Dipartimento di Farmacia
Dipartimento di Eccellenza
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UNIVERSITÀ DEGLI STUDI DI NAPOLI FEDERICO II

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PROJECT TITLE: New Molecules and Modified Aptamers for Targeting Proteins Involved in Pathological Processes

Project description

The present PhD project aims at the synthesis and structural characterization of new molecules capable of selectively modulating the functional activity of proteins involved in complex pathological processes, such as cancer, neurodegenerative diseases, and chronic inflammation. Among the most relevant protein targets, the proteasome[1-3] will be analyzed first, due to its crucial role in protein degradation and in the regulation of cellular homeostasis. The resulting experimental approach will also be extended to other clinically relevant proteins[4-6]. A central element of the project will be the rational development of new molecules, such as derivatives of small organic molecules already known for their affinity towards specific protein targets, or analogues of endogenous ligands – such as proteasome regulatory proteins, miRNA, or siRNA – suitably modified to increase their resistance to proteases/nucleases, their affinity for biological targets, and to modulate the immune response.In parallel, new phosphoramidite building blocks will be synthesized to be used as nucleoside analogues in the automated solid-phase synthesis of nucleic acids, selecting appropriate sequences of therapeutic RNA and/or DNA aptamers. The modifications introduced into the selected sequences will aim to promote the bioactive conformation[7-8] in the recognition of the target protein and to modulate the innate immune response associated with the administration of therapeutic nucleic acids[9,10], through the analysis of the correlations between the cellular response and the introduced modifications. All newly synthesized molecules will undergo in-depth characterization using spectroscopic techniques (CD, UV, NMR) and spectrometric techniques (MS, HRMS, MS^n), employing the advanced instrumentation available at the departmental instrumental analysis laboratories, including the NMR Laboratory and the MS Laboratory. In summary, the project aims to develop an innovative and versatile platform for the production and characterization of molecular regulators – whether small organic molecules or modified nucleic acids – with potential applications in the treatment of complex diseases and in the understanding of the involved molecular mechanisms.

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