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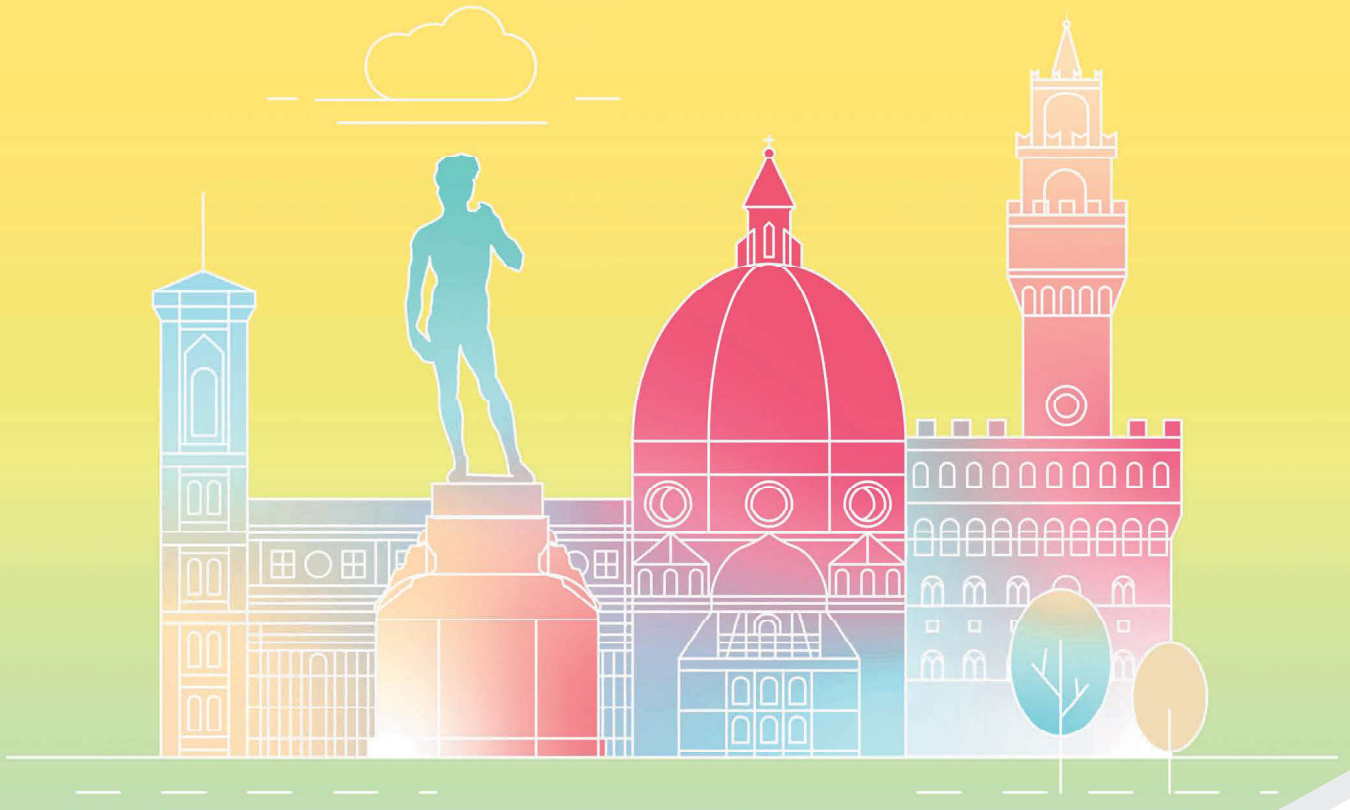

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ID: 739–P2.070 | Evaluation of antimicrobial and anticancer properties of peptides derived from Melittin: Design, synthesis and studies of mechanisms of action

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Animal venoms constitute a rich source of pharmacologically active substances. These molecules act alone or synergistically, being able to bind to different cellular receptors and/or interfere with metabolic pathways. It is known that infectious diseases are among the main causes of death in the world, and the resistance of various strains of microorganisms in relation to their commonly administered medications is a reality, causing an increase in the search for new alternatives for antimicrobial compounds. Furthermore, cancer is one of the leading causes of death in the world, and conventional treatments, such as chemotherapy and radiotherapy, are partially ineffective, producing side effects. Then, the search for alternatives, such as peptides, has been studied to combat tumoral cells and microorganisms. The objective of this work was to synthesize the peptide Melittin and analogues. Furthermore, bioconjugation strategies linking Melittin to aptamer peptides, which present affinity to tumoral markers, were used to overcome the limitations arising from the low specificity and high toxicity of melittin. In the present work, Melittin analogues, developed through rational design, were synthesized and tested for antimicrobial activity against a variety of bacterial strains. Through biological activity, it was possible to observe that all analogues presented antimicrobial activity comparable to Melittin, and in some cases, more promising activity, in addition to a significant improvement in its cytotoxicity, as we can assess in the hemolytic assay. Regarding the anticancer activity, analysis by automated microscopy and flow cytometry showed that the aptamers have affinity to the membrane at different concentrations tested. In the cell viability assay, it was observed that the bioconjugates have selectivity, since they show cytotoxic activity only in tumor cell lines, while cell viability in the non-tumor cell line remains high. With the results obtained, it is possible to observe that the bioconjugation between antitumor peptides with aptamers can be an excellent strategy visualizing a better specificity for the treatment of different types of cancer. Moreover, small analogues were able to mimic the antimicrobial activity of Melittin, reducing its toxicity.

ID: 741–P2.071 | Development of a retro-inverso tetrapeptide collagen modulator as anti-aging active principle

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The increasing demand for innovative cosmeceutical ingredients has brought attention to peptides as a significant category. SA1-III, a decapeptide derived from a serine protease inhibitor (serpin A1), known for its collagen turnover modulation properties, recently approached the cosmetic market [1]. In the present study, we developed a second-generation peptide with improved characteristics. A tetrapeptide candidate underwent modification using the retro-inverso approach, incorporating D-amino acids to enhance stability against dermal enzymes. Surprisingly, the resulted peptide AAT11RI exhibited notably high in vitro activity compared to its precursors when used as treatment for collagen-producing cells, specifically on normal human dermal fibroblasts (NHDFs) [2,3]. Its mode of action was investigated with cell-invasion experiments conducted on NHDFs (reported in Figure), which demonstrated an inhibition of proteases activity, thus a decreasing of collagen degradation. Moreover, AAT11RI demonstrated high stability against dermal enzymes in human skin homogenates, attributed to its carefully designed structure that hinders recognition by most proteases. This study highlights the significance of a rational approach in substantiating claims for the design of new cosmeceutical ingredients, representing a rarity in the field.

References

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