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Ear researchers think like engineers

By Carolyn Y. Johnson |

JOSE JORDAN/AFP/GETTY IMAGES **Promoting research: Ernesto Bertarelli.**

Deep in the recesses of the ear lies a feat of biology and engineering: a delicate, fluid-filled structure where cells translate the vibrations of sound, from bird songs to car horns, into electrical impulses that are sent to the brain, to be perceived as a tweet or a honk.

But this intricate feat of natural neuroengineering can easily go awry, because of damage over a lifetime or because of genetic defects. The hair cells and nerve cells of the inner ear cannot regenerate, leaving limited options for those who lose their hearing.

Now, trans-Atlantic collaborations between Harvard Medical School scientists and Swiss researchers will bring together engineers and neuroscientists to tackle a range of sensory and motor problems, with an emphasis on hearing loss.

The newly announced projects, which will be highlighted during a conference at the end of the week, will be funded by the Bertarelli Foundation, the philanthropic organization of the Swiss-Italian family that controlled the pharmaceutical company Serono SA. It was sold to the German pharmaceutical and chemical company Merck KGaA in 2007 for $13.3 billion.

In addition to Serono's Massachusetts presence, the foundation's copresident, Ernesto Bertarelli, has ties to the state, as a graduate of Babson College and Harvard Business School.

Bertarelli said the neuroengineering program his family's foundation established last year, which is intended to foster collaboration and exchange between the medical school and the Ecole Polytechnique Federale de Lausanne in Switzerland, mirrors his personal experience.

"It relates to the way I was brought up, spending my time half in the US and half in Switzerland and being able to travel across the Atlantic through my studies and through my work,'' Bertarelli said. "Always

seeing the best work, the best ideas come to fruition when you create teams which are diverse in background, and if you yet share common goals.''

He said that because of his work at Serono, which developed a multiple sclerosis therapy, he and his family were acutely aware of the opportunities and needs in neurology and excited by new opportunities to apply engineering to medical problems.

The first six grants awarded by the foundation focus on various problems in sensory and motor disorders, although the majority of them support new approaches to combating hearing loss or deafness, ranging from new attempts to repair or regenerate hair cells to finding solutions that could overcome nerve damage. One of the research teams will combine a variety of approaches to develop treatments for spinal cord injury in rats, with the hope they could be applicable to humans.

Jeffrey Holt, a neuroscientist who recently moved from the University of Virginia to Children's Hospital Boston, said the opportunity to collaborate with experts in different fields and take advantage of unique funding opportunities is one of the reasons he wanted to move to Boston.

Holt is sharing a $600,000, three-year grant with Patrick Aebischer of the Ecole Polytechnique Federale de Lausanne, a leader in the development of gene therapy to correct inherited defects. While gene therapy research has suffered setbacks over the past 20 years, recent successes in using a tool in the eye motivated Holt to think about using it in the inner ear.

Together, Holt and Aebischer will attempt to deliver genes to the inner ear that could repair problems caused by genetic defects. As a first step, they will develop the specialized viruses that can deliver the correct DNA to the hair cells of the inner ear. Once they have developed that tool, they will inject viruses into mice that cannot hear because they carry the same genetic defects that cause deafness in humans. They hope to make deaf mice capable of hearing, and create an approach that could be useful in the clinic.

"We're both coming at it from different angles, hopefully leading to the same eventual end: using viral vectors to treat hearing loss in humans,'' Holt said.

Lisa Goodrich, associate professor of neurobiology at Harvard Medical School who specializes in understanding the development of cells that make up the ear, is partnering with Matthias Lutolf, a bioengineer.

The team will use its combined skills to devise a system to screen rapidly for molecules that influence the development of cells in the ear.

The eventual goal is to use insights into the development of cells in the ear to find agents that could be used to reprogram a mature cell, giving it the ability to regenerate a new hair or nerve cell. "If we can figure out how to use biology, which works so beautifully as it is, and recreate those events, we'll have a much more appropriate way of dealing with diseases,'' Goodrich said.

David Corey, a professor of neurobiology at Harvard Medical School who is organizing the conference, said it is a particularly ripe time for taking neuroengineering approaches to these types of problems.

Unlike many neurological and psychiatric diseases, motor and sensory problems are typically straightforward. They typically involve the translation of physical signals, like light and sound, into inputs to the brain, or neural signals into movement.

The problems are "not necessarily simpler, but more amenable to engineering approaches,'' Corey said.