THE HARTWELL FOUNDATION

2016 Individual Biomedical Research Award

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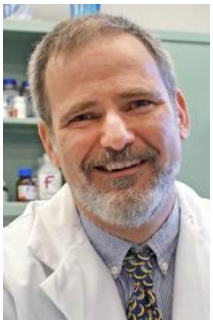

Restoring Hearing in Congenital Deafness

Over 400,000 children living in the U.S. suffer mild to severe hearing loss and each year about 2-3 of every 1,000 children born in the United States have a detectable level of hearing loss in one or both ears. Congenital hearing loss impairs speech and language acquisition, and often contributes substantially to delays social and cognitive development. There are multiple causes for congenital hearing loss, but currently there are no cures. Hearing aids and permanent solutions like an implanted electronic device that provides sound signals to the brain are palliative but inadequate, even when combined with intense speech therapy. Moreover, even in the best case the implants produce only a sensation of hearing, mimicking only a small fraction of the sounds that a healthy ear can perceive. Normal hearing requires the proper development of the cochlea, the hearing portion of the inner ear. The cochlea includes the auditory organ that contains the sensory hair cells responsible for sound detection and the stria vascularis, the "battery" that provides the energy for auditory hair cells to function. In humans, the auditory hair cells and supporting cells are formed during embryogenesis and once they mature, they cannot be replaced if damaged or lost. While over the past decade considerable effort has been made to determine the biology of the sensory hair cells in the mammalian cochlea, with the aim of applying the principles of embryonic development to regenerative therapies, current research has not yielded a translational path to treat deafness. Moreover, while 30 to 40% of congenital hearing loss is accounted for by defects in the stria, the regenerative potential of this complex tissue has been largely unexplored. To address this unmet need, Martin proposes to develop a cell based therapy for restoring hearing. In this regard, he will take advantage of a unique mouse model of congenital strial deafness (caused by the absence of intermediate cells in the stria vascularis), which is the same pathology observed in children with congenital deafness. He hypothesizes that specialized cells isolated from the stria vascularis that have not fully differentiated and still retain many characteristics from their progenitor cells still retain the ability to fully differentiate into functional mature intermediate cells. His plan is to test whether such stem cells will restore hearing when injected into the lateral wall of the cochlea in his strial deafness mouse model. Three strial cell types with distinct embryonic origins will be evaluated: marginal cells; specialized melanocyte-like cells derived from migratory neural crest cells; and basal cells. If Martin is successful, it will be possible to generate equivalent human cell lines and advance clinical translation, with potential to recover the hearing of those children from the large population affected with severe hearing loss due to defects in the stria.