Stanford

Nicolas Grillet, PhD

Assistant Professor of Otolaryngology - Head & Neck Surgery (OHNS)

Otolaryngology (Head and Neck Surgery)

Bio

BIO

2014-present

Assistant Professor, Stanford University, School of Medicine, Stanford, CA, USA

Otolaryngology department

2010-2014

Senior Research Associate, The Scripps Research Institute, La Jolla, CA, USA

Department of Cell Biology and Dorris Neuroscience Center

Advisor: Ulrich Müller

2005-2010

Research Associate, The Scripps Research Institute, La Jolla, CA, USA

Department of Cell Biology and Dorris Neuroscience Center

Advisor: Ulrich Müller

1999-2004

Ph.D. Student, The Institute for Developmental Biology of Marseilles, France

then moved to the Ecole Normale Supérieure, Paris, France

CNRS/ENS “Development and Evolution of the Nervous System”

Advisor: Jean-François Brunet

1998-1999

Graduate Student, The Institute for Developmental Biology of Marseilles, France

INSERM “Development and Pathology of Spinal Motoneuron”

Advisors: Christopher E Henderson, Keith Dudley

ACADEMIC APPOINTMENTS

- Assistant Professor, Otolaryngology (Head and Neck Surgery)
- Member, Bio-X

- Member, Maternal & Child Health Research Institute (MCHRI)

LINKS

- Grillet Lab: https://grilletlab.stanford.edu/

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Genetics of Hearing and Vestibular Impairment

The inner ear contains the sensory cells that detect sound and head motion, the hair cells. In mammals, these cells are generated during the mid-gestation and will never be replaced during the entire life. The hair cells are in constant activity and their dysfunction is a major cause of deafness and peripheral vestibular disorders: they are both the core and the Achilles' heel of the system.
Hearing loss can result from exposure to excessive noise, chemicals and certain medications. However, susceptibility to deafness is generally dictated by genetic transmission. To this date, 136 human loci have been linked to hearing loss, but we know the corresponding affected genes for only 85 of them. These genes are very often required, directly or indirectly, for the proper hair cell function.

We want to identify the comprehensive list of genes required for hearing and head motion detection, and ultimately characterize the function of these genes at the molecular level.

Function of Hair Cells and other Inner Ear Cells

Differently from the sense of Vision, still little is known about Hearing and Balancing at their molecular level. This is due to the technical challenges associated with this organ: the paucity of the inner ear sensory cells, their inaccessibility and their fragility.
The inner ear is composed of two functional parts: the cochlea, which is the auditory organ, and the vestibule, organs responsible for head motion and balancing. In both parts, the sensory epithelia are composed by the sensory hair cells, always surrounded by supporting cells.
We want to characterize down to the molecular level the function of the cells that compose the inner ear, particularly the hair cells.

The hair cells have different functions: 1) to detect the mechanical stimuli induced by sound, and 2), to transmit this information to the central nervous system through their synapses.

Teaching

COURSES

2022-23

- Biology and Physics of Hearing: OTOHNS 204 (Spr)

2021-22

- Biology and Physics of Hearing: OTOHNS 204 (Spr)

2020-21

- Inner Ear Biology: OTOHNS 204 (Aut, Spr)

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biology (School of Humanities and Sciences) (Phd Program)
- Biomedical Informatics (Masters Program)
- Developmental Biology (Phd Program)
- Genetics (Phd Program)
- Human Genetics and Genetic Counseling (Masters Program)
- Neurosciences (Phd Program)

Publications

PUBLICATIONS

- **LOXHD1 is indispensable for coupling auditory mechanosensitive channels to the site of force transmission.** *Research square*
  Wang, P., Miller, K. K., He, E., Dhawan, S. S., Cunningham, C. L., Grillet, N.
  2024

- **High-resolution immunofluorescence imaging of mouse cochlear hair bundles.** *STAR protocols*
  Miller, K. K., Wang, P., Grillet, N.
  2022; 3 (2): 101431

- **Oncofusion-driven de novo enhancer assembly promotes malignancy in Ewing sarcoma via aberrant expression of the stereociliary protein LOXHD1.** *Cell reports*
  Deng, Q., Natesan, R., Cidre-Aranaz, F., Arif, S., Liu, Y., Rasool, R. U., Wang, P., Mitchell-Velasquez, E., Das, C. K., Vinca, E., Cramer, Z., Grohar, P. J., Chou, et al
  2022; 39 (11): 110971

- **High-resolution imaging of the mouse-hair-cell hair bundle by scanning electron microscopy.** *STAR protocols*
  Grillet, N.
  2022; 3 (1): 101213

- **Loxhd1 mutations cause mechanotransduction defects in cochlear hair cells.** *The Journal of neuroscience : the official journal of the Society for Neuroscience*
  Trouillet, A., Miller, K. K., George, S. S., Wang, P., Ali, N., Ricci, A., Grillet, N.
  2021

- **Dimensions of a Living Cochlear Hair Bundle** *Front Cell Dev Biol*
  Miller, K. K., Atkinson, P., Mendoza, K., Ó Maoiléidigh, D., Grillet, N.
  2021; 9: 742529

- **Mechanosensory hair cells express two molecularly distinct mechanotransduction channels** *NATURE NEUROSCIENCE*
  Wu, Z., Grillet, N., Zhao, B., Cunningham, C., Harkins-Perry, S., Coste, B., Ranade, S., Zebarjadi, N., Beurg, M., Fettiplace, R., Patapoutian, A., Muller, U.
  2017; 20 (1): 24-33

- **TMIE Is an Essential Component of the Mechanotransduction Machinery of Cochlear Hair Cells.** *Neuron*
  Zhao, B., Wu, Z., Grillet, N., Yan, L., Xiong, W., Harkins-Perry, S., Müller, U.
  2014; 84 (5): 954-67

- **Using injectoporation to deliver genes to mechanosensory hair cells.** *Nature protocols*
  Xiong, W., Wagner, T., Yan, L., Grillet, N., Müller, U.
  2014; 9 (10): 2438-49

- **TMHS Is an Integral Component of the Mechanotransduction Machinery of Cochlear Hair Cells** *CELL*
  Xiong, W., Grillet, N., Elledge, H. M., Wagner, T. F., Zhao, B., Johnson, K. R., Kazmierczak, P., Mueller, U.
  2012; 151 (6): 1283-1295

- **Mutations in LOXHD1, an Evolutionarily Conserved Stereociliary Protein, Disrupt Hair Cell Function in Mice and Cause Progressive Hearing Loss in Humans** *AMERICAN JOURNAL OF HUMAN GENETICS*

Grillet, N., Schwander, M., Hildebrand, M. S., Sczaniecka, A., Kolatkar, A., Velasco, J., Webster, J. A., Kahrizi, K., Najmabadi, H., Kimberling, W. J., Stephan, D., Bahlo, M., Wiltshire, et al
2009; 85 (3): 328-337

- **The Mechanotransduction Machinery of Hair Cells** *SCIENCE SIGNALING*
  Grillet, N., Kazmierczak, P., Xiong, W., Schwander, M., Reynolds, A., Sakaguchi, H., Tokita, J., Kachar, B., Mueller, U.
  2009; 2 (85)

- **Harmonin Mutations Cause Mechanotransduction Defects in Cochlear Hair Cells** *NEURON*
  Grillet, N., Xiong, W., Reynolds, A., Kazmierczak, P., Sato, T., Lillo, C., Dumont, R. A., Hintermann, E., Sczaniecka, A., Schwander, M., Williams, D., Kachar, B., Gillespie, et al
  2009; 62 (3): 375-387

- **Selection Criteria Optimal for Recovery of Inner Ear Tissues from Deceased Organ Donors.** *Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology*
  Aaron, K. A., Hosseini, D. K., Vaisbuch, Y., Scheibinger, M., Grillet, N., Heller, S., Wang, T., Cheng, A. G.
  2022

- **Oncofusion driven de novo enhancer assembly promotes malignancy in Ewing sarcomavia aberrant expression of the stereociliary protein LOXHD1.**
  Deng, Q., Natesan, R., Cidre-Aranz, F., Arif, S., Liu, Y., Rasool, R., Wang, P., Crammer, Z., Chou, M., Kumar, C., Weber, K., Eisinger, K., Grillet, et al
  AMER ASSOC CANCER RESEARCH.2021

- **Discovery and characterization of LOXHD1 as a highly specific EWS-FLI1 driven oncogene in Ewing sarcoma.**
  Deng, Q., Natesan, R., Arif, S., Rasool, R., Liu, Y., Wang, P., Crammer, Z., Mercadante, M., Gades, T., Cho, M., Eisengher, K., Grillet, N., Asangani, et al
  AMER ASSOC CANCER RESEARCH.2020: 54–55

- **A rare genomic duplication in 2p14 underlies autosomal dominant hearing loss DFNA58.** *Human molecular genetics*
  Lezirovitz, K., Vieira-Silva, G. A., Batissoco, A. C., Levy, D., Kitajima, J. P., Trouillet, A., Ouyang, E., Zebajardi, N., Sampaio-Silva, J., Pedroso-Campos, V., Nascimento, L. R., Sonoda, C. Y., Borges, et al
  2020

- **Dual regulation of planar polarization by secreted Wnts and Vangl2 in the developing mouse cochlea.** *Development (Cambridge, England)*
  Huarcaya Najarro, E., Huang, J., Jacobo, A., Quiruz, L. A., Grillet, N., Cheng, A. G.
  2020

- **Osmotic stabilization prevents cochlear synaptopathy after blast trauma** *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA*
  Kim, J., Xia, A., Grillet, N., Applegate, B. E., Oghalai, J. S.
  2018; 115 (21): E4853–E4860

- **Neuroplastin Isoform Np55 Is Expressed in the Stereocilia of Outer Hair Cells and Required for Normal Outer Hair Cell Function.** *journal of neuroscience*
  Zeng, W., Grillet, N., Dewey, J. B., Trouillet, A., Krey, J. F., Barr-Gillespie, P. G., Oghalai, J. S., Müller, U.
  2016; 36 (35): 9201-9216

- **Two-Dimensional Cochlear Micromechanics Measured In Vivo Demonstrate Radial Tuning within the Mouse Organ of Corti.** *journal of neuroscience*
  Lee, H. Y., Raphael, P. D., Xia, A., Kim, J., Grillet, N., Applegate, B. E., Ellerbee Bowden, A. K., Oghalai, J. S.
  2016; 36 (31): 8160-8173

- **Regulation of PCDH15 function in mechanosensory hair cells by alternative splicing of the cytoplasmic domain** *DEVELOPMENT*
  Webb, S. W., Grillet, N., Andrade, L. R., Xiong, W., Swarthout, L., Della Santina, C. C., Kachar, B., Mueller, U.
  2011; 138 (8): 1607-1617

- **The genetics of progressive hearing loss: a link between hearing impairment and dysfunction of mechanosensory hair cells.** *Future neurology*
  Müller, U., Grillet, N.
  2010; 5 (1): 9-12

- **Regulator of G Protein Signaling-4 Controls Fatty Acid and Glucose Homeostasis** *ENDOCRINOLOGY*
  Iankova, I., Chavey, C., Clape, C., Colomer, C., Guerineau, N. C., Grillet, N., Brunet, J., Annicotte, J., Fajas, L.
  2008; 149 (11): 5706-5712

- **A forward genetics screen in mice identifies recessive deafness traits and reveals that pejvakin is essential for outer hair cell function** *JOURNAL OF NEUROSCIENCE*

  Schwander, M., Sczaniecka, A., Grillet, N., Bailey, J. S., Avenarius, M., Najmabadi, H., Steffy, B. M., Federe, G. C., Lagler, E. A., Banan, R., Hice, R., Grabowski-Boase, L., Keithley, et al

  2007; 27 (9): 2163-2175

- **Sphingosine 1-phosphate (S1P) signaling is required for maintenance of hair cells mainly via activation of S1P(2)** *JOURNAL OF NEUROSCIENCE*

  Herr, D. R., Grillet, N., Schwander, M., Rivera, R., Mueller, U., Chun, J.

  2007; 27 (6): 1474-1478

- **Generation and characterization of Rgs4 mutant mice** *MOLECULAR AND CELLULAR BIOLOGY*

  Grillet, N., Pattyn, A., Contet, C., Kieffer, B. L., GORIDIS, C., Brunet, J. F.

  2005; 25 (10): 4221-4228

- **Dynamic expression of RGS4 in the developing nervous system and regulation by the neural type-specific transcription factor Phox2b** *JOURNAL OF NEUROSCIENCE*

  Grillet, N., Dubreuil, R., Dufour, H. D., Brunet, J. F.

  2003; 23 (33): 10613-10621

- **Responsiveness to neurturin of subpopulations of embryonic rat spinal motoneuron does not correlate with expression of GFR alpha 1 or GFR alpha 2** *DEVELOPMENTAL DYNAMICS*

  Garces, A., Livet, J., Grillet, N., Henderson, C. E., deLapeyriere, O.

  2001; 220 (3): 189-197