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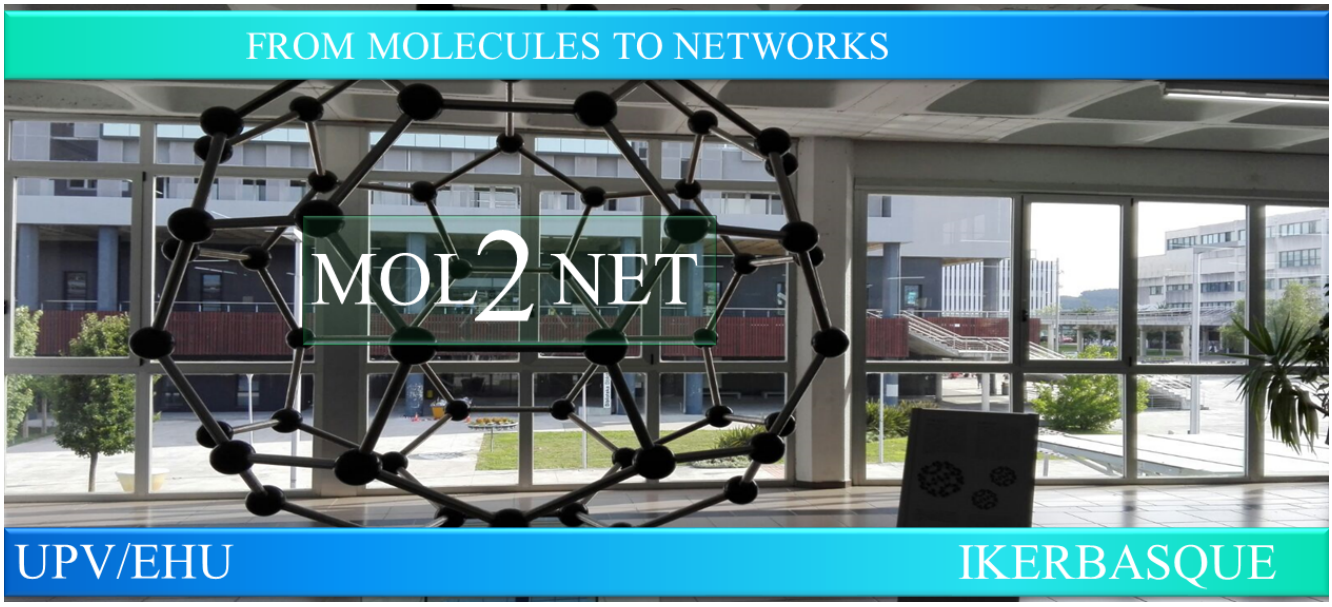

A Novel Network Science and Similarity-Searching-Based Approach for Discovering Potential Tumor-Homing Peptides from Antimicrobials

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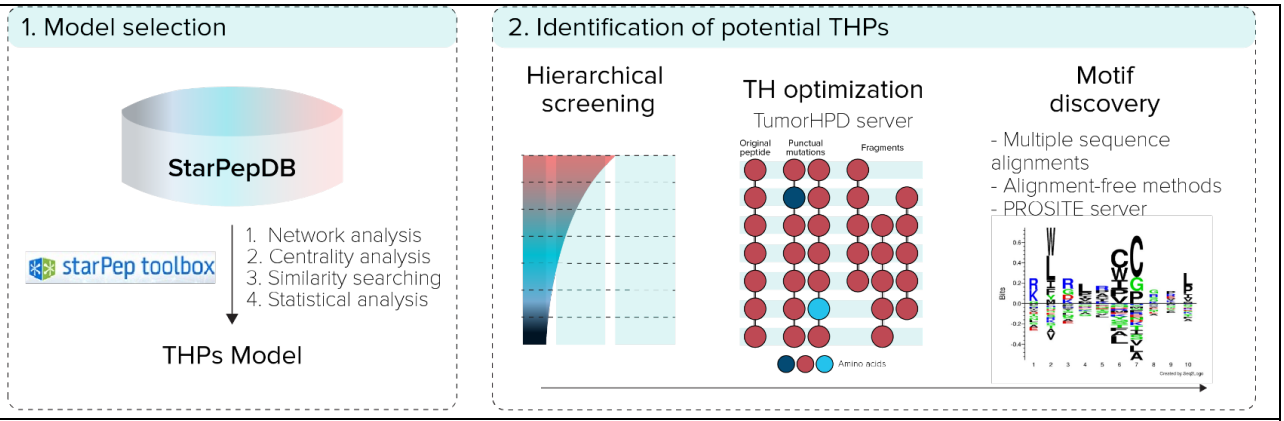
Graphical Abstract



Abstract: Peptide-based drugs are promising anticancer candidates due to their biocompatibility and low toxicity. In particular, tumor-homing peptides (THPs) have the ability to bind specifically to cancer cell receptors and tumor vasculature. Despite their potential to develop antitumor drugs, there are few available prediction tools to assist the discovery of new THPs. Two webservers based on machine learning models are currently active, the TumorHPD and the THPep, and more recently the SCMTHP. Herein, a novel method based on network science and similarity searching implemented in the starPep toolbox is presented for THP discovery. The approach leverages from exploring the structural space of THPs with Chemical Space Networks (CSNs) and from applying centrality measures to identify the most relevant and non-redundant THP sequences within the CSN. Such THPs were considered as queries (Qs) for multi-query similarity searches that apply a group fusion (MAX-SIM rule) model. The resulting multi-query similarity searching models (SSMs) were validated with three benchmarking datasets of THPs/non-THPs. The predictions achieved accuracies that ranged from 92.64 to 99.18% and Matthews Correlation Coefficients between 0.894–0.98, outperforming state-of-the-art predictors. The best model was applied to repurpose AMPs from the starPep database as THPs, which were subsequently optimized for the TH activity. Finally, 54 promising THP leads were discovered, and their sequences were analyzed to encounter novel motifs. These results demonstrate the potential of CSNs and multi-query similarity searching for the rapid and accurate identification of THPs (https://doi.org/10.3390/antibiotics11030401).

The main bibliographic sources used in this paper are listed below [1-10].

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