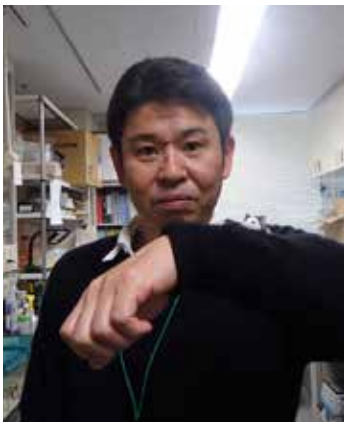
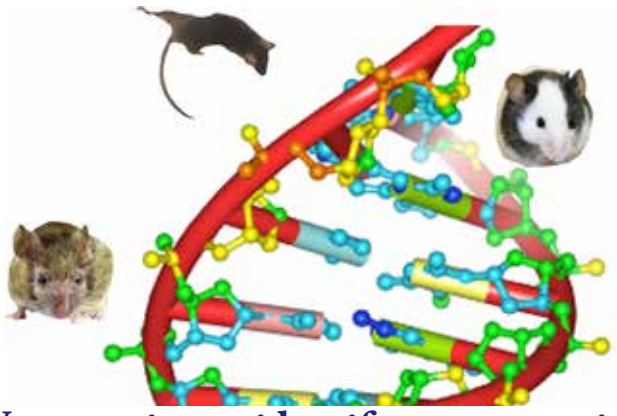


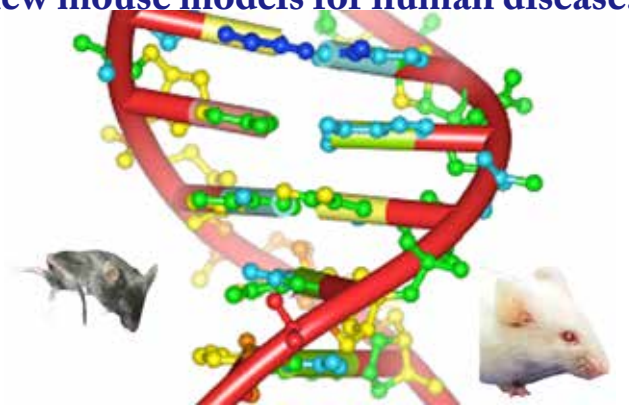
Project Leader **Yoshiaki Kikkawa** Mammalian Genetics Project

Gene discovery: Phenotype- and gene-driven approaches to identify disease-associated genes in mice

Mouse disease models have contributed to the study of pathogenic mechanisms. The demand for mouse disease models will continue to increase because the genetic factors and molecular mechanisms behind many human genetic diseases are still unknown. Mouse disease models are important tools for identifying genes that are responsible for genetic diseases. They are also important for studying the processes that regulate the onset of genetic diseases and for evaluating the effectiveness of new drugs. We aim to develop novel mouse disease models via forward and reverse genetics for the phenotypic analysis of human genetic diseases and for the study of pathogenic mechanisms.



"We are trying to identify genes associated with human diseases using mutant mice and are aiming to develop new mouse models for human disease."



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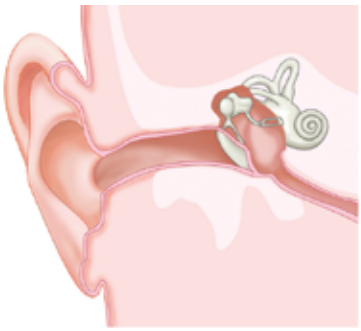
Mammalian Genetics

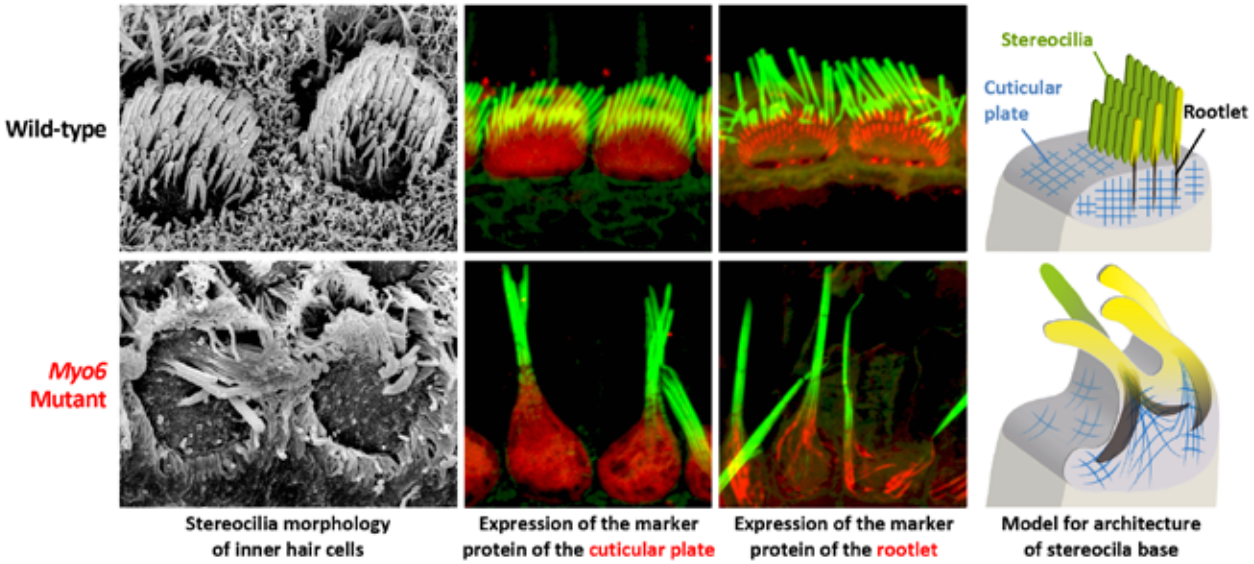
Main project: Genetics of deafness



Hearing loss is the most common sensory disease in humans, which severely affects one's quality of life. We continue to make significant advances in understanding the development, transduction, and homeostasis of the auditory system by studying corresponding mouse mutants. We exploit the similarities between the mouse and human genomes, physiology, and auditory system anatomy to identify and characterize genes related to deafness.

Current focus

Stereociliary fusion in Myo6 mutant mice caused by a disruption of actin networks in the apical region of inner ear hair cells

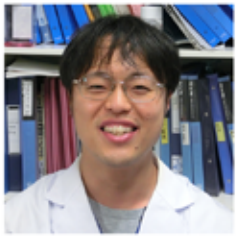


An unconventional myosin encoded by *MYO6*, a myosin VI gene, contributes to hearing loss in humans. Homozygous *Myo6* mutant mice exhibit congenital hearing defects caused by the fusion of stereocilia. We recently identified morphological changes at the base of the stereocilia in *Myo6* mouse mutants by scanning electron microscopy and analysis of the marker proteins of the cuticular plate and rootlet. In wild-type mice, stereocilia have dense rootlets that extend through the taper region of stereocilia to anchor them into the actin mesh of the cuticular plate. These structures are maintained when MYO6 is normally expressed in the stereociliary taper region, cuticular plate, and cytoplasm of the hair cells, but a reduction of MYO6 leads to stereociliary fusion accompanied by deformations of the cuticular plates and the extension of rootlets.

By Yuta Seki

Members

Kunie Matsuoka



Shumpei Yasuda

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