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TRPM8 as a potential target in neurodegenerative diseases

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Abstract

Background: Cholesterol is required by the neuronal cells for a normal brain functions as it affects membrane fluidity and ion channel functions by disrupting calcium homeostasis and neuronal loss[1]. Synthesis of cholesterol occurs in glial cells like astrocytes and get transported into neurons and intracellular organelles. Any deregulation in these transport leads to several neurodegenerative diseases[2,3]. TRPM8 cation channel has been found to contain conserved cholesterol binding motifs in its sequences that indicates its potential role in cholesterol mediated functions[4].

Method: Conservation analysis of cholesterol binding motifs has been performed using CARC and CRAC sequences and docking of cholesterol with TRPM8 Cryo EM structure has been performed in Autodock. For in-vitro studies, peripheral neurons were grown in cholesterol reduced condition. Co-localization has been studied between TRPM8 and lipid-raft marker by immunostaining.

Result: TRPM8 has conserved cholesterol binding motifs in its structure. *In-vitro* study shows that TRPM8 get localized on cholesterol enriched lipid-raft on the plasma membrane more when cholesterol is reduced. The recruitment of TRPM8 protein also seems to increase in neuronal cell line after cholesterol reduction.

Conclusion: TRPM8 might have a cholesterol mediated role in neuronal cell dynamics which can be potential target for neurodegenerative diseases.

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