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Gene therapy to correct surfactant protein B deficiency in newborns

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An article published in *Experimental Biology and Medicine* (Volume 242, Issue 13, July, 2017) reports that gene therapy may be used to as an intermediate therapy for newborns with surfactant protein deficiencies until lung transplantation becomes an option. The study, led by Dr. David Dean in the Division of Neonatology at the University of Rochester in Rochester NY reports that electroporation-mediated delivery of the surfactant B gene to deficient mice improves lung function and survival.

Surfactant is present in the lungs of all humans. This important protein makes it easier for people to breath. Without it, lungs would collapse with each breath. Surfactant protein B (SPB) deficiency is a rare but fatal disease that affects full term babies after an apparently uncomplicated pregnancy and delivery. Babies with SBP deficiency have severe breathing problems from birth, and die in infancy even with aggressive medical treatment. To date the only effective treatment is a lung transplant. Given how quickly these babies become ill, and the limited number of available organs, transplantation is often not even an option.

The most promising therapy for this devastating disease is replacement of the absent SPB gene, a process called gene therapy. Gene therapy approaches using viral-based delivery techniques have not achieved therapeutic levels of SPB protein and induce inflammation, which can exacerbate the disease. The current study used electroporation-based delivery techniques which result in higher levels of transgene expression

and are well-tolerated even in animals with existing lung injury. Delivery of SPB DNA into the lung cells of SPB-deficient mice reduced lung inflammation, improved lung function, and extended survival. Since the DNA is eventually silenced, SPB expression does not last forever and this is approach cannot provide a cure.

Dr. Barnett, a neonatology fellow and coauthor said "although this treatment does not provide lifelong correction, our data suggest that this may be a useful approach for improving the survival and stability of infants until lung transplant can occur." Dr. Dean added "we are excited to help optimize an approach that may treat and someday even cure this and other devastating diseases."

Dr. Steven R. Goodman, Editor-in-Chief of *Experimental Biology and Medicine*, said, "Dean and colleagues provide evidence that gene therapy may restore surfactant activity in SPB deficiency for sufficient time to allow lung transplants in a greater number of affected neonates. This is represents an important advance in this field of research."

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