Title (en)

NOVEL PEPTIDE COMPOSITIONS AND METHODS OF TREATING NEUROLOGICAL INJURY

Title (de)

NEUARTIGE PEPTIDZUSAMMENSETZUNGEN UND VERFAHREN ZUR BEHANDLUNG VON NEUROLOGISCHEN LÄSIONEN

Title (fr)

NOUVELLES COMPOSITIONS DE PEPTIDES ET MÉTHODES DE TRAITEMENT D'UNE LÉSION NEUROLOGIQUE

Publication

EP 4058470 A4 20240228 (EN)

Application

EP 20887138 A 20201116

Priority

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- US 2020060681 W 20201116

Abstract (en)

[origin: WO2021097407A2] TRPM2 is a calcium permeable channel activated by ADPR metabolites and oxidative stress. TRPM2 contributes to neuronal injury in the brain caused by stroke and cardiac arrest among other diseases including pain, inflammation, and cancer. However, the lack of specific inhibitors hinders the study of TRPM2 in brain pathophysiology. Presented is the design of a novel TRPM2 antagonist, tatM2NX and truncated variants thereof, which prevents ligand binding and TRPM2 activation. Mutagenesis of tatM2NX was used to determine the structure-activity relationship and antagonistic mechanism on TRPM2 using whole-cell patch clamp and Ca2+ imaging in HEK293 cells with stable human TRPM2 expression, showing that tatM2NX inhibits over 90% of TRPM2 channel currents at concentrations as low as 2μM. Moreover, tatM2NX is a potent antagonist with an IC50 of 396nM. These results from tatM2NX mutagenesis demonstrate that specific residues within the tatM2NX C-terminus are required to confer antagonism on TRPM2. Therefore, truncated residues of the C-terminus of the peptide tatM2NX represent a new and potent therapeutic for a number of conditions, including neuronal injury and traumatic brain injury.

IPC 8 full level

C07K 14/47 (2006.01); **A61K 38/00** (2006.01); **A61K 38/17** (2006.01); **A61K 47/64** (2017.01); **C07K 14/16** (2006.01)

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A61P 25/00 (2018.01); **C07K 14/705** (2013.01); A61K 38/00 (2013.01); C07K 2319/10 (2013.01)

Citation (search report)

- [XY] WO 2017147298 A1 20170831 - UNIV COLORADO REGENTS [US]
- [Y] WO 2007082053 A2 20070719 - TRUDEAU INST [US], et al
- [Y] WO 2018204764 A1 20181108 - CAMP4 THERAPEUTICS CORP [US]
- [Y] HUANG YIHE ET AL: "Architecture of the TRPM2 channel and its activation mechanism by ADP-ribose and calcium", NATURE,, vol. 562, no. 7725, 24 September 2018 (2018-09-24), pages 145 - 149, XP036605649, DOI: 10.1038/S41586-018-0558-4

Cited by

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