Tonotopic Control of Cochlear Bone Quality by Osteocytes

Christoforos Meliadis, Yoshihiro Obata, Joanna Bons, Laura Müller, Charles Schurman, Michael Sieverts, Barat Q. Achinuq, Edoardo Pedrinazzi, Stéphane Blouin, Peggi Angel, Birgit Schilling, Davide Ruffoni, Claire Acevedo, Pupa U.P.A. Gilbert*, Tamara Alliston*

The cochlea detects sound frequencies through tonotopy, a spatial gradient in mechanical stiffness along the basilar membrane—stiffer base for high frequencies, less stiff apex for low frequencies. Whether cochlear bone also exhibits tonotopic properties is unknown. Because traditional osteoblast and osteoclast remodeling is suppressed in cochlear bone, we hypothesized that osteocytes control cochlear bone properties tonotopically.

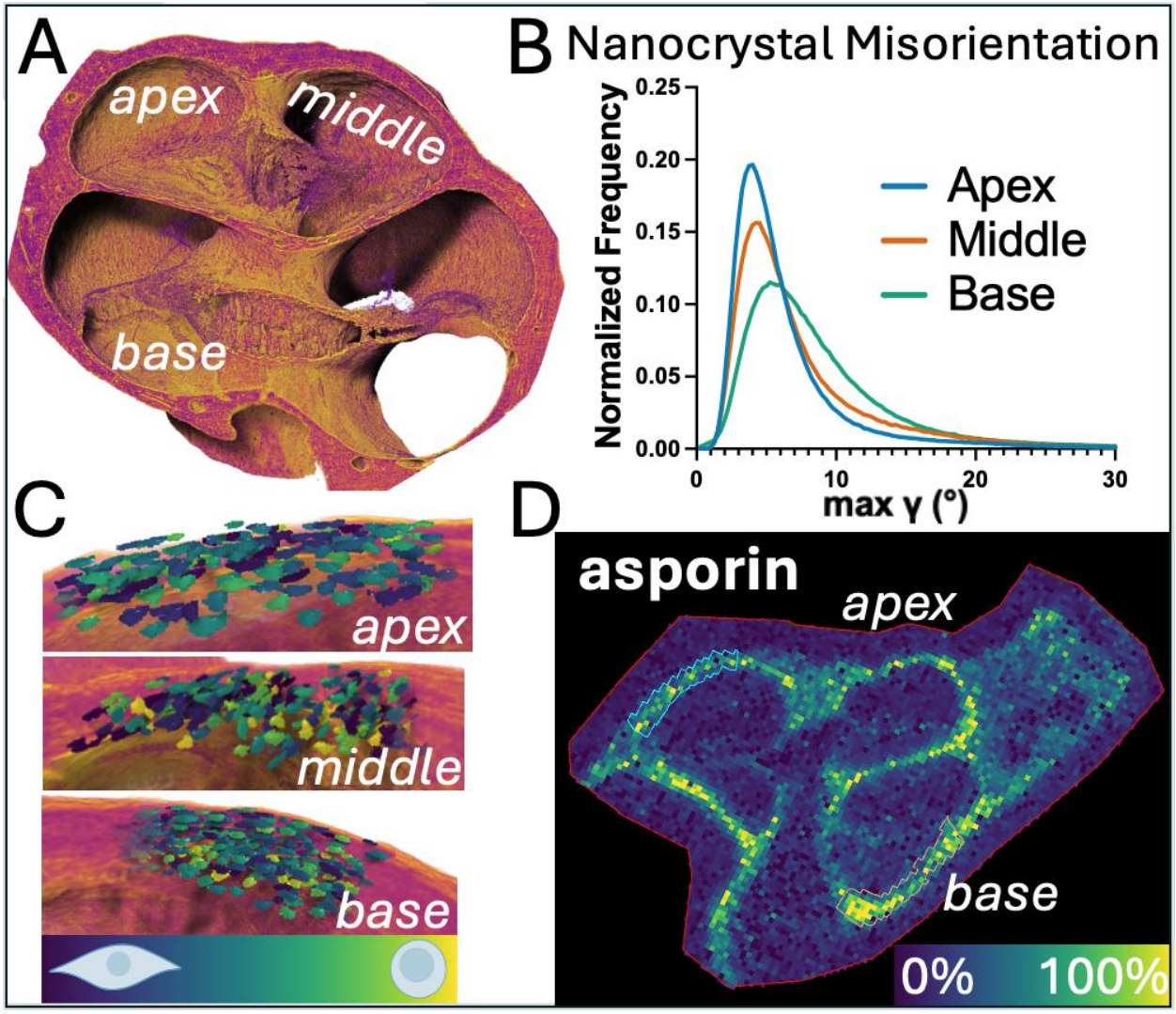
Cochlear bones from female 4-month-old C57BL/6 mice were analyzed. To determine if bone properties align with cochlear frequency regions; collagen organization, mineralization, and mechanical properties were evaluated using second harmonic generation, quantitative backscattered electron imaging, and nanoindentation (n=3). Collagen fibers were more disorganized at the base compared to apex and middle; they were more defined where mineral correlates strongly with material properties. To evaluate how microstructural variations contribute to these regional differences, Synchrotron Radiation micro Computed Tomography (SRμCT) (n=10, Fig. A) and Polarization-dependent Imaging Contrast (PIC) mapping (n=3) were performed. The base showed significantly higher mineral density ($p=0.0292$) and more misoriented adjacent hydroxyapatite nanocrystals ($p=0.0017$) compared to the middle and apex (Fig. B). To test if osteocytes drive these tonotopic differences, we analyzed osteocyte lacunae via SRμCT (n=10). Lacunae were smaller and rounder at the base and larger and more elongated toward the apex (Fig. C), indicating increased perilacunar remodeling (PLR) apically. This pattern strongly suggests osteocytic control through tonotopically distinct PLR activity. MALDI-TOF spatial analysis of peptide distribution identified five potential tonotopic bone quality regulators that were upregulated at the base, including asporin (m/z 1620, n=3, $p<0.05$, Fig. D), a critical regulator of collagen fibrillogenesis and mineralization, suggesting that osteocytes use asporin to precisely tune cochlear bone tonotopy.

This study provides the first evidence of osteocytic control of cochlear bone quality along the frequency map. These findings reveal a novel mechanism of regional bone specialization, suggesting that cochlear bone may contribute to auditory function. This insight may help explain why hearing loss frequently accompanies skeletal disorders like osteogenesis imperfecta and Paget's disease, where mechanisms underlying auditory deficits remain unclear.

Current Version: 2497 characters (including spaces) / 2500 (limit)

Abstract Category: Basic: Mechanobiology, Biomechanics and Bone Quality

Keyword ideas (up to 3): Osteocytes, Mineral Metabolism, Cochlea, Bone Quality, Spatial Proteomics, Hearing, Tonotopy


A
apex
middle
base
B Nanocrystal Misorientation
Normalized Frequency
0.25
0.20
0.15
0.10
0.05
0.00
0
10
20
30
max γ (°)
Apex
Middle
Base
C
apex
middle
base
D
asporin
apex
base
0%
100%