

University of Naples Federico II Department of Pharmacy *Doctoral Course in Pharmaceutical Sciences XL Cycle*



DESIGN, SYNTHESIS, PHYSICOCHEMICAL AND BIOLOGICAL CHARACTERIZATION OF NEW POTENTIAL DRUGS TO COUNTER RESISTANCE TO CANCER THERAPIES.

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In recent years, cancer therapy has significantly advanced in improving selectivity against cancer cells while reducing side effects. Notably, immunotherapy using immune checkpoint inhibitors has undoubtedly revolutionised the treatment of certain incurable tumours, establishing itself as a cornerstone of innovation in cancer therapy. Despite these advancements, the emergence of resistance mechanisms associated with the type of tumour microenvironment remains a major hurdle in achieving successful cancer treatment.

These resistance mechanisms often involve alterations in immune checkpoint modulation systems and abnormalities in the activity of several enzymes, such as arginase and gasotransmitter-producing enzymes (nitrogen monoxide (NO), carbon monoxide (CO) and hydrogen sulfide (H2S)). Therefore, the objective of this research proposal is the design, synthesis and physicochemical characterization and biological evaluation of new potential drugs that can modulate these enzymes activities by counteracting resistance mechanisms. The proposed drugs aim to improve therapeutic responses in cancer patients, enhance the overall success rates of treatments, and contribute to the development of new personalized, patient-centred therapeutic approaches, adaptable to various types of cancer.