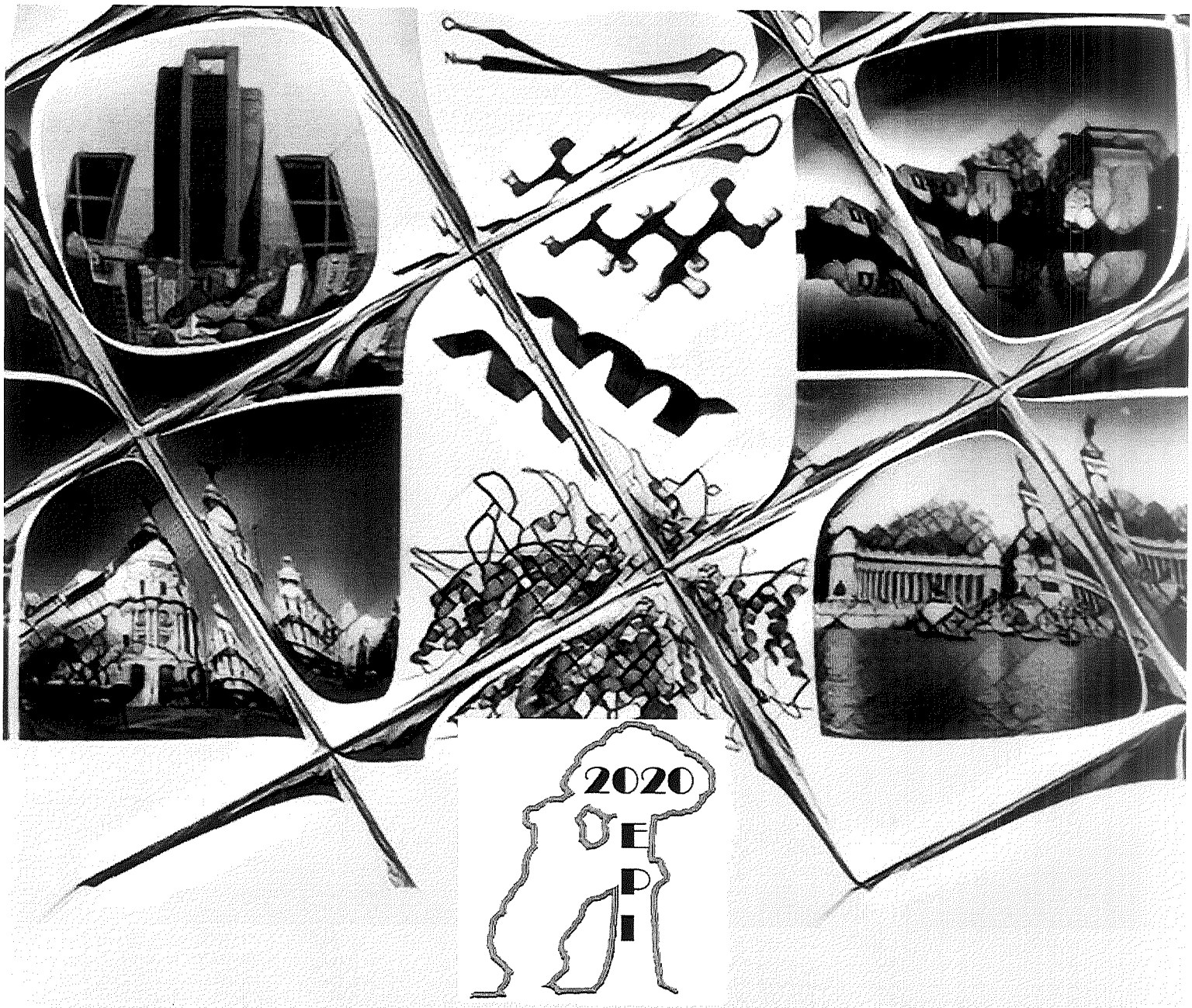


# 17th Iberian Peptide Meeting

# EPI

## IQM-IQFR-CSIC, Madrid, February 5-7th 2020

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IQM/IQFR-CSIC, Madrid, Spain, February 5-7th 2020

# Chiral amino acid-derived TRPM8 antagonists

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Transient Receptor Potential Melastatin type 8 (TRPM8) is a non-selective cationic channel, activated by innocuous cool to cold temperatures (10-28 °C), membrane depolarization, cooling agents, such as menthol and icilin, and different synthetic molecules. Furthermore, it is known that changes or mutations in these channels produce abnormal sensitivity to pain. In addition, overexpression of this channel contributes to the development of various types of cancer, and they are also involved in asthma, cardiovascular, gastrointestinal and neurodegenerative diseases. For these reasons, many pharmaceutical companies and academic researchers are searching for new modulators of TRPM8.[1,2] In this respect, we are working on two series of amino acid-derived, chiral heterocyclic systems having TRPM8 antagonist activity. Some of the first hit compounds were ester derivatives. Considering the low metabolic stability of esters, due to the action of unspecific esterases, we have prepared different amide derivatives in each series. The synthesized amide derivatives have been characterized *in vitro* using a HEK cell line stably expressing TRPM8 channels and a fluorimetry assay to measure the entrance of $Ca^{2+}$ through the cell membrane. Their antagonist activity on TRPM8 channels will be compared to that of the parent esters.

**References**

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