Dipartimento di Farmacia
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PROJECT TITLE

Harnessing Artificial Intelligence and Advanced Computational Methods to Develop Next-Generation Immune Checkpoint Modulators for Immuno-Oncology.

Project description (max 300 words)

Cancer immunotherapy has revolutionized oncology by harnessing the immune system to recognize and eliminate tumor cells. Immune checkpoint receptors such as PD-L1, TIGIT, and LAG-3, along with other key proteins of innate immunity like STING, play crucial roles in immune evasion and tumor progression, making them attractive targets for next-generation therapeutics and diagnostics [1–3]. While monoclonal antibodies have demonstrated clinical success, there is a growing need for alternative modulators, particularly small molecules and peptides, that offer advantages in terms of tumor penetration, cost, and tunability [4].

This PhD project aims to develop novel peptide-based and small-molecule modulators of immune checkpoints, with potential applications as both therapeutic agents, through target-mediated effects or via conversion into radioligands incorporating isotopes such as iridium or lutetium, and diagnostic tools, such as PET tracers. The research will integrate advanced computational methodologies, including bioinformatics, chemoinformatics, molecular and quantum mechanics, and machine learning/artificial intelligence (ML/AI). These tools will be used to model target structures, predict ligand interactions, and guide the design and optimization of modulators with improved affinity, selectivity, and pharmacokinetic properties.

Recent studies from our group have demonstrated the successful application of these approaches to the rational design of PD-L1 inhibitors [5-7]. Building on this expertise, the project will also explore theranostic applications by designing ligands that can both modulate immune checkpoint activity and enable in vivo imaging of tumor immune status.

This multidisciplinary project provides a unique training opportunity in computational drug discovery, chemical biology, and immuno-oncology. The selected candidate will contribute to the development of innovative immunotherapeutic agents and imaging probes, advancing precision medicine at the interface of structural biology, immunology, and translational oncology.

REFERENCES

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