

Unlocking the Potential of the Ear

Researchers at House Ear Institute have found a clue in their search for potential therapeutic targets to regenerate sensory hair cells in the inner ear to restore hearing. Scientists Patricia White, Ph.D., Angelika Doetzlhofer, Ph.D., Neil Segil, Ph.D., and Andy Groves, Ph.D., discovered that a gene called *p27Kip1* is partially responsible for blocking the process of sensory cell regeneration in the mouse hearing organ (cochlea). Their study



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ANDY GROVES, PH.D.

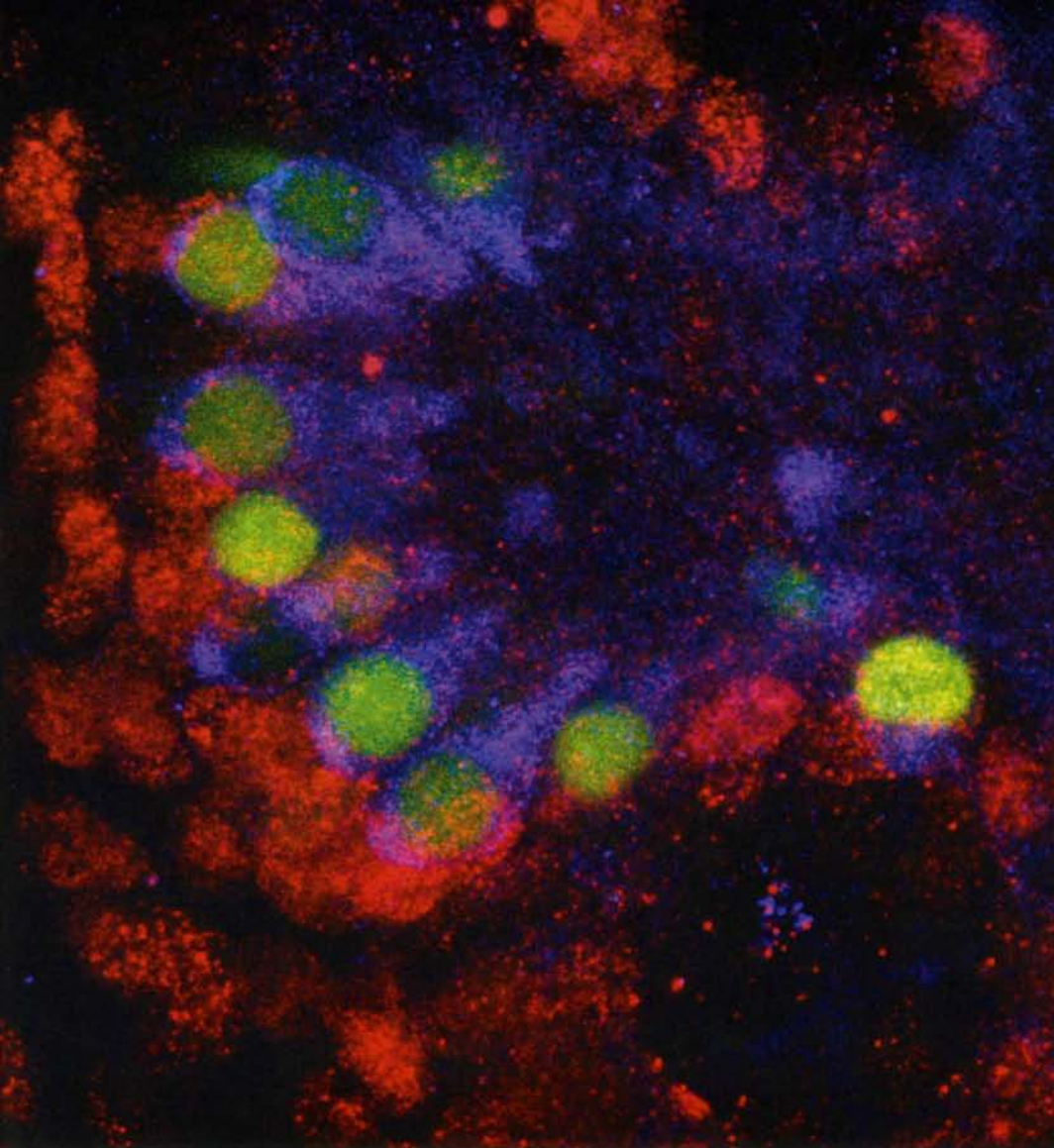
identified and tracked *p27Kip1* through a new research approach that for the first time purified and characterized in isolation the supporting cells that might have the capacity to divide and generate new hair cells in the deafened ear. Segil and Groves are senior authors of a paper outlining the methods and outcomes of this study published in the June 22, 2006 issue of *Nature*.

While sensory cells in the hearing organ (cochlea) of birds and other lower vertebrates have the ability to regenerate after being deafened, the sensory cells in the cochlea of humans and other mammals cannot. Researchers in the hearing health field have long investigated possible methods for stimulating hair cell regeneration in humans as a cure for many forms of deafness. Currently, there is no cure for sensorineural hearing loss, which occurs as a result of

damage to the cochlea’s sensory hair cells from injury, aging, certain medications or infection.

“It’s been suspected for a long time that supporting cells will be the key to hair cell regeneration in humans, but this is the first study to really test the ability of supporting cells to divide and turn into hair cells,” said Andy Groves, Ph.D. “These study results don’t lead directly to the cure for deafness, but they reveal the challenges we’ll have to overcome if hair cell regeneration is ever to become a reality.”

The investigators developed new techniques to identify and purify supporting cells from mice to test whether they have the capacity to divide, and for how long this capacity persists as mice get older. They found that in newborn mice, *p27* was switched off when the cells were grown in a culture dish, and this allowed the supporting cells to divide and make hair cells. In older mice (two weeks old), *p27* was not switched off and thus, cell division was blocked. However, when cells



research scientist Andy Groves, Ph.D. “What I like in art, I like in science.” He admires Picasso, Stravinsky, Miles Davis and Tom Waits because of their willingness to try new things. Andy likes to explore and enjoys solving new problems in his work.

One of Andy’s heroes in science is Francis Crick, who started out designing magnetic mines for the Navy in WWII, but later moved on to biology, proteins, DNA, and more. Another science hero is Seymour Benzer, who was one of the first to develop semiconductors in the 1940s, moved on to molecular biology research and other disciplines, and now works on aging and longevity.

Raised in England, the son of two schoolteachers, Andy was the only person in his family to go to college. He thought about studying medicine, but decided biology was more interesting. He studied biochemistry at Cambridge and cellular neurobiology at University College in London. His primary

were taken from two-week old mice lacking p27, they were once more able to divide and make hair cells. These experiments identified p27 as a block to regeneration and therefore, a possible target for therapy.

“In addition to showing that mammalian auditory supporting cells can turn into hair cells we’ve also identified one of the key obstacles that prevent supporting cells in the damaged inner ear from dividing,” said Neil Segil, Ph.D. “Our study results suggest that p27Kip1 is one culprit preventing cell division, and this raises the potential for therapeutically switching it off so that it can’t block this necessary part of the regeneration process in the inner ear.” ❖

SCIENTIST PROFILES

Andy Groves, Ph.D.

“A good artist is like a good scientist, not doing the same thing over and over again,” says Institute



“Our study results suggest that p27Kip1 is one culprit preventing cell division.”

NEIL SEGIL, PH.D.

interest for the past 20 years has been developmental biology. “I became interested in how living things develop and change over time, becoming more complicated,” he says. “Every part of us started off as a single cell containing all the information needed to build us, but what happens when the system goes wrong and you lose cells? This led me to the study of hearing loss and cell regeneration. A bird can regenerate lost cells to restore its own hearing, but a human can’t. Why not? There has to be an explanation for this.”

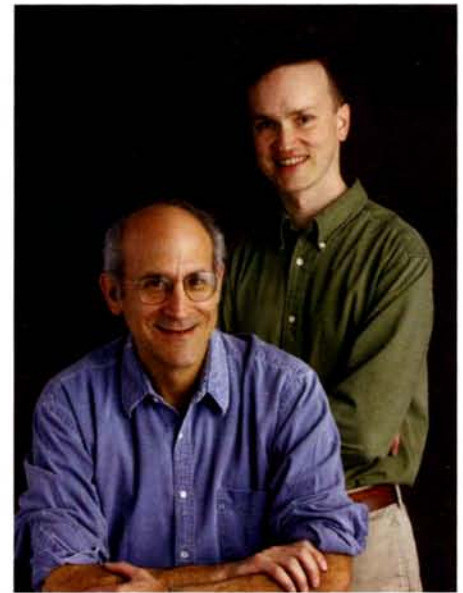
It is this that Andy researches at the Institute with colleague Neil Segil, Ph.D. Andy feels that he and Neil complement each other well as research partners because Neil came from a molecular biology background while Andy’s background was in developmental

and embryological studies. When not in the lab working on their collaborative research studies on hair cell regeneration of the inner ear, Andy and Neil are often hiking one of the many trails winding through the mountains of Alta Dena or cooking for their families.

Andy is married to a scientist. Joanna, whom he met in the science lab at Cal Tech in Pasadena, researches Alzheimer’s disease. While a graduate student, Andy sang with the London Philharmonic Choir and shared the stage with many renowned conductors including Sir Georg Solti, Sir Simon Rattle and Zubin Mehta. He and Joanna enjoy listening to music, attending the symphony and going to movies.

Neil Segil, Ph.D.

It is the nature of scientists to be unconventional, always questioning the status quo, yet they must also recognize basic truths. For Neil Segil, Ph.D., managing both concepts is natural. He personifies



Neil Segil and Andy Groves

the compatible blend of styles that makes a true scientist...inquisitive, yet grounded.

Neil’s early education was a precursor of this untraditional formula: He went to Hampshire College where there were very few classes, no grades, and a curriculum designed to teach students how to learn rather than what to learn. Science wasn’t his focus at that time; that occurred later, after hiking

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Hair Cells and Hearing Loss

A FEW FACTS

Sensorineural hearing loss (SNL) – the loss of sensory cells in the inner ear (cochlea) that help sound impulses reach the brain – is one of the most prevalent disabling conditions in the United States. Twenty million Americans have sensorineural hearing loss, which not only affects their hearing, but can also affect cognitive, behavioral and social functions. The sensory cells, also known as “hair cells,” can be destroyed by exposure to certain medications, illnesses and loud sound. Once destroyed,

these cells cannot be replaced, leading to hearing loss and deafness.

There were nearly 3,000 cases of sensorineural hearing loss reported in the House Clinic last year. While hearing aids or implantable auditory devices can help improve quality of life for people with SNL, finding a way to regenerate the lost hair cells in the ear and thereby restore natural hearing would be a miraculous achievement. ❖

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behind Steve's ear. Then, still suffering temporary facial paralysis, Steve began the post-op recovery period at home, acclimating to his Baha, and spending quality time with Wrigley.

Forever grateful to his canine friend, Steve says, "I have to give credit to the doctor who first detected my tumor and to the House Clinic and Drs. Brackmann and Hitselberger for successfully removing it, but I'm convinced that Wrigley was looking out for me and I feel very blessed to

have her in my life."

Dr. Brackmann does not discount the olfactory abilities of his patient's special dog, and believes that whether it was luck or science we don't understand, it is possible that dogs have the ability to sense or smell things we can't. "I've seen a hunting dog running at a full clip suddenly freeze dead in his tracks because he smells a quail 20 yards away – a good indicator of canine olfactory abilities," says Dr. Brackmann.

"Although we may never understand what exactly Wrigley was sensing, we are certainly grateful that her actions brought Steve to successful treatment at the House Clinic."

Steve's facial nerve has now regained most of its function, and he is acclimating well to his Baha. He is also enjoying music again via his new MP3 player attachment that is an accessory to the device. "Life is good," says Steve. ❖

SCIENTIST PROFILES

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and sailing around the northeast. The science bug bit when he went to graduate school at Columbia University. It was only after a stint in Vienna, and post-doctoral training at Rockefeller University, that Neil ultimately gravitated to the molecular world of hair cell regeneration when he was recruited to the House Ear Institute.

Neil devoted himself to more than just science while studying. He met Greta, his wife-to-be, while in Vienna. It was not only her shared passion for science that hooked Neil, but her Viennese pastries as well! In 1996 they joined HEI together as a team, and Dr. Segil's lab is now a hive of activity in sensory cell development and regeneration. Since then, there has been a steady progression of accomplishments

to justify the lab's efforts studying how hair cells might regenerate in humans. Neil was pleased when his work with colleague Andy Groves, Ph.D., recently culminated in a cover story for *Nature*.



But new discoveries in science pale in comparison to discovering the world anew through the eyes of Nathan, Neil and Greta's 4-year-old son. On Saturdays, Nathan's favorite destination is the park. En route, dad stops at the farmers' markets, and the Middle Eastern and Armenian specialty stores to stock up on goodies to indulge Neil's love of cooking. Neil cooks and Greta bakes (but "not often enough") for family and friends. The group effort, the collaboration, the recollections of home with old world tastes and smells, all appeal to the Segils. And Nathan gets an introduction to international taste treats.

A scientist with positive expectations for an unknown future, Dr. Neil Segil is a solid reflection of how past, present and future meld together in harmony. ❖