

# Salicylates, a class of NSAIDs, stop vestibular schwannomas growth

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Researchers from Massachusetts Eye and Ear and the Harvard Medical School/ Massachusetts Institute of Technology's Program in Speech and Hearing Bioscience and Technology have demonstrated that salicylates, a class of non-steroidal inflammatory drugs (NSAIDs), reduced the proliferation and viability of cultured vestibular schwannoma cells that cause a sometimes lethal intracranial tumor that typically causes hearing loss and tinnitus.

The research is described in "Non-steroidal Anti-inflammatory Medications are Cytostatic Against Human Vestibular Schwannomas" online in *Translational Research*.

"These pre-clinical data based on cultured primary vestibular schwannoma cells, combined with our previously published work on aspirin intake correlating with halted growth of vestibular schwannomas (also known as acoustic neuroma), motivate a future prospective clinical trial," said Konstantina Stankovic, M.D., Ph.D., F.A.C.S., principal investigator at the Eaton-Peabody Laboratories at Mass. Eye and Ear who led the research. Dr. Stankovic is also an assistant professor of Otology and Laryngology at Harvard Medical School. Other authors are her trainees, Drs. Sonam Dilwali, Shyan-Yuan Kao, Takeshi Fujita and Lukas D. Landegger.

Vestibular schwannomas are the most common tumors of the cerebellopontine angle and the fourth most common intracranial tumors. Although vestibular schwannomas are histologically non-malignant, they

can lead to substantial morbidity, including sensorineural hearing loss, vestibular dysfunction and facial nerve paralysis. Large vestibular schwannomas can cause additional paralysis of other cranial nerves, brainstem compression and death, the authors write.

Currently, patients with symptomatic or growing vestibular schwannomas can undergo surgical resection or radiotherapy. Both of these procedures can result in serious complications. Effective drug therapies that can limit growth would greatly advance health care for these patients.

Salicylates are attractive therapeutics because they are clinically relevant, well-tolerated and commonly used against pathologies such as pain and arthritis. Furthermore, in some cases, chronic intake of salicylates has led to a significant reduction in the incidence and burden of various tumors, such as colorectal cancer.

"In our study, we focused on salicylates because a mechanism of their action is inhibition of cyclooxygenase 2 (COX-2), and a previous study reported that immunohistochemical expression of COX-2 correlated with vestibular schwannoma growth rate. We assessed the efficacy of three different salicylates against vestibular schwannoma: aspirin, sodium salicylate (NaSal) and 5-aminosalicylic acid (5-ASA)," Dr. Stankovic said.

The team found COX-2 to be aberrantly expressed in human vestibular schwannomas and primary human vestibular schwannoma cells in comparison to control human nerve specimens and primary Schwann cells (SCs), respectively. Further, levels of prostaglandin E2, the downstream enzymatic product of COX-2, correlated with primary VS culture proliferation rate. Changes in proliferation, cell death and cell viability were analyzed in primary vestibular schwannoma cultures treated with aspirin, NaSal or 5-ASA. These drugs decreased

proliferation and viability of vestibular schwannoma cells without increasing cell death or affecting healthy SCs. The cytostatic effect of aspirin in vitro was in concurrence with Dr. Stankovic's previous clinical finding that vestibular schwannoma patients taking aspirin demonstrate reduced tumor growth.

"Overall, this work suggests that COX-2 is a key modulator in vestibular schwannoma cell proliferation and survival, and highlights salicylates as promising pharmacotherapies against vestibular schwannoma," the authors concluded.

Provided by Massachusetts Eye and Ear Infirmary

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