

52. Elucidating protein function and mechanism

1 unit, Melinda Diver, November 12, 2025

Learning Goals: To explore how protein function and mechanism can be elucidated using the discovery and subsequent characterization of somatosensory ion channels as an example.

Introduction to somatosensory ion channels

TRP channels (TRPA1, TRPV1, TRPM8)

Piezo channels

Identification of somatosensory ion channels for temperature and touch

Awarded the 2021 Nobel Prize in Physiology or Medicine

Channelopathies (i.e., human diseases that results from defects ion channel function)

Exploiting natural product and synthetic chemical modulators to probe protein function

Protein structure-function analysis to elucidate mechanism

Amino acid chemistry

Assaying ion channel function

How mutagenesis (point and deletions) can inform about the functional domains of proteins

ex. Role of calcium binding in TRPM8 activation and/or desensitization

Discussion Paper:

Caterina MJ, Schumacher MA, Tominaga M, Rosen TA, Levine JD, Julius D. The capsaicin receptor: a heat-activated ion channel in the pain pathway. *Nature* 389, 816-824, 1997.

Background Paper:

Gao Y, Cao E, Julius D, and Cheng Y. TRPV1 structures in nanodiscs reveal mechanisms of ligand and lipid action. *Nature* 534, 347-351, 2016.

Review Paper:

Julius D. TRP channels and pain. *Annu. Rev. Cell Dev. Biol.* 29, 355-384, 2013.