womb, during the first month of fetal growth. Each year in the United States about 1,500 babies are born with the condition. The most severe and most common form of spina bifida, myelomeningocele (MMC), occurs when part of the spinal cord and spinal nerves are exposed through an opening on the back, which if left unprotected will cause progressive nerve damage and long term disabilities, including loss of mobility due to paralysis; brain malformations and associated learning disorders; as well as bladder, bowel and gastrointestinal complications. There is no cure for spina bifida, as current treatments only help manage the defect by preventing complications. While Spina bifida is largely preventable if the mother gets enough folate before and during pregnancy, there still exists a population predisposed to genetic and environmental factors. Babies born with spina bifida require surgery within the first few days of life to repair or minimize the spinal defect. If diagnosed early, surgical intervention *in utero* is sometimes possible before birth (about 20% of cases). During surgery the spinal cord and nerves are tucked back into the spine, and covered with muscle and skin to help prevent further nerve damage and infection. Unfortunately, surgery cannot undo damage that's already occurred. Recent advances in fetal surgery offer the expectation of improved clinical outcomes in spina bifida repair; but due to the risks of a complex and challenging procedure it is not performed until late in the second trimester, a delay that limits rescue of neurologic damage and leaves over half of all infants born with this intervention unable to walk. The solution to this problem would be to intervene earlier in gestation; an intervention with minimal risk and available to all spina bifida babies. To address this need David proposes to inject small synthetic particles made from a biocompatible substance into the amniotic cavity that will bind to the surface of the exposed spinal cord and release a growth factor to mediate fetal wound healing and induce skin closure over the defect in order to protect the spinal cord. To optimize this intervention, he proposes to adjust the loading dose of growth factor within the particles, the total particle dose delivered, as well as the timing of intra-amniotic injection during gestation. Based upon his preliminary observations in a rat model, it appears that the size and charge characteristics of the particles can be adjusted to improve their binding to the the exposed spinal cord and surrounding tissues. Most important, he has found no detectable accumulation of injected particles in the lung, liver, skin or gut, which is cricital for limiting off-target effects of the therapy. If the intervention David envisions is successful and a neurologic improvement can be demonstrated, larger animal testing and clinical translation will follow, which would represent a potential cure for the many children afflicted with this debilitating birth defect.