Hong-Bo Zhao, PhD/MD Professor (tenured) Department of Surgery – Otolaryngology Yale University Medical School Curriculum Vitae

Working Address:

Dept. of Surgery – Otolaryngology Yale University Medical School 310 Cedar Street, BML 227 New Haven, CT 06510

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Present and Previous Positions:

2022 -	Professor (tenured), Dept. of Surgery/ENT, Yale University Medical School
2019 - 2022	Professor (tenured), Richard C. Haydon Endowed Chair in Otolaryngology
	Dept. of Otolaryngology, University of Kentucky Medical School
2007 - 2019	Associate Professor (tenured), Richard C. Haydon Endowed Chair in Otolaryngology
	Dept. of Otolaryngology, University of Kentucky Medical School
2002 - 2007	Assistant Professor (tenure track), Dept. of Surgery/ENT, University of Kentucky
	Medical School
1999 - 2002	Instructor, Dept. of Otorhinolaryngology, Baylor College of Medicine
1982 - 1986	Doctor, the Fourth People's Hospital of Yichang, P.R. of China

Education and Training:

1982:	MD, Medicine, Yichang Medical College, China
1989:	MS, Biomedical Engineering, Huazhong University of Science & Technology, China
1992:	PhD, Neuroscience, Shanghai Institute of Physiology, Chinese Academy of Sciences
1993 – 1995	Postdoctoral Fellow, Neuroscience, University of Connecticut Health Center
1995 – 1999	Postdoctoral Fellow, Neuroscience, Yale University Medical School

Awards and Honors:

- 1978 1982 National Doctor Scholarship, Ministry of Public Health, China
- 1986 1992 National Graduate Student Scholarship, State Education Commission, China
- 1990 Technique Advancement Award, Shanghai Institute of Physiology, Chinese Academy of Sciences, Shanghai, China
- 2000 Research Award, National Organization for Hearing Research
- 2008 2013 Professorship, University of Kentucky Medical Center
- 2018 2022 University of Kentucky Wethington Research Award

Grant Reviewers (selected in recently):

- 2024 Ad hoc Member, NIH ZAG1 AN-K (55), CDRC, and BTEN study sections
- 2023 Ad hoc Member, NIH ZAG1 ZIJ, AN-Q (55), and AUD study sections
- 2022 Member, NIH ZDC1 SRB-X and NIDCD NHERN study sections
- 2021 *Ad hoc* Member, NIH NTRC study section
- 2020 2021 Member, NIH ZRG1 IFCN-E study section

2020	Member, NIH study section, NIDCD Special Emphasis Panel, ZDC1 SRB-E
2020	Member, Grant Review Panel, Swiss National Science Foundation, Switzerland
2019	Member, Discovery Project Grant Review Panel, The Royal National Institute for
	Deaf People, London, United Kingdom.
2018 - 2020	Member, Grant Review Panel, Department of Defense Congressionally Directed
	Medical Research Programs (CDMRP), USA
2018	Member, Medical Research Council (MRC) grant review panel, United Kingdom
2015 - 2017	Member, Biotechnology and Biological Sciences Research Council (BBSRC) grant review panel, United Kingdom
2015 - 2019	Ad hoc Member, Grant Review Panel, National Natural Science Foundation of China
2015	Member, Netherlands Organization for Science & Research grant, Netherlands
Committees:	

2024 -	Member, the Board of Permanent Officers (BPO), Yale University Medical
	School
2024 -	Member, ARO Travel Award Committee.

Editorial Board Member of International Journals:

Editorships:

2015 -	Editorial Board Member	<scientific reports=""></scientific>
2022 -	Associate Editor	<frontiers in="" molecular="" neuroscience=""></frontiers>

Reviewer (selected):

<Science>; <Nature Neuroscience>; <PNAS>; <J. of Neuroscience>; <Neuroscience>;
<Biophysics J>; <J. of Physiology> (London); <Hearing Research>; <ORL, J. for Oto-Rhino-Laryngology>; <The Laryngoscope>; <Brain Research>; <Cellular and Molecular Life Sciences>;
<Neuroscience Letter>; <JARO>; <J. of Neuroscience Methods>; <Audiology & Neurotology>;
<European Journal of Human Genetics>; <Plos One>; <Neurobiology of Disease>; <The Journal of Perinatology>; <Frontiers in Cellular Neuroscience>; <American Journal of Pathology>; <Medical & Biological Engineering & Computing>; <Gene Therapy & Molecular Biology>; <Current Biology>; <J of Cell Science>; <J. of Perinatology>; <Experimental Gerontology>; <Current Research in Neurobiology of Aging>; <J. of Alzheimer's Disease>; <Nature Aging>

Publications:

Selected key publications:

- 1. **Zhao HB**, Santos-Sacchi J. (1999) Auditory collusion and a coupled couple of outer hair cells. *Nature* 399: 359-362.
- 2. Oghalai JS, **Zhao HB**, Kutz Jr JW, Brownell WE. (2000) Voltage and tension-dependent lipid mobility in the outer hair cell plasma membrane. *Science* 287: 658-661.
- 3. **Zhao HB**, Yu N, Fleming CR. (2005) Gap junctional hemichannel-mediated ATP release and hearing controls in the inner ear. *Proc Natl Acad Sci USA* 102: 18724-18729.

- Zhao, H.B. page 3 (2013) Active cochlear amplification
- Zhu Y, Liang C, Chen J, Zong L, Chen GD, Zhao HB. (2013) Active cochlear amplification is dependent on supporting cell gap junctions. <u>Nat Commun.</u> 4: 1786 doi: 10.1038/ncommuns2806.
- Zhao HB, Zhu Y, Liu LM. (2021) Excess extracellular K⁺ causes inner hair cell ribbon synapse degeneration. <u>*Commun Biol.*</u> 4(1):24. doi: 10.1038/s42003-020-01532-w. PMID: 33398038.
- Liu LM, Liang C, Chen J, Fang S, Zhao HB. (2023) Cx26 heterozygous mutations cause hyperacusis-like hearing oversensitivity and increase susceptibility to noise. <u>Sci Adv.</u> 9(6):eadf4144. doi: 10.1126/sciadv.adf4144. PMID: 36753545

Complete list of publications:

https://www.ncbi.nlm.nih.gov/myncbi/hong-bo.zhao.1/bibliography/public/

- 1. **Zhao HB**, Yang Y. (2024) Hearing loss promotes Alzheimer's disease. <u>*Nat Aging*</u>. 4(4):443-444. doi: 10.1038/s43587-024-00606-2. PMID: 38491290.
- Liu LM, Liang C, Chen J, Fang S, Zhao HB. (2023) Cx26 heterozygous mutations cause hyperacusis-like hearing oversensitivity and increase susceptibility to noise. <u>Sci Adv</u>. 9(6):eadf4144. doi: 10.1126/sciadv.adf4144. PMID: 36753545
- Zhao HB, Liu LM, Yu N, Zhu Y, Mei L, Chen J, Liang C. (2022) Efferent neurons control hearing sensitivity and protect hearing from noise through the regulation of gap junctions between cochlear supporting cells. *J Neurophysiol*. 127: 313-327. doi: 10.1152/jn.00468.2021. PMID: 34907797.
- Mei L, Liu LM, Chen K, Zhao HB (2021). Early functional and cognitive declines measured by auditory evoked cortical potentials in mice with Alzheimer's disease. <u>Front. Aging</u> <u>Neurosci.</u> 13:710317. doi: 10.3389/fnagi.2021.710317. PMID: 34588972
- Zhao HB, Zhu Y, Liu LM. (2021) Excess extracellular K⁺ causes inner hair cell ribbon synapse degeneration. <u>Commun Biol.</u> 4(1):24. doi: 10.1038/s42003-020-01532-w. PMID: 33398038
- Liu Y, Fang S, Liu LM, Zhu Y, Li CR, Chen K, Zhao HB. (2020) Hearing loss is an early biomarker in APP/PS1 Alzheimer's disease mice. <u>Neurosci. Lett.</u> 134705. doi: 10.1016/j.neulet.2019.134705.
- Chen J, Liang C, Zong L, Zhu Y, Zhao HB. (2018) Knockout of Pannexin-1 induces hearing loss. *Int. J. Mol. Sci.* 19(5). pii: E1332. doi: 10.3390/ijms19051332.
- Zhu Y, Beudez J, Yu N, Grutter T, Zhao HB. (2017) P2X2 dominant deafness mutations have no negative effect on wild-type isoform: Implications for functional rescue and in deafness mechanism. <u>Front. Mol. Neurosci.</u> 10:371. doi: 10.3389/fnmol.2017.00371.
- 9. Mei L, Chen J, Zong L, Zhu Y, Liang C, Jones RO, Zhao HB. (2017) A deafness mechanism

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- Zong L, Chen J, Zhu Y, Zhao HB. (2017) Progressive age-dependence and frequency difference in the effect of gap junctions on active cochlear amplification and hearing. <u>Biochem</u> <u>Biophys Res Commun.</u> 489: 223-227. doi: 10.1016/j.bbrc.2017.05.137.
- Zhao HB. (2017) Hypothesis of K⁺-recycling defect is not a primary deafness mechanism for Cx26 (*GJB2*) deficiency. *Front. Mol. Neurosci.* 10:162. doi: 10.3389/fnmol.2017.00162
- Zong L, Zhu Y, Liang RQ, Zhao HB. (2016) Gap junction mediated miRNA intercellular transfer and gene regulation: A novel mechanism for intercellular genetic communication. <u>Sci</u> <u>Rep.</u> 6: 19884. doi: 10.1038/srep19884.
- 13. **Zhao HB**. (2016) Expression and function of pannexins in the inner ear and hearing. <u>BMC</u> <u>cell biology</u>. 17 Suppl 1:16.
- Zhu Y, Chen J, Liang C, Zong L, Chen J, Jones RO, Zhao HB. (2015) Connexin26 (*GJB2*) deficiency reduces active cochlear amplification leading to late-onset hearing loss. <u>Neuroscience</u> 284: 719-729.
- Zhu Y, Zong L, Mei L, Zhao HB. (2015) Connexin26 gap junction mediates miRNA intercellular genetic communication in the cochlea and is required for inner ear development. <u>Sci Rep.</u> 5: 15647. doi: 10.1038/srep15647.
- Wingard JC, Zhao HB. (2015) Cellular and deafness mechanisms underlying connexin mutation induced hearing loss – a common hereditary deafness. *Front. Cell. Neurosci.* 9: 202. doi: 10.3389/fncel.2015.00202
- 17. **Zhao HB**, Zhu Y, Liang C, Chen J. (2015) Pannexin 1 deficiency can induce hearing loss. *Biochem Biophys Res Commun.* 463: 143-147.
- Chen J, Zhu Y, Liang C, Chen J, Zhao HB. (2015) Pannexin1 channels dominate ATP release in the cochlea ensuring endocochlear potential and auditory receptor potential generation and hearing. <u>Sci Rep.</u> 5: 10762. doi: 10.1038/srep10762.
- 19. Chen J, Chen J, Zhu Y, Liang C, **Zhao HB.** (2014) Deafness induced by Connexin26 (*GJB2*) deficiency is not determined by endocochlear potential (EP) reduction but is associated with cochlear developmental disorders. <u>*Biochem Biophys Res Commun.*</u> 448: 28-32.
- 20. Chen J, **Zhao HB**. (2014) The role of an inward rectifying K⁺ channel (Kir4.1) in the inner ear and hearing. *Neuroscience* 265: 137-146.
- 21. Yan D, Zhu Y, Walsh T, Xie DH, Yuan HJ, Sirmaci A, Fujikawa T, Wong ACY, Loh TL, Du LL, Grati M, Vlajkovic SM, Blanton S, Ryan AF, Chen ZY, Thorne PR, Kachar B, Tekin M, Zhao HB, Housley GD, King MC, Liu XZ. (2013) Mutation of the ATP-gated P2X2 receptor

leads to progressive hearing loss and increased susceptibility to noise. <u>*Proc Natl Acad Sci USA*</u> 110: 2228-2233.

- 22. Liang C, Hong Q, Jiang TT, Gao Y, Yao XF, Luo XX, Zhuo XH, Shinn JB, Jones RO, Zhao HB, Lu GJ. (2013) The effects and outcomes of electrolyte disturbances and asphyxia on newborns hearing. *Int J Pediatr Otorhinolaryngol*. 77: 1072-1076.
- Zhu Y, Liang C, Chen J, Zong L, Chen GD, Zhao HB. (2013) Active cochlear amplification is dependent on supporting cell gap junctions. <u>Nat Commun.</u> 4: 1786 doi: 10.1038/ncommuns2806.
- 24. Liang C, Zhu Y, Zong L, Lu GJ, **Zhao HB.** (2012) Cell degeneration is not a primary causer for Connexin26 (*GJB2*) deficiency associated hearing loss. <u>Neurosci Lett.</u> 528: 36-41.
- 25. Zhu Y, **Zhao HB.** (2012) ATP activates P2X receptors to mediate gap junctional coupling in the cochlea. *Biochem Biophys Res Commun.* 426: 528-532.
- 26. Sosinsky GE, Boassa D, Dermietzel R, Duffy HS, Laird DW, MacVicar BA, Naus CC, Penuela S, Scemes E, Spray DC, Thompson RJ, Zhao HB, Dahl G. (2011) Pannexin channels are not gap junction hemichannels (*Commentary*). <u>Channels (Austin)</u>. 5: 193-197.
- 27. Zhu Y, **Zhao HB.** (2010) ATP-mediated potassium recycling in the cochlear supporting cells. *Purinergic Signal.* 6: 221-229.
- 28. Wang XH, Streeter M, Liu YP, **Zhao HB.** (2009) Identification and characterization of Pannexin expression in the mammalian cochlea. *J Comp Neurol.* 512: 336-346.
- 29. Yu N, **Zhao HB.** (2009) Modulation of outer hair cell electromotility by cochlear supporting cells and gap junctions. <u>*PLoS One*</u> 4(11): e7923.
- 30. Yu N, Zhao HB. (2008) ATP activates P2x receptors and requires extracellular Ca⁺⁺ participation to modify outer hair cell nonlinear capacitance. <u>*Pflugers Arch: Eur J Physiol.*</u> 457: 453-461.
- 31. Liu YP, **Zhao HB.** (2008) Cellular characterization of Connexin 26 and Connexin 30 expressions in the cochlear lateral wall. <u>Cell & Tissue Res.</u> 333: 395-403.
- 32. Gossman DG, **Zhao HB.** (2008) Hemichannel-mediated inositol 1, 4, 5-trisphosphate (IP₃) release in the cochlea: A novel mechanism of IP₃ intercellular signaling. <u>*Cell Commun Adhes.*</u> 15: 305-315.
- Yu N, Zhu ML, Johnson B, Liu YP, Jones RO, Zhao HB. (2008) Prestin up-regulation in chronic salicylate (aspirin) administration: An implication of functional dependence of prestin expression. <u>Cell Mol Life Sci.</u> 65: 2407-2418.
- Chen GD, Zhao HB. (2007) Effects of intense noise exposure on the outer hair cell plasma membrane fluidity. <u>*Hear Res.*</u> 226: 14-21.

- 35. **Zhao HB,** Yu N. (2007) Inner ear connexin gap junctional function and deafness mechanisms. <u>*Chinese J Otology.*</u> 5: 26-30. (In Chinese).
- 36. **Zhao HB,** Yu N. (2006) Distinct and gradient distributions of connexin26 and connexin30 in the cochlear sensory epithelium of guinea pigs. *J Comp Neurol.* 499: 506-518.
- Zhao HB*, Kikuchi T*, Ngezahayo A*, White TW.* (2006) Gap junctions and cochlear homeostasis. <u>J Memb Biol.</u> 209: 177-186. (An invited review; * all authors contributed equally to this article).
- Yu N, Zhu ML, Zhao HB. (2006) Prestin is expressed on the whole outer hair cell basolateral surface. *Brain Res.* 1095: 51-58. (selected as a cover story)
- 39. **Zhao HB**, Yu N, Fleming CR. (2005) Gap junctional hemichannel-mediated ATP release and hearing controls in the inner ear. *Proc Natl Acad Sci USA* 102: 18724-18729.
- Zhao HB. (2005) Connexin26 is responsible for anionic molecule permeability in the cochlea for intercellular signaling and metabolic communications. <u>*Eur J Neurosci.*</u> 21: 1859-1868. (selected as a cover story)
- Huang ZW, Luo YY, Wu ZY, Tao ZZ, Jones RO, Zhao HB. (2005) Paradoxical enhancement of cochlear active mechanics in long-term administration of salicylate. <u>J Neurophysiol.</u> 93: 2053-2061.
- Santos-Sacchi J, Zhao HB. (2003) Excitation of fluorescent dyes inactivates the outer hair cell integral membrane motor protein prestin and betrays its lateral mobility. <u>*Pflugers Arch:*</u> <u>*Eur J Physiol.*</u> 446: 617-622.
- Lue AJC, Zhao HB, Brownell WE. (2001) Chlorpromazine alters outer hair cell electromotility. <u>Otolaryngology- Head and Neck Surgery</u> 125: 71-76.
- 44. **Zhao HB**. (2001) Long-term natural culture of cochlear sensory epithelia of guinea pigs. <u>Neurosci Lett.</u> 315: 73-76.
- 45. Oghalai JS, **Zhao HB**, Kutz Jr JW, Brownell WE. (2000) Voltage and tension-dependent lipid mobility in the outer hair cell plasma membrane. <u>Science</u> 287: 658-661.
- 46. **Zhao HB,** Santos-Sacchi J. (2000) Voltage gating of gap junctions in cochlear supporting cells: Evidence for nonhomotypic channels. *J Memb Biol.* 175: 17-24.
- 47. **Zhao HB.** (2000) Directional rectification of gap junctional voltage gating between Deiters cells in the inner ear of guinea pig. *Neurosci Lett.* 296: 105-108.
- Zhao HB, Santos-Sacchi J. (1999) Auditory collusion and a coupled couple of outer hair cells. <u>Nature</u> 399: 359-362.

- 49. **Zhao HB**, Santos-Sacchi J. (1998) Effect of membrane tension on gap junctional conductance of supporting cells in Corti's organ. *J Gen Physiol*. 112: 447-455.
- Parham K, Zhao HB, Ye Y, Kim DO. (1998) Responses of anteroventral cochlear nucleus neurons of the unanesthetized decerebrate cat to click pairs as stimulated echoes. <u>*Hear Res.*</u> 125: 131-146.
- 51. **Zhao HB**, Liang ZA. (1997) Temporal encoding and transmitting of amplitude and frequency modulations in dorsal cochlear nucleus. *Hear Res.* 106: 83-94.
- 52. Parham K, **Zhao HB**, Kim DO. (1996) Responses of auditory nerve fibers of the unanesthetized decerebrate cat to click pairs as stimulated echoes. *J Neurophysiol*. 76: 17-29.
- 53. **Zhao HB**, Liang ZA. (1996) Processing of modulation frequency in the dorsal cochlear nucleus of the guinea pig: Sinusoidal frequency modulated tones. *Hear Res.* 95: 120-134.
- 54. Zhao HB, Parham K, Ghoshal S, Kim DO. (1995) Projections from small neurons in the vestibular nerve root to the granule-cell-layer/small-cell-cap of the anteroventral cochlear nucleus in the cat. <u>Brain Res.</u> 700: 295-298.
- 55. **Zhao HB**, Liang ZA. (1995) Processing of modulation frequency in the dorsal cochlear nucleus of the guinea pig: Amplitude modulated tone. *Hear Res.* 82: 244-256.
- 56. **Zhao HB**, Liang ZA. (1993) Response patterns of single units in guinea pig cochlear nucleus to click and sound bursts. *Chin J Physiol Sci.* 9: 136-144.

Selected Invited Professorships and Lectureships (Recently):

Zhao HB (2023). "Early biomarkers of Alzheimer's disease in the auditory system", Yale University Medical School, New Haven, CT

Zhao HB. (2022) Heterozygous carriers of Cx26 (GJB2) mutations are susceptible to noise leading to hearing loss. The 20th International Gap Junction Conference. A Coruna, Spain, July 16- 20, 2022.

Zhao HB (2022) "A new method to record auditory evoked cortical potential (AECP) in mice to assess mouse brain function and Alzheimer's disease development", Dept. of Otolaryngology, Southeast University, Nanjing, China (zoom meeting)

Zhao HB (2022). "The effect of hidden hearing loss on Alzheimer's disease development and progression". Invited talk in NIDCD/NIA Webinar: Sharing our Science: Alzheimer's Disease and Related Dementias. April 7, 2022

Zhao HB (2022) "Mechanisms of GJB2 (Cx26) mutations induced hearing loss", Baylor College of Medicine, Houston, TX

Zhao HB (2020) "Gap junction connexin hearing function and deafness mechanisms", Invited seminar, Dept. of Otolaryngology, University of Utah, Salt Lake City, Utah, USA

Zhao HB (2019) "Cx30 is required for neural and synapse development in the inner ear". The 19th International Gap Junction Conference. Victoria, BC, Canada, July 27- August 1, 2019.

Zhao HB (2017) "Diagnosis of hidden hearing loss", Dept. of Communication Science & Disorders, University of Cincinnati, Cincinnati, OH

Zhao HB. (2017) "Deafness mechanisms underlying connexin deficiency induced hearing loss and K⁺-recycling impairment is not a primary deafness mechanism for connexin deficiency induced hearing loss". The 18th International Gap Junction Conference. Glasgow, United Kingdom, July 29- August 2, 2017.

Zhao HB (2015) "Deafness Mechanisms Underlying Nonsyndromic Hearing Loss", Cincinnati Children's Hospital Medical Center, Cincinnati, OH

Zhao HB (2015) "The role of supporting cell gap junctions in active hearing", Dept of Otolaryngology, Northwestern University Medical School, Chicago, IL

Research Supports:

<u>Activated:</u> 1. NIH/NIA R01 AG080587 (PI) "Hearing Biomarkers in Alzheimer's disease"

07/01/2023 - 06/30/2028

2. NIH/NIA RF1 AG082216 (PI) 04/01/2023 – 03/31/2028 "The effect of noise induced hearing loss on Alzheimer's disease development and progression"

3. NIH/NIDCD R01 DC019687 (PI) 06/01/2021 – 05/31/2027 "Connexin function and mechanisms of Cx26 deficiency induced hearing loss"

4. NIH/NIDCD R01 DC017025 (PI)

04/01/2018 - 03/31/2025

"ATP-purinergic mechanisms underlying noise-induced cochlear synaptopathy and hearing loss"