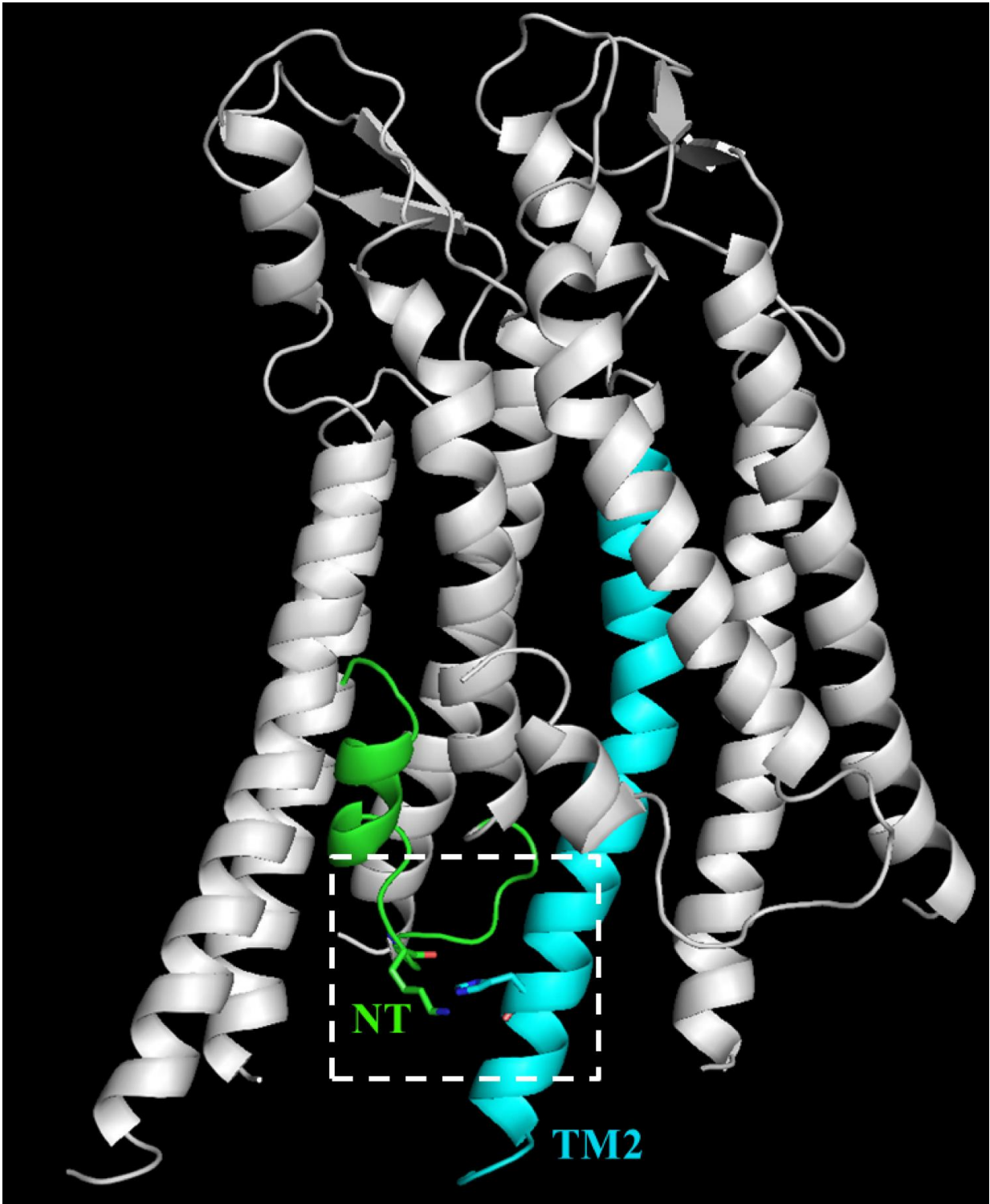


Why KID Syndrome patients experience different sets of symptoms

June 27 2016



The X-ray crystallographic structure of two Cx26 subunits suggests that the N14K mutation in the protein's N-terminal domain (green) may stabilize the hemichannel's open state by interacting with a transmembrane domain (blue) of a

neighboring subunit. Credit: Sanchez *et al.*, 2016

A team of New York-based researchers has compared the effects of two disease-causing mutations, potentially explaining why patients with the rare genetic disorder keratitis-ichthyosis-deafness (KID) syndrome can experience different sets of symptoms. The study, "Syndromic deafness mutations at Asn 14 differentially alter open stability of Cx26 hemichannels," will be published online June 27, 2016 in *The Journal of General Physiology*.

Connexin proteins form "hemichannels" in the plasma membrane of cells that allow ions and small molecules to pass between a cell and its surroundings, or between two neighboring cells, if the hemichannels of both cells are aligned. Mutations in Connexin 26 (Cx26) cause KID syndrome, which is associated with profound deafness, visual problems, and skin abnormalities. Patients carrying the N14Y mutation, in which an asparagine residue in Cx26's N-terminal domain is mutated to tyrosine, experience all these symptoms. But patients carrying the N14K mutation, in which the same asparagine residue is changed to lysine, experience a different set of symptoms. These patients do not suffer vision loss, but they do develop problems in various mucosal tissues, such as the lips, gums, and lining of the tongue.

To understand why the N14Y and N14K [mutations](#) have distinct effects in patients, Helmuth Sanchez and Vytas Verselis, from the Albert Einstein College of Medicine, together with Nefeli Slavi and Miduturu Srinavas from the SUNY College of Optometry, expressed the mutant proteins in cells and investigated how they affected the properties of Cx26 hemichannels.

Hemichannels containing the N14Y mutation showed much lower ion

conductance than normal, wild-type hemichannels, perhaps because the mutation destabilizes the channel's open, ion-conducting, state. N14K, in contrast, appeared to stabilize hemichannels in their open state, thereby allowing robust ion conductance. Wild-type Cx26 channels close in response to a reduction in pH, but N14K-containing channels remained open at a variety of pH levels.

"The effects of hemichannel opening would therefore be exacerbated in acidic environments, as seen in many mucosal tissues," says Vytas Verselis. "This might explain the unusual mucocutaneous manifestations described in patients carrying the N14K mutation."

The researchers nevertheless want to investigate other potential effects of the N14Y and N14K mutations, determining, for example, how they affect the passage of ions and small molecules between [cells](#), and whether they alter the expression or localization of Cx26 channels in patient tissues.

More information: Helmuth A. Sanchez et al, Syndromic deafness mutations at Asn 14 differentially alter the open stability of Cx26 hemichannels, *The Journal of General Physiology* (2016). [DOI: 10.1085/jgp.201611585](https://doi.org/10.1085/jgp.201611585)

Provided by Rockefeller University Press

Citation: Why KID Syndrome patients experience different sets of symptoms (2016, June 27) retrieved 3 May 2024 from <https://medicalxpress.com/news/2016-06-kid-syndrome-patients-symptoms.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.
