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Study finds protein that helps nematodes avoid salt may also be involved in mammalian hearing

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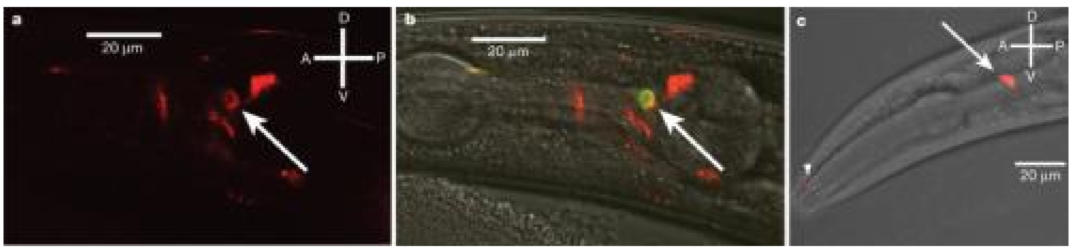

Expression of TMC-1 in chemosensory neurons. Credit: (c) *Nature* (2013) doi:10.1038/nature11845

(Medical Xpress)—A research team with members from Cambridge University in the U.K. and Korea University College of Medicine, has found that a protein expressed in nematodes may also be responsible for controlling an ion channel involved in hearing in mammals. In their study, described in the journal *Nature*, the team found that a protein expressed due to the TMC-1 gene, allows nematodes to avoid areas of high salt concentrations. Because TMC-1 genes have been linked with hearing problems in mammals, the researchers suggest that the same protein found in nematodes might be responsible for controlling ion channels in mammalian hearing.

In studying nematode reactions to high salt concentrations, the researchers manipulated the DNA of a specimen to remove the TMC-1, gene. Doing so they found, removed the nematode's ability to sense high salt concentrations, a necessary ability to ensure its survival. Looking deeper, they discovered that the presence of the TMC-1 gene caused the nematode to produce a certain kind of protein that was involved in controlling an ion channel. Conversely, the absence of that protein meant the nematode was no longer able to avoid entering areas where high salt concentrations would spell its doom. This finding has led the researchers to wonder if the same protein might be involved with hearing in mammals.

Prior research has shown that the TMC-1 gene is involved somehow in hearing in mammals, including humans. Problems with it generally mean problems with hearing. Up till now however, the mechanism involved has not been clear. This new research with the nematodes suggests that it might be possible that the same protein, or one very much like it, might be expressed in mammals, due to the TMC-1 gene – and that the protein might be responsible for controlling ion channels in the ears that serve as communication conduits between the tips of cilia in the ears and neurons that carry signals to the brain. If this is correct, it might mean researchers are on the right path to developing a way to treat people who have missing or impaired TMC-1 genes, and their related hearing problems.

At this time, the connection between TMC-1 and ion channel control in mammals, is still speculative, but the team's findings have alerted the health community to the possibility, which means that future research will likely be dedicated to investigating more closely the types of proteins found in the ears and the channels that carry sound information to the brain.

More information: tmc-1 encodes a sodium-sensitive channel required for salt chemosensation in C. elegans, *Nature* (2013) doi:10.1038/nature11845

Abstract

Transmembrane channel-like (TMC) genes encode a broadly conserved family of multipass integral membrane proteins in animals1, 2. Human TMC1 and TMC2 genes are linked to human deafness and required for hair-cell mechanotransduction; however, the molecular functions of these and other TMC proteins have not been determined3, 4, 5, 6. Here we show that the Caenorhabditis elegans tmc-1 gene encodes a sodium sensor that functions specifically in salt taste chemosensation. tmc-1 is expressed in the ASH polymodal avoidance neurons, where it is required for salt-evoked neuronal activity and behavioural avoidance of high concentrations of NaCl. However, tmc-1 has no effect on responses to other stimuli sensed by the ASH neurons including high osmolarity and chemical repellents, indicating a specific role in salt sensation. When expressed in mammalian cell culture, C. elegans TMC-1 generates a predominantly cationic conductance activated by high extracellular sodium but not by other cations or uncharged small molecules. Thus, TMC-1 is both necessary for salt sensation in vivo and sufficient to generate a sodium-sensitive channel in vitro, identifying it as a probable ionotropic sensory receptor.