The Hugh Knowles Prize for Distinguished Achievement

Christine Petit, MD PhD
College de France
Institut Pasteur

In association with her award, Dr. Petit will deliver a lecture entitled:

**Understanding hearing mechanisms: avenues opened up by deafness genes**

**TUESDAY, MAY 10, 2016 • 5:00 PM**

McCormick Tribune Center Forum
1870 Campus Drive
Northwestern University • Evanston Campus

Reception to follow the lecture.

The traditional approach to the neurophysiology of hearing has been mostly elaborated by physicists and biophysicists on the basis of the responses of the auditory system to pure tones. Whilst this approach revealed the exquisite spectrotemporal analyses carried out by the cochlea, the last three decades saw the emergence of a complementary approach focusing on natural and behaviorally significant sounds, which revealed their specific acoustic features and optimal processing by the auditory system. The cellular and molecular mechanisms underpinning these properties remained, however, largely unknown; the paucity of the cells involved prevented biochemical and molecular genetic analyses.

We initiated a genetic approach to pinpoint the proteins essential to the development and the functioning of the auditory system based on the identification of the genes responsible for monogenic forms of sensorineural deafness in humans. We assembled these basic components into molecular complexes and machineries, and gradually revealed their roles and modes of action through multidisciplinary approaches largely based on the use of specifically engineered mouse mutants. Hence, the cohesion of the hair bundle, the sensory antenna of the auditory sensory cells, was shown to depend critically on stereociliary fibrous links, which were also unmasked as essential for the hair bundle’s functional polarity, the control of the stereocilia length, and the property of cochlear suppressive masking. The intrinsic properties of the hair cell synapse, that contribute to the fast operating speed and the extremely precise temporal encoding of sound features by the auditory system, could be related to the unusual molecular composition of its synaptic vesicle exocytosis machinery. Enlightening the way the auditory system withstands the continuous stress of the environmental noise, it was found to be endowed by a dynamic adaptive proliferation/fission of peroxisomes buffering harmful oxidative stress. Based on the knowledge generated by these studies, the management of hearing impairment has greatly improved and strategies for treating the various forms of deafness are now being developed.