Use of NR for the Prevention and Treatment of Hearing Loss

Kevin Brown, Anthony Sauve and Samie R. Jaffrey, Weill Cornell Medical College, New York, NY

Diverse medical conditions involve hearing loss
- Meniere's disease (200/100,000 prevalence)
- Hearing loss associated with antibiotics (aminoglycoside) and chemotherapy (cis-platin, ~10%)
- Sudden hearing loss (10/100,000 per year)

Hair cell damage and axon degeneration in hearing loss
- Hair cells undergo cell death after hearing loss
- Hair cells are highly sensitive to cis-platin and antibiotics
- Hair cells release excess neurotransmitter causing neurite degeneration
- Hair cells are enriched in mitochondria
- Reactive oxygen species and mitochondrial dysfunction is the common feature of these diseases
- No approach is currently being explored that targets mitochondria

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Nicotinamide riboside (NR)
- NAD+ activates sirtuin enzymes that control cell survival
- NAD+ is very unstable in serum
- NR is a stable NAD+ precursor
- NR rapidly elevates cellular NAD+ levels

NR prevents hearing loss
- Profound protective effect of NR
- NR can be administered after acoustic trauma

NR acts on the SIRT3 in the mitochondria

NR enables direct control of ROS production via SIRT3

Treatment is intratympanic injection of steroids
- High concentrations can be achieved in labyrinth fluid
- Drugs remain in fluid for weeks
- Steroid injection is common for each condition

Diverse approaches to improve treatment
- Auris Medical: NMDA-R antagonist; JNK inhibitor
- Sound Pharmaceuticals: Glutathione peroxidase mimetics
- Otonomy: sustained-release dexamethasone

Advantages of the technology
- Novel compounds with no toxicity
- Directly target the cause of hair cell loss - dysfunctional mitochondria

Cornell IP
- NR in hearing loss

Licensing contact: Brian Kelly, Director, Technology Licensing, WCMC Office, (212)746-6189, bjk44@cornell.edu