Curriculum Vitae

Personal Information

- ***Name*****:** Yilai Shu ***Gender*****:** Male
- ***Academic title*****:** Professor, Physician Scientist, Chief Physician
- ***Position*****:** Deputy Dean of Eye & ENT Hospital of Fudan University
- ***Address*****:** No.83 Fenyang Road, Xuhui District, Shanghai, 200031, China
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Education Profile

- 2010.10-2012.06 Joint training program student between Harvard Medical School and Fudan University
- 2007.09- 2012.06 M.D. and Ph.D. Degree in Otolaryngology, Fudan University
- 1999.09-2004.07 Bachelor's Degree in Medicine, University of South China

Work Experience

2022/12–Present	Professor, Eye & ENT Hospital of Fudan University
2022/12–Present	Chief Physician, Department of Otolaryngology, Eye & ENT Hospital of Fudan University
2018/12–Present	Principal Investigator, Eye & ENT Hospital of Fudan University
2018/08–Present	Principal Investigator, State Key Laboratory of Medical Neurobiology, Fudan University
2017/12–2022/11	Deputy Chief Physician, Department of Otolaryngology, Eye & ENT Hospital of Fudan University
2019/03–2019/10	Clinic Visiting Scholar, Stanford Medicine
2014/07–2017/11	Attending Physician, Department of Otolaryngology, Eye & ENT Hospital of Fudan University
2012/07–2014/07	Postdoctoral Fellows, Massachusetts Eye and Ear, Harvard Medical School
2004/07–2007/08	Resident Physician, Department of Otolaryngology, The First Affiliated Hospital of University of South China

Clinical Focus

- Otolaryngology - Head & Neck Surgery (Ear, Nose and Throat)
- Hearing Loss
- Acoustic Neuroma
- Facial Nerve

Curriculum Vitae

- Cholesteatoma
- Skull Base Neoplasms
- Otitis Media
- Otosclerosis

Research Focus

Current estimates indicate more than 10,000 kinds of rare diseases affect humanity. One of ten people are living with rare diseases. 80% of rare diseases are attributed to genetic factors. According to the World Health Organization, more than 1.5 billion people worldwide suffer from varying degrees of hearing impairments, which imposes a serious burden on patients and society. It is reported hearing loss is affected by over 200 genes. The number of patients with a specific deafness gene mutation is actually low. My interests include deafness mechanism, gene therapy for hearing loss, hair cell regeneration, and clinical translation research in rare diseases.

Research Narrative

As a physician-scientist in the field of otolaryngology and the director of Shanghai Key Laboratory of Gene Editing and Cell Therapy for Rare Diseases, I have devoted myself to the research on the pathogenesis, prevention, and clinical translation of deafness in response to the serious inadequacy of clinical treatments for hearing loss, contributing to the accurate diagnosis and treatment of rare diseases and developing gene therapy drugs for rare diseases.

My critical research findings include:

I. Clinical translation. Congenital hearing loss affects approximately 26 million individuals worldwide, with genetic factors accounting for 60% of cases. There are no pharmacological treatments available in clinical practice. *OTOF* mutation is one of the most common genetic factors for auditory neuropathy. After decades of effort, we have developed an *OTOF* gene therapy drug (AAV1-hOTOF) delivered by dual-AAV vectors to treat autosomal recessive deafness 9 (DFNB9), which can significantly improve hearing in a mouse model of deafness. We have also engineered a precision-targeted, minimally invasive intracochlear drug delivery platform utilizing microinjection technology. By evaluating the effect of the drug on hearing function and combining the safety assessment including blood, tissue distribution, histopathology, and neurotoxicity in mice and non-human primates, no obvious toxicity or side effects were observed. As the principal investigator, responsible for the first-in-human clinical trial to investigate the safety and efficacy of gene therapy for congenital hearing loss, I directed the successful administration of *OTOF* gene therapy drug to 11 pediatric patients with DFNB9, marking the world's first clinical application of inner ear gene therapy. The data showed that the drug was safe in patients, and successfully recovered the auditory function and speech perception in 10 patients. This groundbreaking milestone establishes a new paradigm for treating hearing disorders, with the findings published in ***The Lancet***

(Cover story) and ***Nature Medicine*** in year 2024. For the first time, the auditory function and speech perception in congenitally deafness humans was recovered by precise gene therapy; and, dual-AAV gene therapy was conducted in humans successfully for the first time.

Furthermore, non-invasive tests, including functional near infrared spectroscopy, electroencephalography, and mental development assessment were used to observe changes in neural response to sound in patients with congenital deafness before and after receiving AAV1-hOTOF gene therapy. This study elucidates neural processing of various sound stimuli in patients with congenital deafness at different stages after gene therapy (***Nature Human Behaviour,*** 2025), providing the first central-level evidence of functional auditory pathway reconstruction in children with congenital deafness after gene therapy, revealing dynamic neural remodeling in the auditory cortex and developmental improvement, and establishing a critical scientific foundation for precision treatments of congenital deafness. We also revealed that ABR and ASSR are reliable objective tools for assessing hearing recovery in patients after gene therapy. ABR displayed positive changes in the auditory pathway over time after gene therapy, enhancing our understanding of the impact of gene therapy on auditory pathway recovery (***Med***, 2025, cover story). Currently, our cohort study comparing gene therapy (GT) and cochlear implantation (CI) in pediatric patients with congenital deafness, which included auditory and speech perception, music perception, sound source localization, auditory information processing ability, and quality of life, demonstrated that GT patients achieved stable hearing recovery and exhibited more rapid improvements in auditory and speech performance than in CI patients, while outperforming CI in speech in noise performance and music perception, offering functional evidence for future clinical decision-making. (***JAMA Neurology,*** 2025).

II. Pathogenesis. As the most prevalent genetic etiology of hereditary hearing loss, *GJB2* mutations present unique modeling challenges due to embryonic lethality in knockout murine models. To address this critical barrier, we pioneered the first viable animal model recapitulating human *GJB2*-related deafness through tetraploid embryo complementation coupled with CRISPR-Cas9 genome editing (***Cell Mol Life Sci***, 2023), establishing an essential platform for mechanistic interrogation and therapeutic development. Additionally, our structural biology investigations elucidated molecular pathogenesis in two key auditory disorders: 1) Determined the cryo-EM structure of pendrin (SLC26A4), defective in large vestibular aqueduct syndrome, revealing novel ion transport regulation mechanism; 2) Characterized pathogenic variants in potassium channel KCNQ4 underlying progressive hearing loss, identifying critical gating domain perturbations through electrophysiological mapping (***Nat Commun***, 2023; ***Neuron***, 2022; ***Clin Genet***, 2022).

III. Inner ear Delivery. Due to the complexity of the inner ear structure, it is challenging to deliver drugs to the inner ear safely and efficiently. We explored multiple routes of gene therapy delivery in mice, guinea pigs, or monkeys, such as the lateral wall of the cochlea, the posterior semicircular canal (PSCC), round window membrane (RWM), and tubing-RWM+PSCC (t-RP), etc., and also studied the delivery efficiencies of 16 AAVs,

3 Ads, and 6 non-viral vectors in the inner ear, etc. We have developed a series of new injection routes and new vectors to deliver gene therapy drugs into the inner ear (***Hum Gene Ther***, **Cover story**, 2016; ***Hum Gene Ther***, **Cover story**, 2022; ***Neural Plast***, 2016; ***Front Cell Neurosci***, 2019; ***Cell Discov***, 2019; ***Mol Ther Methods Clin Dev***, 2020; ***Nanoscale***, 2022; ***Biomolecules***, 2023)**.** Additionally, we have independently developed a precise delivery device for the inner ear and opened up a new surgery pathway for gene therapy in patients with hearing loss (***Otology & Neurotology, 2024***).

IV. Prevention and treatment.

(1) Autosomal dominant hearing loss. Collaborate in the first CRISPR/Cas9 gene editing study of inner ear hair cells (***Nat Biotechnol***, 2014) and in the first CRISPR/Cas9-based treatment of dominant hereditary hearing loss in *Tmc1* mutant mice (***Nature***, 2017). Clarify that the *MYO6 p.C442Y* mutation is the dominant negative effect pathogenesis (***Hear Res***, 2019), and design the SaCas9-KKH therapeutic system, specifically disrupting the $Myo6^{C442Y}$ allele and sustainably restoring the hearing in mutant mice for 10 months (***Mol Ther***, 2022). Clinically diagnose a large deaf family, discover a novel mutation in *KCNQ4*, construct a mouse model that recapitulated the pathogenesis of the DFNA2 patient (***Clin Genet***, 2022), and develop a CRISPR/Cas9-based precise and specific knockout treatment system, which resulted in significant hearing restoration in mice at all frequencies (***Mol Ther Nucleic Acids***, 2022). Develop a highly efficient RNA editing therapeutic system with specific knockdown of *Tmc1* transcripts, improving the hearing in the *Tmc1* mutant mouse model (***Signal Transduct Target Ther***, 2022). Develop a novel RNA single-base editing tool, which can efficiently and accurately convert base A to I on RNA, and accurately correct the mutation site in $Myo6^{C442Y}$ deaf mice, leading to the significant hearing improvement (***Sci Transl Med***, 2022).

(2) Autosomal recessive deafness. We develop an adenine base editor targeting the prevalent *OTOF p.Q829X* mutation, restoring the level of the otoferlin protein in 88% of the inner hair cells and stably rescuing the auditory function of the mice to near-wild-type levels for over 1.5 years, which is the longest study to date to observe hearing recovery (***Nat Biomed Eng***, 2024). We overcame the low repair efficiency of homologous recombination via optimized homology-directed repair and ameliorated the hearing in recessive deaf mice by CRISPR/Cas9-mediated homologous recombination for the first time (***Cell Res***, 2022). To treatment DFNB9 caused by mutations in the *OTOF* gene (~6 kb cDNA), a dual-AAV gene therapy strategy on the basis of protein trans-splicing recombinant was developed, overcoming the difficulty of the delivery of large gene and successfully restoring the hearing in a mouse model of DFNB9 (***Hum Genet,*** 2023). Develop an antisense oligonucleotide candidate drug to significantly elevate the proportion of normal transcript in mononuclear cells from *SLC26A4* patients (***Mol Ther Nucleic Acids***, 2022). Develop a PAM-flexible base editor to rescue hearing loss in a mouse model of autosomal recessive deafness 111 (DFNB111) (***Nat Commun***, 2025).

(3) Acquired sensorineural hearing loss, hair cell regeneration and biomaterials. Aminoglycoside antibiotics (AGs) are ototoxic drugs. Based on DNA and RNA editing tools, developed therapeutic system targeting the *Htra2* gene to improve the auditory function in AG-exposed mice (***Genome Biol***, 2021; ***Mol Ther***

Nucleic Acids, 2022), which is the first successful study to combat acquired deafness with CRIPSR/Cas9. Regeneration in the adult mammalian inner ear remains a major challenge. We elucidated that overexpression of Notch and C-Myc could reprogram mature supporting cells and hair cells to enter the cell cycle and regenerate the living hair cells (***Nat Commun***, 2019). Tympanic membrane perforation is one of the most common clinical symptoms of conductive hearing disorders. A novel multifunctional GelMA-TA double-crosslinked electrostatically spun hydrogel was developed to promote tympanic membrane regeneration and restoration of auditory function (***Chem Eng J***, 2021). Local drug delivery is an effective method for disease therapy in fine organs including ears, eyes, and noses. We developed a type of dexamethasone sodium phosphate-encapsulated gelatin methacryloyl (Dexsp@GelMA) microgel particles, with finely tunable size through well-designed microfluidics, which could be used as a drug delivery vehicle for treatment of hearing loss (***ACS Appl Mater Interfaces***, 2022).

V. Clinical diagnosis and treatment. Report a clinical case of auricular chondritis infection causing cartilage necrosis ear deformity and propose a standardized clinical diagnostic and treatment process for auricular chondritis (***The British Medical Journal***, 2023). Based on the genetic screening of more than 4,000 cases of patients with hereditary hearing loss, we have established a domestic hereditary deafness data website in China, which is accessible to hospitals and patients at all levels across the country, making it convenient for grassroots doctors to study and educate patients. We have also established a birth defects alliance with a reproduction center and combined it with third-generation *in vitro* fertilization (IVF) technology to block the births of deaf babies. We established Shanghai Key Laboratory of Gene Editing and Cell Therapy for Rare Diseases, coordinated academic forums on rare diseases and advocated rare disease directory, advancing the clinical diagnosis and treatment of rare diseases.

Interests & Activities

- Participate actively in voluntary medical consultation
- Regular Blood Donor since 2005
- Enjoy music, swimming, dancing, badminton and other physical activities

Honors and Awards

- XPLORER PRIZE (2025)
- ARO Award for Clinical Innovation (2025)
- The First Prize of the 13th DBN Science and Technology Award (2025)
- Shanghai Youth Outstanding Science and Technology Contribution Award (2024)
- Shanghai Municipal Hospital Clinical Innovation Award (First Completer) (2024)

Curriculum Vitae

• The 4th Golden Snail Award for Rare Disease Medical Contribution（2024）

• China Hospital Association Hospital Science and Technology Innovation Award for R&D Innovation (First Completer) (2023)

• Huaxia Youth Medical Science and Technology Award (2023)

• First Prize of the "Chunsheng Cup" Medical Innovation Talent Competition (Growth Group) (2023)

• Second Prize of Shanghai Medical Science and Technology Award (First Completer）(2023)

• First Prize of "One Health Foundation" Outstanding Teachers (2023)

• Second Prize of the Third Fudan University Teaching Innovation Competition for Teachers (2023)

• Second Prize of the Eighth PBL Teaching Plan Writing Competition of Shanghai Medical College of Fudan University (2022)

• National Natural Science Foundation of China for National Science Fund for Distinguished Young Scholars (2022)

• Shanghai Youth May 4th Medal (2020)

• Shanghai Silver Snake Award for the highest honor of young talents in health system (2019)

• National Natural Science Foundation of China for Excellent Young Scientists Fund Program (2018)

• Excellent Oral Presentation of National Youth Annual Meeting of Otolaryngology (2018)

• Excellent Oral Presentation of Annual meeting of Otolaryngology - Head & Neck Surgery in Shanghai (2018)

• ARO Poster Blitz Podium (2018)

• Travel Award of Association for Research in Otolaryngology (2015, 2017,2018)

• Excellent Poster of National Annual Meeting of Otolaryngology of Chinese Medical Association (2017)

• The Pujiang Talen of Shanghai (2015)

• Outstanding Graduate of Fudan University (2012)

Academic Appointments

• Chairman of the Expert Committee on Deafness Prevention, Chinese Integrative Medicine Otorhinolaryngology Branch, Chinese Association of Integrative Medicine (2024-2026)

• Committee member, Chinese Society of Otolaryngology-Head and Neck Surgery, (2023-2026)

• Standing Committee Member, the Second Committee, Otology Section, Chinese Society of Geriatrics (2024-2029)

• Committee member, Long Range Planning of ARO (2018-2021)

• Committee member, International Committee of ARO (2015-2018)

• Standing committee member, Hearing, Speech and Communication Studies Academic Subgroup of the

Biophysical Society of China, (2021-2025)

• Chairman of the Expert Committee for Auditory Medicine Innovation and Translation of Audiology Development Foundation of China, (2023-2027)

• Committee member, Shanghai Medical Association Otolaryngology-Head and Neck Surgery Specialty Branch, (2023-2027)

• Committee member, Shanghai Medical Association Rare Diseases Specialty Branch(2023-2027)

• Corresponding Editor of the Second Editorial Board, World Journal of Otorhinolaryngology-Head and Neck Surgery(WJO-HNS) (2023-2027)

• Communicating Editor of the 12th Editorial Board, Chinese Journal of Otorhinolaryngology-Head and Neck Surgery (2023-2027)

Grant Support

Ongoing Grants as PI：

- National Natural Science Foundation of China (NSFC), ￥4,000,000, 202301-202712.
- the National Key R&D Program of China, ￥4,580,000, 202011-202510.
- the Science and Technology Commission of Shanghai Municipality, ￥3,000,000, 202312-202611.
- National Natural Science Foundation of China (NSFC), ￥570,000, 202201-202512.

Finished Grants as PI：

- National Natural Science Foundation of China (NSFC), ￥1,300,000, 201901-202112.
- National Natural Science Foundation of China (NSFC), ￥560,000, 201801-202112.
- National Natural Science Foundation of China (NSFC), ￥230,000, 201401-201612.
- the Science and Technology Commission of Shanghai Municipality, ￥500,000, 201804-202103
- the Science and Technology Commission of Shanghai Municipality, ￥200,000, 201705-202004
- the Science and Technology Commission of Shanghai Municipality, ￥200,000, 201507-201706

Representative Publications (**#** first author, * corresponding author)

1.Jun Lv#, Hui Wang#, Xiaoting Cheng#, Yuxin Chen#, Daqi Wang#, Longlong Zhang, Qi Cao, Honghai Tang, Shaowei Hu, Kaiyu Gao, Mengzhao Xun, Jinghan Wang, Zijing Wang, Biyun Zhu, Chong Cui, Ziwen Gao, Luo Guo, Sha Yu, Luoying Jiang, Yanbo Yin, Jiajia Zhang, Bing Chen, Wuqing Wang*, Renjie Chai*, Zheng-Yi Chen*, Huawei Li*, and **Yilai Shu***. AAV1-hOTOF Gene Therapy for Autosomal Recessive Deafness 9: a single-arm trial. ***The Lancet***, 403(10441):2317-2325, 2024. (Cover story)

2.Hui Wang#, Yuxin Chen#, Jun Lv#, Xiaoting Cheng#, Qi Cao#, Daqi Wang, Longlong Zhang, Biyun Zhu, Min Shen, Chunxin Xu, Mengzhao Xun, Zijing Wang, Honghai Tang, Shaowei Hu, Chong Cui, Luoying Jiang, Yanbo

Yin, Luo Guo, Yi Zhou, Lei Han, Ziwen Gao, Jiajia Zhang, Sha Yu, Kaiyu Gao, Jinghan Wang, Bing Chen, Wuqing Wang*, Zheng-Yi Chen*, Huawei Li*, **Yilai Shu***. Bilateral gene therapy in children with autosomal recessive deafness 9: single-arm trial results. ***Nature Medicine***,30(7):1898-1904, 2024.

3.Xiaoting Cheng#, Kevin A Peng, Bing Chen, **Yilai Shu***. A teenager with auricular infection secondary to piercing. ***The British Medical Journal***, 380:e071715, 2023.

4.Chong Cui#, Shengyi Wang#, Daqi Wang#, Jingjing Zhao, Bowei Huang, Biyun Zhu, Yuxin Chen, Honghai Tang, Yu Han, Cheng Ye, Dan Mu, Chengdong Zhang, Yuan Yang, Yihan Bao, Jun Lv, Shuang Han, Geng-Lin Li, Huawei Li, **Yilai Shu***. A base editor for the long-term restoration of auditory function in mice with recessive profound deafness. ***Nature Biomedical Engineering***, 9(1):40-56, 2025.

5.Jiajia Zhang#, Zengzhi Guo#, Changjie Pan#, Chunchun Hu#, Xinyang Weng#, Yang-wenyi Liu, Xiaoting Cheng, Jun Lv, Qi Cao, Hui Wang, Yuxin Chen, Daqi Wang, Shaowei Hu, Mengzhao Xun, Longlong Zhang, Zijing Wang, Honghai Tang, Biyun Zhu, Luo Guo, Sha Yu, Xiaoling Hu, Lin Chen, Bing Chen, Zheng-Yi Chen, Shan Sun*, Xiu Xu*, Huawei Li*, Fei Chen* and **Yilai Shu***. Preliminary evidence for enhanced auditory cortex activation and mental development after gene therapy in children with autosomal recessive deafness 9. ***Nature Human Behaviour***, 9(7):1457-1469, 2025.

6.Xiaoting Cheng#, Jiake Zhong#, Jiajia Zhang#, Chong Cui#, Luoying Jiang#, Yang-wenyi Liu#, Yuxin Chen, Qi Cao, Daqi Wang, Guiqing Cheng, Yuxin Zong, Min Shen, Chunxin Xu, Jun Lv, Hui Wang, Longlong Zhang, Biyun Zhu, Honghai Tang, Jinghan Wang, Xintai Fan, Yanqing Fang, Luo Guo, Jiawei Guo, Liheng Chen, Yanbo Yin, Zijing Wang, Lei Han, Shaowei Hu, Shengyi Wang, Guoyou Qin, Xuezhong Liu, Jinqiu Sang, Fangang Zeng, Wuqing Wang*, Bing Chen*, Zheng-Yi Chen*, Huawei Li*, **Yilai Shu***. Gene Therapy vs Cochlear Implantation in Restoring Hearing Function and Speech Perception for Individuals With Congenital Deafness. ***JAMA Neurology***, 2025 July 21.

7.Yuxin Chen#, Jiake Zhong, **Yilai Shu***. Gene therapy for deafness: we can do more. ***Nature Reviews Genetics***. 26(4):225-226, 2025.

8.Qingquan Xiao#, Zhijiao Xu#, Yuanyuan Xue#, Chunlong Xu#, Lei Han, Yuanhua Liu, Fang Wang, Runze Zhang, Shuang Han, Xing Wang, Geng-Lin Li, Huawei Li*, Hui Yang*, **Yilai Shu***. Rescue of autosomal dominant hearing loss by in vivo delivery of mini dCas13X-derived RNA base editor. ***Science Translational Medicine***, 14(654):eabn0449, 2022.

9.Xi Gu#, Xinde Hu#, Daqi Wang#, Zhijiao Xu, Fang Wang, Di Li, Geng-lin Li, Hui Yang, Huawei Li*, Erwei Zuo* and **Yilai Shu***. Treatment of autosomal recessive hearing loss via in vivo CRISPR/Cas9-mediated optimized homology-directed repair in mice. ***Cell Research***, 32(7):699-702,2022.

10.Longlong Zhang#, Dingding Dong#, Yanbo Yin#, Honghai Tang#, Jun Lv, Qi Cao, Wuqing Wang, Bing Chen*, Yunfeng Wang*, Huawei Li*, Daqi Wang*, **Yilai Shu***. Audiological characteristics following gene therapy in patients with autosomal recessive deafness 9. ***Med***, 6(8):100696, 2025. (Cover story)

11.Shao Wei Hu#, Sohyang Jeong#, Luoying Jiang#, Hansol Koo#, Zijing Wang, Won Hoon Choi, Biyun Zhu, Heeyoung Seok, Yi Zhou, Min Gu Kim, Dan Mu, Huixia Guo, Ziyi Zhou, Sung Ho Jung, Yingting Zhang, Ho

Byung Chae, Liheng Chen, Sung-Yeon Lee, Luo Guo, Myung-Whan Suh, Yang Xiao, Moo Kyun Park, Honghai Tang, Jae-Jin Song, Xi Chen, Ai Chen, Jun Ho Lee, Sangsu Bae*, Sang-Yeon Lee*, **Yilai Shu***.PAM-flexible adenine base editing rescues hearing loss in a humanized MPZL2 mouse model harboring an East Asian founder mutation. ***Nature Communications***, 16(1):7186, 2025.

12.Yuanyuan Xue#, Xinde Hu#, Daqi Wang#, Di Li#, Yige Li, Fang Wang, Mingqian Huang, Xi Gu, Zhijiao Xu, Jinan Zhou, Jinghan Wang, Renjie Chai, Jun Shen, Zheng-Yi Chen, Geng-Lin Li, Hui Yang, Huawei Li*, Erwei Zuo*, and **Yilai Shu***. Gene editing in a Myo6 semi-dominant mouse model rescues auditory function. ***Molecular Therapy***, 30(1):105-118, 2022.

13.Ziwen Zheng#, Guo Li#, Chong Cui#, Fang Wang, Xiaohan Wang, Zhijiao Xu, Huiping Guo, Yuxin Chen, Honghai Tang, Daqi Wang, Mingqian Huang, Zheng-Yi Chen, Xingxu Huang, Huawei Li, Geng-Lin Li*, Xiaoxiang Hu* and **Yilai Shu***. Preventing autosomal-dominant hearing loss in Bth mice with CRISPR/CasRx-based RNA editing. ***Signal Transduction and Targeted Therapy***, 7(1):79, 2022.

14.Qianying Liu#, Xiang Zhang#, Hui Huang#, Yuxin Chen#, Fang Wang, Aihua Hao, Wuqiang Zhan, Qiyu Mao, Yuxia Hu, Lin Han, Yifang Sun, Meng Zhang, Zhimin Liu, Geng-Lin Li, Weijia Zhang, **Yilai Shu***, Lei Sun*, Zhenguo Chen*. Asymmetric pendrin homodimer reveals its molecular mechanism as anion exchanger. ***Nature Communications***, 14(1):3012, 2023.

15.You Zheng#, Heng Liu#, Yuxin Chen#, Shaowei Dong#, Fang Wang, Shengyi Wang, Geng-Lin Li, **Yilai Shu***, Fei Xu*. Structural insights into the lipid and ligand regulation of a human neuronal KCNQ channel. ***Neuron***, 110(2): 237-247, 2022.

16.Shao Wei Hu#, Jun Lv#, Zijing Wang#, Honghai Tang#, Hui Wang, Fang Wang, Daqi Wang, Juan Zhang, Longlong Zhang, Qi Cao, Yuxin Chen, Ziwen Gao, Yu Han, Wuqing Wang, Geng-Lin Li*, **Yilai Shu***, Huawei Li*. Engineering of the AAV-Compatible Hair Cell-Specific Small-Size Myo15 Promoter for Gene Therapy in the Inner Ear. ***Research***, 7:0341, 2024.

17.Long Long Zhang#, JingHan Wang#, Zi Wen Gao#, Jun Lv, Luo Ying Jiang, Chong Cui, Zi Jing Wang, Da Qi Wang, Yu Xin Chen, Xin Tai Fan, Cheng Ye, Hui Wang, Bing Chen*, Wu Qing Wang*, Hua Wei Li*, **Yi Lai Shu***. A Novel Delivery Approach of Clinical Inner Ear Gene Therapy. ***Otology & Neurotology***, 46(1):31-38, 2025.

18.Luoying Jiang#, Daqi Wang#, Yingzi He*, **Yilai Shu***. Advances in gene therapy hold promise for treating hereditary hearing loss. ***Molecular Therapy***, 31(4):934-950, 2023.

19.Hui Wang#, Mengzhao Xun#, Honghai Tang#, Jingjing Zhao, Shaowei Hu, Longlong Zhang, Jun Lv, Daqi Wang, Yuxin Chen, Jianping Liu, Geng-lin Li, Wuqing Wang*, **Yilai Shu***, Huawei Li*. Hair cell-specific Myo15 promoter-mediated gene therapy rescues hearing in DFNB9 mouse model. ***Molecular Therapy Nucleic Acids***, 35(1), 35(1):102135, 2024.

20.Luoying Jiang#, Shaowei Hu#, Zijing Wang#, Yi Zhou, Honghai Tang, Yuxin Chen, Daqi Wang, Xintai Fan, Lei Han, Huawei Li, Dazhi Shi, Yingzi He*, **Yilai Shu***. Hearing restoration by gene replacement therapy for a multisite-expressed gene in a mouse model of human DFNB111 deafness. ***The American Journal of Human***

Genetics. 111(10):2253-2264, 2024.

21.Chong Cui#, Daqi Wang#, Bowei Huang#, Fang Wang#, Yuxin Chen, Jun Lv, Luping Zhang, Lei Han, Dong Liu, Zheng-Yi Chen, Geng-Lin Li, Huawei Li, **Yilai Shu***. Precise detection of CRISPR-Cas9 editing in hair cells in the treatment of autosomal dominant hearing loss. ***Molecular Therapy-Nucleic Acids***, 29:400-412, 2022.

22.Qing Li#*, Chong Cui#, Rongyu Liao, Xidi Yin, Daqi Wang, Yanbo Cheng, Bowei Huang, Liqin Wang, Meng Yan, Jinan Zhou, Jingjing Zhao, Wei Tang, Yingyi Wang, Xiaohan Wang, Jun Lv, Jinsong Li, Huawei Li*, **Yilai Shu***. The pathogenesis of common Gjb2 mutations associated with human hereditary deafness in mice. ***Cellular and Molecular Life Sciences***, 80(6):148, 2023.

23.Jiali Wang#, Chong Wang, Qiao Wang, Zhuohao Zhang, Hui Wang, Shengyi Wang, Zhangcai Chi, Luoran Shang*, Wuqing Wang*, **Yilai Shu***. Microfluidic Preparation of Gelatin Methacryloyl Microgels as Local Drug Delivery Vehicles for Hearing Loss Therapy. ***Acs Applied Materials & Interfaces***, 14(41):46212-46223, 2022.

24.Pengchao Feng#, Zhijiao Xu#, Jialin Chen, Meizhen Liu, Yu Zhao, Daqi Wang, Lei Han, Li Wang, Bo Wan, Xingshun Xu, Dali Li, **Yilai Shu***, Yimin Hua*. Rescue of mis-splicing of a common SLC26A4 mutant associated with sensorineural hearing loss by antisense oligonucleotides. ***Molecular Therapy-Nucleic Acids***, 28:280-292, 2022.

25.Yang Guo#, Lei Han#, Shuang Han, Honghai Tang, Shengyi Wang, Chong Cui, Bing Chen*, Huawei Li*, **Yilai Shu***. Specific knockdown of Htra2 by CRISPR-CasRx prevents acquired sensorineural hearing loss in mice. ***Molecular Therapy-Nucleic Acids***, 28:643-655, 2022.

26.Xinde Hu#, Jinghan Wang#, Xuan Yao#, Qingquan Xiao#, Yuanyuan Xue, Shaoran Wang, Linyu Shi, **Yilai Shu***, Huawei Li*, Hui Yang*. Screened AAV variants permit efficient transduction access to supporting cells and hair cells. ***Cell Discovery***, 5:49, 2019.

27.Xi Gu#, Daqi Wang#, Zhijiao Xu#, Jinghan Wang, Luo Guo, Renjie Chai, Genglin Li, **Yilai Shu***, Huawei Li*. Prevention of acquired sensorineural hearing loss in mice by in vivo Htra2 gene editing. ***Genome Biology***, 22(1):86, 2021.

28.**Yilai Shu#**, Wenyan Li#, Mingqian Huang#, Yi-Zhou Quan#, Deborah Scheffer, Chunjie Tian, Yong Tao, Xuezhong Liu, Konrad Hochedlinger, Artur A. Indzhykulian, Zhengmin Wang, Huawei Li, Zheng-Yi Chen*. Renewed proliferation in adult mouse cochlea and regeneration of hair cells. ***Nature Communications***, 10(1):5530, 2019.

29.Jinghan Wang#, Liping Zhao#, Xi Gu#, Yuanyuan Xue, Shengyi Wang, Ru Xiao, Luk H. Vandenberghe, Kevin A. Peng, **Yilai Shu***, Huawei Li*. Efficient Delivery of Adeno-Associated Virus into Inner Ear In Vivo Through Trans-Stapes Route in Adult Guinea Pig. ***Human Gene Therapy***, 33(13-14):719-728, 2022. (Cover story)

30.Honghai Tang#, Hui Wang#, Shengyi Wang#, Shao Wei Hu#, Jun Lv, Mengzhao Xun, Kaiyu Gao, Fang Wang, Yuxin Chen, Daqi Wang, Wuqing Wang*, Huawei Li*, **Yilai Shu***. Hearing of Otof-deficient mice restored by trans-splicing of N- and C-terminal otoferlin. ***Human Genetics***, 142(2):289-304, 2023.

31.Longlong Zhang#, Hui Wang#, Mengzhao Xun#, Honghai Tang#, Jinghan Wang, Jun Lv, Biyun Zhu, Yuxin

Chen, Daqi Wang, Shaowei Hu, Ziwen Gao, Jianping Liu, Zheng-Yi Chen, Bing Chen*, Huawei Li*, **Yilai Shu***. Preclinical evaluation of the efficacy and safety of AAV1-hOTOF in mice and nonhuman primates. ***Molecular Therapy Methods & Clinical Development***, 31:101154, 2023.

32.Shuang Han#, Zhijiao Xu#, Shengyi Wang, Honghai Tang, Shaowei Hu, Hui Wang, Guofang Guan*, **Yilai Shu***. Distributional comparison of different AAV vectors after unilateral cochlear administration. ***Gene Therapy***, 31(3-4):154-164, 2024.

33.Bing Wang#, Tianwen Xin#, Lang Shen, Kun Zhang, Dan Zhang, Hui Zhang, Jisheng Liu, Bing Chen*, Wenguo Cui*, **Yilai Shu***. Acoustic transmitted electrospun fibrous membranes for tympanic membrane regeneration. ***Chemical Engineering Journal***, 419, 129536, 2021.

34.**Yilai Shu#**, Yong Tao, Zhengmin Wang, Yong Tang, Huawei Li, Pu Dai, Guangping Gao, Zheng-Yi Chen*. Identification of Adeno-Associated Viral Vectors That Target Neonatal and Adult Mammalian Inner Ear Cell Subtypes. ***Human Gene Therapy***, 27(9):687-99, 2016. (Cover story)

Patents

1. **Yilai Shu** (1/4). CRISPR/Cas9 Gene Editing System and Its Application in Developing Therapeutics for Hereditary Sensorineural Deafness. 07/25/2023, ZL 2021 1 0691504.2
2. **Yilai Shu** (1/5). Application of Htra2 Gene Expression Inhibitors in Preventing Acquired Sensorineural Deafness. 11/29/2022, ZL 2021 1 0288529.8
3. **Yilai Shu** (1/6). CRISPR/CasRx-based Gene Editing Methods and Their Applications. 01/24/2023, ZL 2021 1 0919746.2
4. **Yilai Shu** (1/5). The Applications of sgRNA and CRISPR/CasRx System for Targeted Knockdown of Htra2 Transcripts.01/02/2024, ZL 2022 1 0500081.6
5. **Yilai Shu** (1/6). CRISPR/Cas9 Gene Editing System for Repairing Klhl18^{lowf} Mutant Genes and Its Applications.02/13/2024, ZL 2022 1 0107537.2
6. **Yilai Shu** (1/10). Micro-dosing Device for the Inner Ear. 01/26/2024, ZL 2023 2 1758105.4
7. **Yilai Shu** (1/10). Low Residual Micro-syringe.09/24/2024, ZL 2024 2 0328358.6
8. **Yilai Shu** (2/10). Low Residual Micro- infusion Tubing. 10/25/2024, ZL 2024 2 0328214.0
9. **Yilai Shu** (2/10). Micro-infusion Pump. 09/24/2024, ZL 2024 2 0328515.3

Oral or Poster in International Conference

[1].**Yilai Shu.** Gene Therapy Restores Hearing for Autosomal Recessive Deafness 9: a Multicenter Clinic Trial. 96th Annual Meeting of the German Society of Oto-Rhino-Laryngology, Head and Neck Surgery 2025, May 28-31, 2025, Frankurt, Germany. Oral presentation. Invited lecture.

[2].**Yilai Shu.** Gene Therapy in DFNB9 Patients. 96th Annual Meeting of the German Society of Oto-Rhino-Laryngology, Head and Neck Surgery 2025, May 28-31, 2025, Frankurt, Germany. Oral presentation. Invited lecture.

[3].**Yilai Shu.** Gene therapy in Otoferlin mutation-related congenital sensorineural hearing loss. 34th Politzer Society Meeting 2024, Oct 13-16, 2024, Rome, Italy. Instructional Course.

[4].**Yilai Shu**, Jun Lv, Hui Wang, Xiaoting Cheng, Yuxin Chen, Daqi Wang, Longlong Zhang, Qi Cao, Honghai Tang, Shaowei Hu, Kaiyu Gao, Mengzhao Xun, Jinghan Wang, Zijing Wang, Biyun Zhu, Chong Cui, Ziwen Gao, Luo Guo, Sha Yu, Luoying Jiang, Yanbo Yin, Jiajia Zhang, Bing Chen, Wuqing Wang, Renjie Chai, Zheng-Yi Chen, Huawei Li. AAV1-hOTOF Gene Therapy for Autosomal Recessive Deafness 9. ESGCT 2024, Oct 22-25, 2024, Rome, Italy. Oral presentation. (PLENARY)

[5].**Yilai Shu**, Jun Lv, Hui Wang, Xiaoting Cheng, Yuxin Chen, Daqi Wang, Longlong Zhang, Qi Cao, Honghai Tang, Shaowei Hu, Kaiyu Gao, Mengzhao Xun, Jinghan Wang, Zijing Wang, Biyun Zhu, Chong Cui, Bing Chen, Wuqing Wang, Renjie Chai, Zheng-Yi Chen, Huawei Li. AAV1-hOTOF Gene Therapy for Children with Autosomal Recessive Deafness 9. ASGCT 2024, May 7-11, 2024, Baltimore, MD, USA. Oral presentation.

[6].**Yilai Shu**. AAV1-HOTOF Gene Therapy for Children with Autosomal Recessive Deafness 9. ARO 2024, Feb 03 - 07, 2024 Anaheim, CA, USA. Presidential Symposium.

[7].**Yilai Shu**, Jun Lv, Hui Wang, Xiaoting Cheng, Yuxin Chen, Daqi Wang, Longlong Zhang, Qi Cao, Honghai Tang, Shaowei Hu, Kaiyu Gao, Wuqing Wang, Zheng-Yi Chen, Huawei Li. AAV1-HOTOF Gene Therapy for Autosomal Recessive Deafness 9 (DFNB9). ARO 2024, Feb 03-07, 2024 Anaheim, CA, USA, Poster.

[8].**Yilai Shu**, Jun Lv, Hui Wang, Xiaoting Cheng, Yuxin Chen, Daqi Wang, Longlong Zhang, Qi Cao, Honghai Tang, Shaowei Hu, Kaiyu Gao, Wuqing Wang, Huawei Li, Zheng-yi Chen. AAV1-hOTOF gene therapy trial for autosomal recessive deafness 9(DFNB9). ESGCT 2023, Oct 24-27, 2023, Brussels, Belgium, Oral presentation.

[9].**Yilai Shu**, Chong Cui, Shengyi Wang, Daqi Wang, Geng-Lin Li, Huawei Li. In vivo adenine base editing restores long-term auditory function in a mouse model of recessive profound deafness. IEB 2023, September 2-5, 2023, London, UK, Oral presentation.

[10].**Yilai Shu**, Qingquan Xiao, Zhijiao Xu, Yuanyuan Xue, Chunlong Xu, Xinde Hu, Daqi Wang, Di Li, Chong Cui, Bowei Huang, Fang Wang. Gene Therapy for Heating Loss.The 16th Annual Meeting of Chinese Neuroscience Society & The 2nd CJK International Meeting 2023, Zhuhai, China, Oral presentation.

[11].**Yilai Shu**, Yang Guo, Lei Han, Shuang Han, Honghai Tang, Shengyi Wang, Chong Cui, Bing Chen, Huawei Li. Specific knockdown of Htra2 by CRISPR-CasRx prevents acquired sensorineural hearing loss in mice. EES2022 .Dec 5-8，2022, Kyoto, Japan. Oral presentation.

[12].**Yilai Shu**, Xi Gu, Daqi Wang, Xinde Hu, Zhijiao Xu, Fang Wang, Geng-lin Li, Hui Yang, Erwei Zuo and Huawei Li. Treatment of Autosomal Recessive Hearing Loss via in Vivo CRISPR/Cas9-Mediated Optimized Homology-Directed Repair in Mice. ARO 2022, Virtual conference, San Jose, California USA, Oral presentation.

[13].**Yilai Shu,** Yuanyuan Xue, Daqi Wang, Jinghan Wang, Huawei Li. Restoration of hearing in a Myo6 genetic

deafness model using CRISPR/Cas9. ARO 2021, Orlando, Virtual Meeting, Oral presentation.

[14].**Yilai Shu,** Jinghan Wang, Jun Shen, Cheng Chen, Renjie Chai, Huawei Li**.** A humanized mouse model demonstrated that apparently autosomal dominant deafness caused by MYO6 p.C442Y is inherited in a semi-dominant pattern. The 19th International Association of Physicians in Audiology. Egypt. 2018. Oral presentation.

[15].**Yilai Shu**, Wenyan Li, Yizhou Quan, Mingqian Huang, Zhengmin Wang, Huawei Li, Zheng-Yi Chen. Induction of proliferation in adult and aged mouse cochlea. San Diego, USA, ARO 2018, PS 215 Poster Blitz Podium.

[16].**Yilai Shu**, Wenyan Li, Yong Tao, Huawei Li, David Liu, Zheng-Yi Chen. Gene Therapy for genetic deafness. The 15th International and Chinese Biophysics Congress.2017.11.06. Shanghai. Oral presentation.

[17].**Yilai Shu,** John Zuris, David Thompson, Yong Tao, David Liu, Zheng-Yi Chen. Efficient Delivery of Functional Genome Editing Proteins into Mammalian Inner Ear In Vivo. ARO 2015 9:30 PD-88. Oral presentation.

[18].**Yilai Shu,** John A Zuris, David B Thompson, Yong Tao, Wenyan Li, Zhengmin Wang, Huawei Li, David R Liu, Zheng-Yi Chen. Efficient Delivery of CRISPR/Cas9 Proteins into Mammalian Inner Ear In Vivo and Neuron Stem Cells in Vitro. 52nd Inner Ear Biology. Rome, Italy,2015.9.12-9.15. Oral presentation.

[19].**Yilai Shu,** Yong Tao, Margie Li, Zhengmin Wang, Huawei Li, David Liu and Zheng-Yi Chen Highly efficient functional protein with a peptide into neonatal and adult mammalian inner ear in vivo. The 10th Molecular Biology of Hearing and Deafness. Cambridge, UK. 2016.5.17-20. Oral presentation.

[20].**Yilai Shu,** Xi Gu, Xinde Hu, Daqi Wang, Zhijiao Xu, Fang Wang, Di Li, Geng-Lin Li, Hui Yang, Huawei Li, Erwei Zuo. Treatment of autosomal recessive hearing loss via in vivo CRISPR/Cas9-mediated optimized homology-directed repair in mice. EES2022, December 5-8, 2022, Kyoto, Japan, Poster, 1296.

[21].**Yilai Shu**, jinghan wang, Xinde Hu, Yuanyuan Xue Hui Yang, huawei Li Screened AAV Variants Permit Efficient Transduction Access to Inner Ear Cells for Gene therapy. ARO 2020, PS 405, Poster

[22].**Yilai Shu,** Jinghan Wang, Xi Gu, Yuanyuan Xue, Luo Guo, Wenyan Li, Renjie Chai, Huawei Li, Efficient delivery of AAV into mammalian inner ear in vivo via trans-stapes injection in adult guinea pig, ARO 2019, PS 705, Poster

[23].**Yilai Shu***,* Lijuan Wang, Jun Shen, Zhengmin Wang, Huawei Li, Weiguo Zou, Bing Chen. A Novel NOG Mutation (P170L) Impairs Noggin Secretion and Causes Autosomal Dominant Congenital Conductive Hearing Loss. Baltimore, USA, ARO 2017, Poster

[24].**Yilai Shu,** Yong Tao, Margie Li, Zhengmin Wang, Huawei Li, David Liu and Zheng-Yi Chen Highly efficient delivery of functional protein with a peptide into mammalian inner ear in vivo. PS908, Volume 39，P535, 2016.2.19-24. ARO 2016. Poster.

[25].**Yilai Shu,** Na Lu, Marco Petrillo, Wenyan Li, Guanping Gao, Huawei Li, Zhengmin Wang and Zheng-Yi Chen. Identification of Adeno-associate viral vectors (AAV) that target mammalian cochlear cells.

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