



Università degli Studi *Magna Græcia* di Catanzaro - Dipartimento di Scienze della Salute -- Dottorato di Ricerche in Scienze della Vita -- Scuola di Specializzazione in Farmacia Ospedaliera -

SEMINARIO CORSO CV_S_053 DEVELOPMENT OF SMALL MOLECULES TARGETING TUBULIN: FROM BOOKS TO THE BENCH



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In the last decades, both natural and synthetic products have appreciably contributed to the development of a large number of anticancer drugs. Among these, tubulin-binding molecules represent an important class of antineoplastic agents, with broad activity in both solid and hematologic malignancies. Such chemotherapeutic agents block cell division at the metaphase/anaphase junction of mitosis bv affecting microtubule dynamics and interfering with the function of the mitotic spindle, thus leading to cell death. The therapeutic potential of anti-microtubule agents (including taxanes, vinca alkaloids, macrolides and peptides) has been extensively exploited in clinical practice. However, limitations in the use of these molecules are often related to their short half-life and the frequent incidence of tumor cell resistance, as well as to the development of severe toxicity. Based on the evidence that small molecule therapeutic drugs are generally highly specific, exhibit best efficacy and mostly contain heterocyclic scaffolds, we have devoted our efforts as synthetic medicinal chemists to develop new small molecules with antitumor properties. In particular we investigated [1,2]oxazole derivatives and we identified several classes of compounds able to impair microtubule assembly during mitosis, in a vinca alkaloid-like manner, inducing a dose- and time-dependent cell cycle arrest at the G2/M compartment, which was paralleled by an induction of apoptosis.

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