Scientists reveal similarities between gut microvilli and inner ear hair cell

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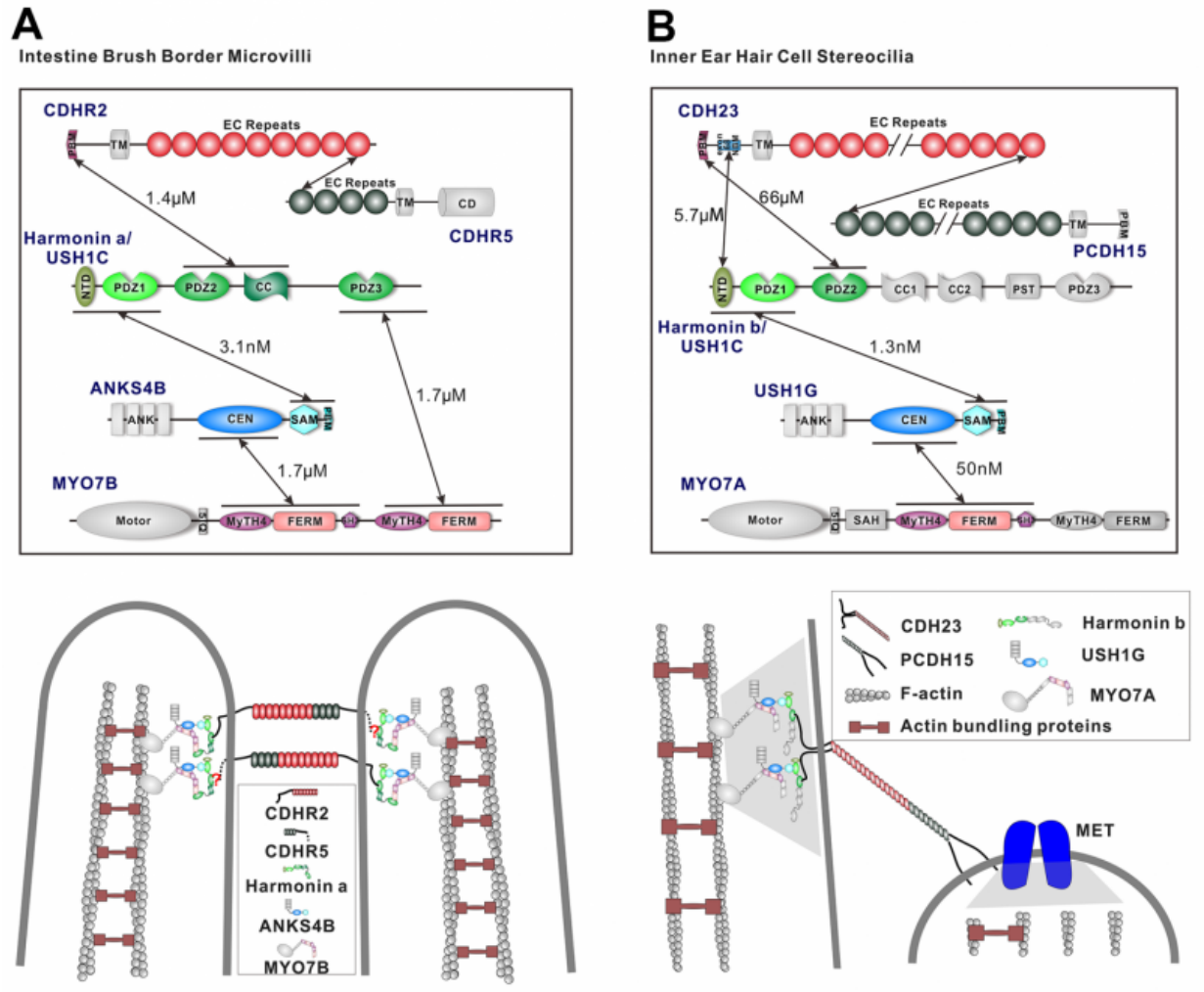

(A) The top panel summarizes the detailed protein interaction network governing the assembly of the inter-microvillar tip-link. Except for the extracellular cadherin repeat-mediated hetero-dimerization interaction between CDHR2 and CDHR5 identified recently by Tyska's group (Crawley et al., 2014b), the rest of

the interactions marked by two-way arrows have been characterized quantitatively in this study. The bottom panel is a cartoon summary of the protein interaction network in microvilli.(B) The protein interaction network governing the inner ear stereocilia tip-link complex (also known as the USH1 complex) assembly. The figure is adapted from an earlier review by Pan and Zhang (2012). The bottom panel is a cartoon summary of the protein interaction network in stereocilia adapted from an earlier review by Lu et al. (2014). Credit: HKUST Division of Life Science

Brush border microvilli are microscopic cellular membrane protrusions that increase the surface area of cells and carry out a wide variety of functions, including absorption, secretion and cellular adhesion. Stereocilia, on the other hand, are mechanosensing organelles of hair cells, which respond to fluid motion in numerous types of animals for various functions, including hearing and balance. The two structures are located in separate parts of the human body and perform vastly different functions, despite the very-similar looks and features they have.

The similarities between the two, in fact, are far more than just looks. Mechanistically, the two resembles one another just as close.

HKUST structural biologist Mingjie Zhang and his team have found that the microvilli and the stereocilia tip-link complexes, despite only having Harmonin in common, are formed via strikingly similar interaction modes. Their findings were published in the January 25, 2016 issue of the journal *Developmental Cell*.

"While brush border microvilli resemble the relatively well-characterized stereocilia of hair cells, the mechanistic basis of tip-link complex organization in brush border microvilli is poorly understood," said Professor Mingjie Zhang.

In the study, the team of HKUST researchers performed systematic biochemical and structural characterizations of the protein interaction network residing at the cytoplasmic face of the brush border inter-microvilli tip- link. The researchers found that both the brush border inter-microvillar tip link complex and the inner ear stereocilia tip link complex both utilize adhesive, heteromeric cadherin family proteins to build filamentous inter-microvillar/ inter-stereocilia tip links that can sustain mechanical strains. Both systems use two scaffold proteins that include Harmonin as the hub to organize the respective multi-protein complex within each system.

"These results not only provide insight into the mechanistic bases of brush border microvilli formation and maintenance, but may also be valuable for understanding of some gut and/or kidney diseases caused by perturbations of brush border microvilli structures," said Professor Zhang. "A single mutation of genes encoding the stereocilia tip link complex can cause a disease as debilitating as Usher syndrome, while corresponding mutations in gut microvilli do not appear to cause obvious diseases in our guts. The results of our study can help scientists and clinicians to identify mutations of genes that may cause digestive diseases."

More information: *Developmental Cell*, dx.doi.org/10.1016/j.devcel.2015.12.020

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