Unlocking the therapeutic potential of SLC13 transporters

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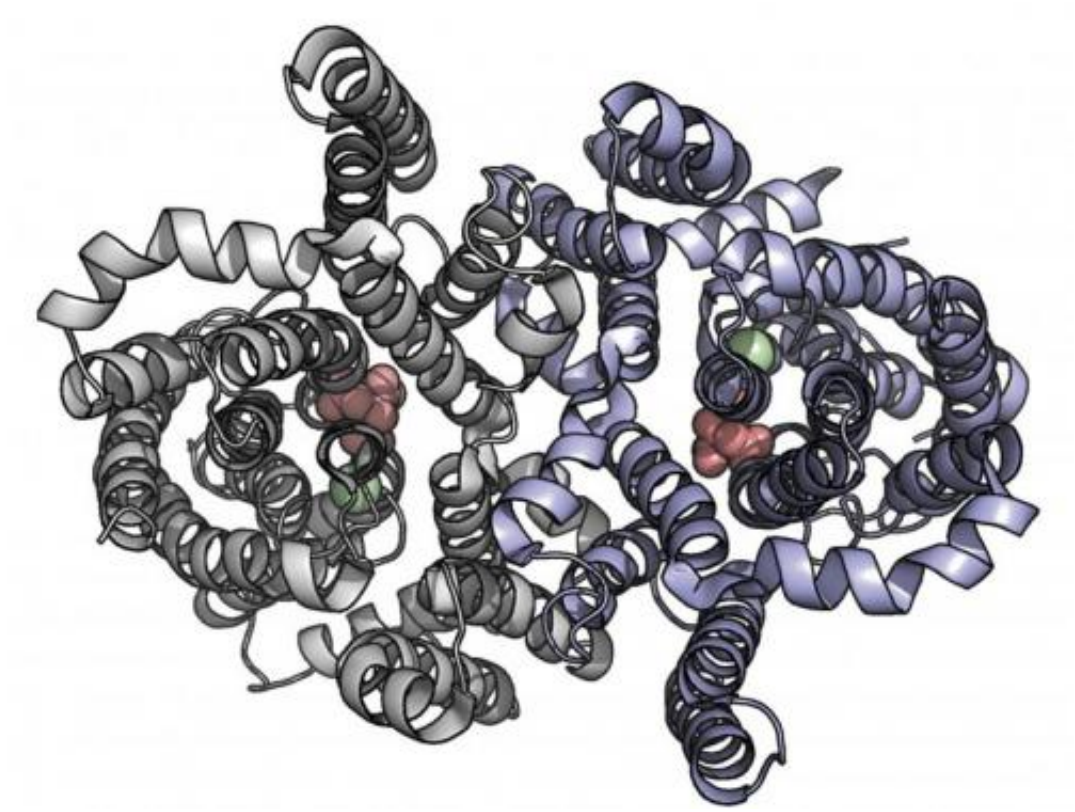

Researchers analyzed the functional properties of VcINDY (pictured), laying the groundwork for future studies of a family of transporters implicated in diabetes, obesity, and lifespan. Credit: Mulligan et al., 2014; structure from Protein Data Bank accession no. 4F35

Researchers have provided the first functional analysis of a member of a family of transporter proteins implicated in diabetes, obesity, and

lifespan. The study appears in the June issue of *The Journal of General Physiology*.

Members of the SLC13 transporter family play a key role in the regulation of fat storage, insulin resistance, and other processes. Some SLC13 transporters mediate the transport of Krebs cycle intermediates—compounds essential for the body's metabolic activity—across the cell membrane. Previous studies have shown that loss of one member of this family protects mice against obesity and insulin resistance, and loss of another results in reduced fat storage and extended lifespan in fruit flies. These findings hint at the therapeutic potential of targeting these transporters to combat metabolic disease, obesity, diabetes, and other conditions.

A recently obtained high-resolution structure of VcINDY—a member of the SLC13 family found in the bacteria that causes cholera—has provided key structural insights, but understanding how these transporters function at the cellular level remains a mystery. To find out more, researchers from the National Institute of Neurological Disorders and Stroke (NINDS) reconstituted VcINDY into small synthetic vesicles called liposomes that allowed them to monitor its activity in isolation. Led by Joseph Mindell, the team was thereby able to analyze the properties of VcINDY as a transporter and provide a model that lays the groundwork for future studies of SLC13 transporters, potentially providing the key that will enable researchers to unlock their therapeutic potential.

More information: Mulligan, C., et al. 2014. *J. Gen. Physiol*. DOI: 10.1085/jgp.201311141

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