Someya Lab

Lab Members
Principal Investigator:
Someya, Shinichi, PhD

Postdoctoral Fellow:
Chul Han, PhD

Graduate Student:
Mi-Jung Kim

Undergraduate Student:
Logan Walker

Technician:
Lorraine Koerper

Research Interests
Hearing loss is caused by genetic defects, noise exposure, ototoxic drugs, and/or aging and is the third most prevalent chronic health condition in adults. A major question being studied in our laboratory is why and how hearing deteriorates with age at the molecular level. We are particularly interested in understanding how cochlear hair cells, spiral ganglion neurons, and/or stria vascularis cells are continually lost or degenerated throughout life. To answer these questions, we study the molecular basis of hearing loss as well as hearing function under normal/healthy conditions using various transgenic and knockout mice and cultured mouse inner ear cell lines. A second question being studied in our laboratory is can hearing loss progression be slowed? We are also interested in whether hearing can be improved at specific frequencies. To find these answers, we study the effects of calorie restriction, exercise, and sensory training on hearing in various mouse models of hearing loss.

Current Projects
Role of the glutathione system in maintaining hearing function
Glutathione acts as the major small molecule antioxidant in cells and is found mostly in the reduced form (GSH) in healthy mitochondria. During aging, oxidized glutathione (GSSG) accumulates, and hence an altered ratio of mitochondrial GSH:GSSG is thought to be a marker of both oxidative stress and aging. Of the glutathione enzymes, glutathione reductase (GSR) plays a critical role in preventing accumulation of GSSG and maintaining the appropriate redox environment in the mitochondria through regeneration of GSH, thereby enhancing the glutathione antioxidant defense system. The overall aim of this research project is to investigate the role of the GSH system in maintaining hearing function. We are particularly interested in investigating: 1) whether a decline in the GSH system results in the degeneration of sensory hair cells, spiral ganglion neurons, and/or stria vascularis cells in the cochlea, leading to hearing loss, and 2) whether the GSH system is essential for cochlear oxidative stress reduction and hearing loss prevention by caloric restriction.

Role of the mitochondrial thioredoxin system in maintaining hearing function
There are two major antioxidant defense systems in mitochondria: the GSH and thioredoxin (TXN) systems. These systems work with each other to protect cells from oxidative stress. There are two major players in the mitochondrial TXN antioxidant defense system: thioredoxin 2 (TXN2) and thioredoxin reductase 2 (TXNRD2). In mitochondria, NADPH-dependent TXNRD2 regenerates
reduced TXN2 from oxidized TXN2. When TXN2 is in a reduced state, it interacts with peroxiredoxin 3 (PRDX3) to remove hydrogen peroxide (H₂O₂). The overall aim of this research project is to investigate the role of the mitochondrial TXN system in maintaining hearing function. We are particularly interested in investigating: 1) whether the mitochondrial TXN and GSH systems function in a redundant manner, and 2) whether a decline in the TXN system results in the degeneration of sensory hair cells, spiral ganglion neurons, and/or stria vascularis cells in the cochlea, leading to hearing loss. We are also investigating whether the TXN system is essential for cochlear oxidative stress reduction and hearing loss prevention by caloric restriction.

Role of NADPH in the auditory system
NADPH is a major cellular reductant and is central to cell survival and cellular antioxidant defenses because NADPH is required for regeneration of reduced glutathione from oxidized glutathione, and reduced thioredoxin from oxidized thioredoxin, and for the activity of catalase. There are 2 major enzymatic sources of NADPH: G6PD (glucose 6-phosphate dehydrogenase) in the Pentose Phosphate Pathway and IDH2 (isocitrate dehydrogenase 2) in the TCA (tricarboxylic acid) Cycle. The overall aim of this research project is to investigate the role of NADPH in regulating cochlear cell survival and maintaining hearing function under normal/healthy conditions or during aging. We are currently investigating which pathway/cycle is the principle source of NADPH for the cochlear cellular antioxidant defenses and whether G6PD or IDH2 is essential for maintaining hearing function.