University of Naples Federico II

Department of Pharmacy

International PhD course in

Nutraceuticals, Functional Foods and Human Health

Regulation of the interaction of Hyaluronic Acid with the CD44 protein by identifying new modulating agents by NMR and other biophysical techniques

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Project description

Hyaluronic acid (HA) is a major component of the extracellular matrix, involved in tissue hydration, cellular signaling, and inflammation. Beyond its physiological role, HA has gained attention in the field of nutraceuticals due to its beneficial effects on skin health, joint function, and tissue regeneration. Orally administered HA has shown promise in supporting dermal elasticity and reducing joint discomfort, suggesting systemic bioactivity [1]. However, HA's biological effects also extend to pathological contexts, particularly cancer.

CD44, a transmembrane glycoprotein, is the principal receptor of HA. The HA–CD44 interaction is crucial in cancer progression, where it promotes tumor cell adhesion, migration, metastasis, and resistance to therapies [2]. CD44 is also a recognized marker of cancer stem cells and plays a role in remodeling the tumor microenvironment [3]. While HA is often used in cosmetic and nutraceutical formulations, its interaction with CD44 may influence tumor biology, underlining the importance of understanding and potentially modulating this axis.

This project aims to identify small-molecule or peptide ligands that can modulate the HA–CD44 interaction, with the goal of developing chemical probes or therapeutic leads. The HA-binding domain (HABD) of CD44 will be recombinantly expressed both unlabeled and isotopically enriched (^{15}N, ^{13}C) for NMR studies.

Initial screening will involve ligand-based NMR techniques (STD-NMR, WaterLOGSY), followed by HSQC titrations for hit validation [4]. High-affinity ligands will be characterized using microscale thermophoresis (MST), surface plasmon resonance (SPR), and fluorescence polarization (FP) to define kinetic and thermodynamic parameters [5].

By combining structural and biophysical approaches, this project seeks to uncover novel modulators of the HA–CD44 interaction, offering insights into cancer biology and the broader implications of HA in health and disease.

REFERENCES

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