Simple recipe to make sensory hair cells in the ear

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Scientists at the Molecular Medicine Institute in Lisbon, Portugal, and at the University College London Ear Institute, United Kingdom, have developed a simple and efficient protocol to generate inner ear hair cells, the cells responsible for our hearing and sense of balance. This study is an important step for the future production of large numbers of these cells for use in cell transplantation therapies or large-scale drug screens. The research has just been published in the scientific journal *Development*.

Sensory hair cells located in the inner ear are vital for our sense of hearing and balance. As these cells are unable to regenerate, millions of people worldwide have permanent hearing and balance impairments. Previous studies had already reported the successful generation of hair cells in the lab, but the protocols used were complex and inefficient. To overcome these problems, the team led by Domingos Henrique, whose Neural Development lab is also associated with the Champalimaud Centre for the Unknown in Lisbon, decided to follow a different strategy. "We explored the extensive knowledge on the various regulatory proteins that control hair cell development in the embryo to design an effective combination of three transcription factors able to induce the formation of these cells", said Dr Henrique and Aida Costa, the graduate student involved in the work.

The team applied this simpler approach to mouse embryonic stem cells in a dish, which have the potential to become any cell type. They were able to convert these cells into hair cells, more successfully and with higher efficiencies than previously reported. Excitingly, when the team added the three players to cells in the ear of a developing chick embryo they were also able to induce the formation of many new hair cells, including in areas where they do not form normally, suggesting that a similar strategy might work in vivo.

"Hair cells get their name from the bundle of hair-like structures that protrude from the cell. These protrusions have mechanosensitive ion channels that allow hair cells to transform vibrational movements into electrical signals. We observed that the hair cells we produced are also able to develop similar protrusions, but with an immature and disorganized morphology", said the authors. "However, we have some evidence suggesting that functional mechanosensitive ion channels are already present in these cells, and that the genes expressed by normal hair cells and those produced by us in a dish are very similar."

Future work will focus both on improving this protocol to produce fully mature hair cells, and on applying the method to human cells that can be produced in large quantities. "Producing large numbers of hair cells will allow the development of high-throughput drug screening to discover new compounds that can promote hair cell regeneration. In the long term, they can also be used as a starting point to develop cell replacement therapies that could successfully restore the lost or damaged hair cells in the inner ear", conclude the authors.

More information: Costa, A., Sanchez-Guardado, L., Juniat, S., Gale, J. E., Daudet, N., Henrique, D. (2015). Generation of sensory hair cells by genetic programming with a combination of transcription factors. *Development*, 11, 1948-1959. dev.biologists.org/content/142/11/1948

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