Gene discovery in fruit flies 'opens new doors' for hearing loss cure in elderly

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Scientists at UCL have discovered sets of regulatory genes, which are responsible for maintaining healthy hearing. The finding, made in fruit flies, could potentially lead to treatments for age-related hearing loss (ARHL) in humans.

Globally one third of people (1.23 billion people) aged over 65 experience hearing impairment, and while there are thought to be more than 150 candidate genes which may affect hearing loss, there is no unified view on how to use these to develop novel preventive or curative hearing loss therapies.

In the study, published in *Scientific Reports*, researchers at the UCL Ear Institute assessed the hearing ability of the common fruit fly (Drosophila melanogaster) across its life span (around 70 days), to see if their hearing declines with age.

The fruit fly is a powerful model in biology and its ear shares many molecular similarities with the ears of humans, which make it an ideal tool for the study of human hearing loss. However, so far, no study had assessed the fruit flies' hearing across their life course.

Using advanced biomechanical, neurophysiological and behavioral techniques, the researchers found that the antennal ears of fruit flies also display ARHL with nearly all measures of sensitive hearing starting to decline after 50 days of age.

With this knowledge, the researchers turned their interest to the time before flies developed ARHL: they wanted to know if there were any 'age-variable' genes in the flies' Johnston's Organ (their 'inner ear'), which have kept the ears healthy for 50 days of their lives.

Using a combination of molecular biology, bioinformatics and mutant analysis, the researchers identified a new set of transcriptional regulator genes: these are so called 'homeostasis genes', meaning they are the genetic actuators, so they control the activity which keeps the ear sensitive.

For researchers, one of the principle advantages of the fruit fly model is that it allows for easily testing the roles of individual genes by either increasing their function (overexpression) or silencing them (RNAi interference). Exploiting these tools, researchers also found that manipulating some of the homeostasis genes could prevent the flies from getting ARHL.

Lead author Professor Joerg Albert (UCL Ear Institute) said: "While many studies have been conducted into the hearing function of fruit flies, ours is the first to look at the mechanistic and molecular detail of their auditory life course.

"Our twin discoveries that fruit flies experience age-related hearing loss and that their prior auditory

health is controlled by a particular set of genes, is a significant breakthrough. The fact that these genes are conserved in humans will also help to focus future clinical research in humans and thereby accelerate the discovery of novel pharmacological or gene-therapeutic strategies.

"Building on our findings from Drosophila, we have already started a follow-up drug discovery project designed to fast-track novel treatments for human ARHL."

Dr. Ralph Holme, Executive Director of Research at Action on Hearing Loss, said: 'We urgently need to find effective treatments able to prevent or slow the loss of hearing as we age.

"Hearing loss affects 70% of people aged over 70 years old, cutting people off from friends and family.

"Action on Hearing Loss is proud to have been able to support this exciting research that has identified genes involved in maintaining hearing.

"It not only advances our understanding of why hearing declines with age, but importantly also opens the door to the future development of treatments to prevent it."

More information: Alyona Keder et al, Homeostatic maintenance and age-related functional decline in the Drosophila ear, *Scientific Reports* (2020). DOI: 10.1038/s41598-020-64498-z

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