

## SYMPOSIUM REVIEW

## TRPM2: a multifunctional ion channel for calcium signalling

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The transient potential receptor melastatin-2 (TRPM2) channel has emerged as an important  $\text{Ca}^{2+}$  signalling mechanism in a variety of cells, contributing to cellular functions that include cytokine production, insulin release, cell motility and cell death. Its ability to respond to reactive oxygen species has made TRPM2 a potential therapeutic target for chronic inflammation, neurodegenerative diseases, and oxidative stress-related pathologies. TRPM2 is a non-selective, calcium ( $\text{Ca}^{2+}$ )-permeable cation channel of the melastatin-related transient receptor potential (TRPM) ion channel subfamily. It is activated by intracellular adenosine diphosphate ribose (ADPR) through a diphosphoribose hydrolase domain in its C-terminus and regulated through a variety of factors, including synergistic facilitation by  $[\text{Ca}^{2+}]_i$ , cyclic ADPR,  $\text{H}_2\text{O}_2$ , NAADP, and negative feedback regulation by AMP and permeating protons (pH). In addition to its role mediating  $\text{Ca}^{2+}$  influx into the cells, TRPM2 can also function as a lysosomal  $\text{Ca}^{2+}$  release channel, contributing to cell death. The physiological and pathophysiological context of ROS-mediated events makes TRPM2 a promising target for the development of therapeutic tools of inflammatory and degenerative diseases.

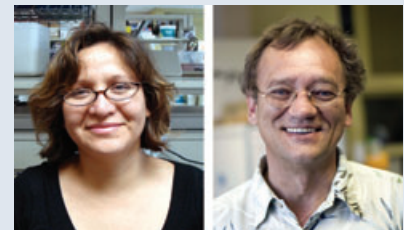
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**Corresponding author** R. Penner: Center for Biomedical Research, The Queen's Medical Center, University of Hawaii, 1301 Punchbowl Street – UHT 8, HI 6813, USA. Email: rpenner@hawaii.edu**Introduction**

Transient receptor potential (TRP) proteins represent a large superfamily of six-transmembrane (6TM) mono-

valent and divalent cation-permeable ion channels that are homologues of the *Drosophila melanogaster* TRP protein, a  $\text{Ca}^{2+}$ -permeable channel that is essential for phototransduction (Ramsey *et al.* 2006; Nilius, 2007;

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