Dipartimento di Farmacia
Dipartimento di Eccellenza
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Università degli Studi di Napoli Federico II

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PROJECT TITLE
Identification of Novel Ligands for the Cancer-Related Protein CD44 Using NMR and Other Biophysical Techniques

Project description
CD44 is a transmembrane glycoprotein involved in cell adhesion, migration, and signaling. It plays a crucial role in cancer progression, including tumor growth, metastasis, and resistance to therapy. CD44 is widely recognized as a marker for cancer stem cells and is implicated in the regulation of the tumor microenvironment. Targeting CD44 offers promising therapeutic potential for several aggressive cancers, such as breast, pancreatic, and colorectal malignancies [1,2].
This project aims to identify and characterize novel ligands for the CD44 protein, to develop potential modulators or inhibitors of its function. In particular, the hyaluronic acid binding domain (HABD) of CD44 will be recombinantly expressed in the proponent's laboratory both in unlabeled and isotopically labeled forms (^{15}N and ^{13}C), to enable comprehensive structural and interaction studies.
Selected peptide or small-molecule libraries will be screened to identify potential ligands. Screening procedures will integrate both ligand-based and protein-based Nuclear Magnetic Resonance (NMR) techniques: ligand-based methods, such as Saturation Transfer Difference NMR (STD-NMR) and WaterLOGSY, will be employed as primary screening assays, while protein-based approaches (e.g., ^{1}H-^{15}N HSQC) will be used to map ligand-binding epitopes and, where possible, determine binding affinities [3]. High-affinity ligands for CD44 will also be analyzed using complementary interaction techniques, including Surface Plasmon Resonance (SPR), Microscale Thermophoresis (MST), and Fluorescence Polarization (FP), to assess the kinetic and thermodynamic parameters of ligand/CD44 complex formation [4]. Selected candidate ligands will be further evaluated for their functional impact on CD44-mediated cellular processes. In particular, cell migration assays will be conducted to assess the ability of these compounds to modulate CD44-dependent cell motility, a key feature of metastatic behavior [5].
By integrating structural, biophysical, and functional approaches, this project aims to develop high-affinity and selective ligands for CD44, either as potential therapeutic agents or as chemical probes to study the role of CD44 in cancer biology.
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