Company profile

Acousia Therapeutics: medicines for deafness

Deafness is one of the most common sensory disorders in the world: in Germany alone, around eleven million people suffer from hearing loss. So far there is no real therapy, the symptoms can only be alleviated to a greater or lesser degree with hearing aids or assistive devices. This is what researchers from the Tübingen-based company Acousia Therapeutics want to change: they have identified drug candidates that can protect sensory hair cells and support their function. Clinical trials are currently in preparation and funds totalling ten million euros have recently been secured.

Hearing loss, or hearing impairment, can affect many of us. Worldwide, about 300 million people are hard of hearing; in Germany, hearing loss affects around 16% of all adults*, and the number of people with hearing loss is rising. The disorder is not just age related, but can have multiple causes. For example, malformations, inflammation or the use of certain medications can severely damage the ear and lead to hearing impairments, including total deafness.

All parts of the ear can be affected, from the auricle to the auditory nerves. However, damage to the hair cells in the inner ear, also known as sensorineural hearing loss, is particularly critical and is the most frequent type of hearing loss. The hair cells are very sensitive and the human body is unable to regenerate these cells when they are damaged or deficient. To date, there is no clinical therapy that can fully regenerate damaged hair cells. Standard management involves the use of hearing aids or cochlear implants. However, both devices only amplify ambient noises, so that individual voices cannot be clearly discerned from other people talking in a noisy environment.

Two decades looking for treatment possibilities

In the search for a solution to hearing impairments, Prof. Dr. Hubert Löwenheim, medical director of the Department of Otolaryngology at the University Hospital in Tübingen, has spent many years researching regenerative therapies for treating sensorineural hearing loss. Around twenty years ago, Löwenheim was the first to describe the role of certain cell cycle regulators in the growth and differentiation of hair cells and neighbouring cochlear cells. In 1998, Löwenheim and physicist Dr. Christoph Antz founded a company called Otogene AG in Tübingen to further advance Löwenheim's findings. Based on their basic idea, they founded another company in Tübingen called Acousia Therapeutics GmbH in 2012.

"W  d to work on a therapy for curing hearing loss," says Antz, who has been at the helm of Acousia since 2017. "Back then, our idea was to manipulate molecular switches involved in cell division processes. Birds are able to regenerate and regrow their hair cells, an ability that humans and other mammals do not have. Mammalian and human hair cells are terminally differentiated and cannot be renewed. Despite promising laboratory results, back then the researchers were unable to transfer this approach into the clinic."

Dr. Christoph Antz is the CEO of Acousia Therapeutics GmbH in Tübingen.
© DICS Ringeisen & Schupp GbR, Langheckenstraße 30, 69245 Bammental

Support from many sides

A few years passed before Löwenheim, together with EMC microcollections GmbH and the Boehringer Ingelheim Venture Fund, founded another company, Acousia Therapeutics GmbH in 2012. "With EMC microcollections GmbH and the Boehringer Ingelheim Venture Fund, we had experienced and powerful partners right from the start," says Antz. Furthermore, the company's second managing director, medical chemist Dr. Michael Bös, brought the necessary expertise on board to actually develop optimised leads and promising clinical drug candidates. In recent years, the Acousia researchers have been able to focus on the search for drug candidates for the cure of sensorineural hearing loss. Shortly after company establishment, the founders received financial support from the Kreditanstalt für Wiederaufbau KfW and Axxam SpA in Milan, which also provided funding for the researchers in Tübingen to screen for candidate molecules for inner ear therapy.

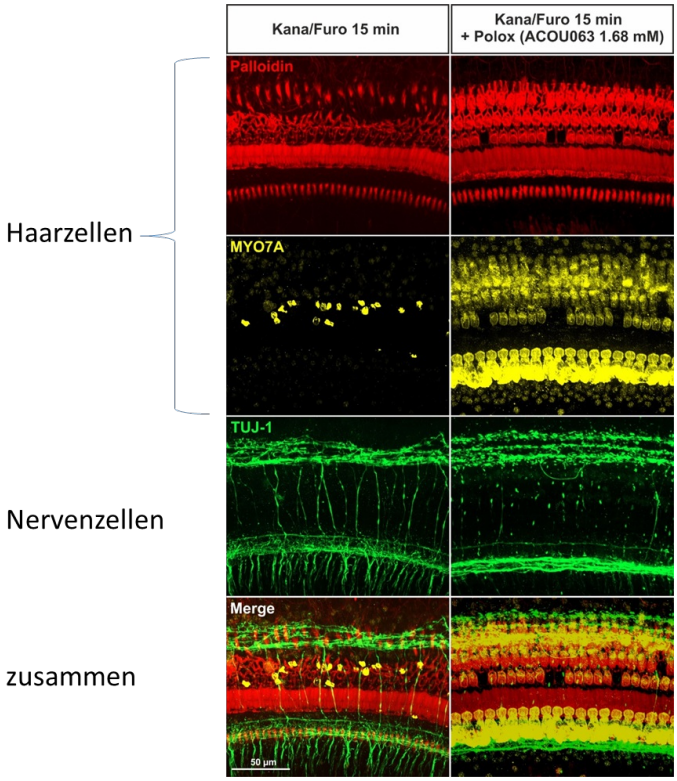
Acousia itself has only a handful of employees. "A service agreement with Tübingen University Hospital gives us access to the infrastructures we need for our work. This is a very fortunate situation. This framework agreement guarantees that we can use model systems and organisms, measurement devices, laboratory facilities, staff and many other things in the Department of Otolaryngology for our work," explains Antz.

Drug candidate protects and regenerates hair cells at the same time

And the researchers' search was successful: using a top-down approach, the scientists screened genes involved in sensorineural hearing loss and identified a small molecule that, when applied to

the ear, protects the hair cells against toxins. “There are many ototoxic substances, i.e. compounds that damage the ear,” explains Antz. One of these compounds, cisplatin, is a very potent chemotherapeutic agent that is highly likely to cause massive hearing damage. The same applies to aminoglycosides which are prescribed as antibiotics, for example for treating tuberculosis. In such cases, the drug we have identified has the potential to protect the hair cells from damage.”

This has already been confirmed in a preclinical trial: guinea pigs displayed significantly better hearing abilities after the drug had been applied. "In addition, the drug appears to be able to increase the sensitivity of existing hair cells – or in other words, achieve an enhancement effect. This is also very exciting for us, and we now want to examine to what extent this property, coupled with cellular protection, can also help to remedy age-related hearing loss. Overall, this would open up huge application opportunities. And we also hope that we can enable the patient to discriminate speech. This would be absolutely terrific.”



Damage/protection experiment in guinea pigs: a mixture of kanamycin and furosemide is applied locally. After cell damage, the application of a drug candidate called ACOU063 in a special poloxamer gel leads to considerable improvement in the sensory cell structures (hair cells and nerve cells).
© Acousia Therapeutics GmbH

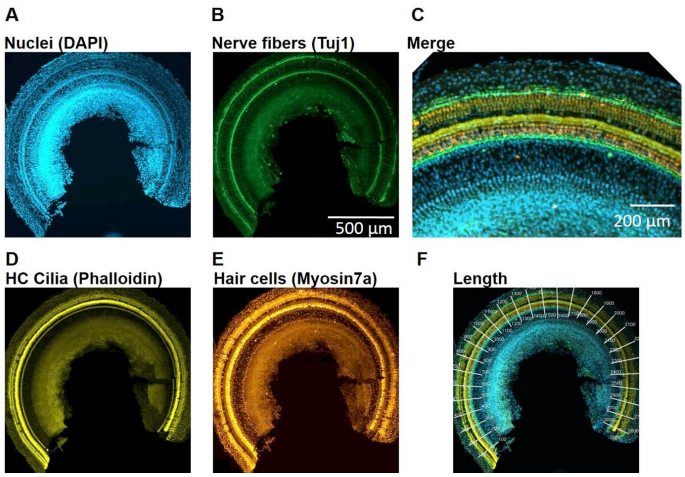
Globally unique approach comes from Tübingen

Therapy involves application of the drug locally in the inner ear, something that is not a problem, as Antz reports: "This can be much more effective than administering the drug orally. This topical application does not hurt and the procedure is part of the treatment spectrum of ENT doctors. "

Acousia already has some competitors. Antz comments: "There are between five and ten companies around the world that are working on inner ear therapies. However, that’s not many, as it is extremely hard to get into the ear, and this has been a major obstacle for quite some time. But the unique thing about our approach is that one single drug provides protection and sensorineural enhancement at the same time.”

Clinical phase to begin in 2020

Now that the results from the preclinical studies are available, the Tübingen researchers are busy preparing a clinical trial plan; concrete studies are planned to commence in 2020. At the same time, the scientists are currently testing a mouse model of accelerated ageing in order to determine to what extent the drug candidate is able to significantly slow down the ageing process of the hair cells. "The risk associated with clinical development is always very high. An exceptionally high number of trials that focused on the inner ear have failed over the years,” says Antz. "But in our case, we are very confident because we have outstanding preclinical results and the protective



Immunohistological stains of a guinea pig cochlea (blue: DAPI), nerve cells (green: Tuj19), hair cells (orange: myosin7a) and associated cilia (yellow: phalloidine) as well as the combination of all colour channels. The marks between equidistant sections (lower right-hand side) are used to count existing hair cells as part of the quantitative evaluation of the experiments.
© Acousia Therapeutics GmbH

effects achieved with our compounds are very robust and significant."

It was not until May 2018 when Acousia was able to secure follow-up financing of ten million euros for the next three years that the scientists were able to start the clinical trial. In addition to the original investors, other investors include Landesbank Baden-Württemberg (LBBW), Creathor Ventures and Bregua Corporation. "We now want to use this money to enter Phase I/IIa trials and hope to come up with reasonable data, which will then either help acquire further funds or perhaps even allow us to sell the company."

* P. von Gablenz, E. Hoffmann, I. Holube: "Prävalenz von Schwerhörigkeit in Nord- und Süddeutschland", HNO (2017) Issue 8, 663 – 670.

Article

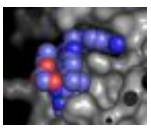
31-Jul-2018
Dr. Petra Neis-Beeckmann
© BIOPRO Baden-Württemberg GmbH

Further information

Dr. Christoph Antz
Acousia Therapeutics GmbH
Sindelfingerstr. 3
72070 Tübingen
Phone: +49 (0)7071 298 8186
E-mail: antz(at)acousia.com

- Acousia Therapeutics GmbH

The article is part of the following dossiers



Drug screening - higher throughput, quicker and more effective thanks to automation

No new drugs to be placed on the market without clinical trials

financing

prevention

clinical trial

company foundation

therapy

active pharmaceutical ingredient