# TUBULIN: A TARGET FOR SEVERAL ANTINEOPLASTIC DRUGS

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Since the introduction in clinical practice of vinca alkaloids, tubulin has became a good target for antineoplastic chemotherapy. Microtubules are essential to separate the duplicated chromosome pairs during mitosis but they are also involved in intracellular transportation, cell signaling and cell movement. Microtubules are cytoskeletal polymers built by self-associated alpha and beta-tubulin dimers in a dynamic equilibrium which is the crucial requirement in the mitotic spindle assembly and functionality. Thus microtubules are among the most interesting targets for anticancer drugs.
Paclitaxel, a chemotherapeutic drug belonging to the taxanes family, has been for several years the only microtubule depolymerization inhibitors known in literature. Only in 1995 a second class of cytotoxic natural compounds acting with similar mechanism as taxanes was discovered and named epothilones. Binding the beta-tubulin subunit taxanes, natural epothilones and its synthetic analogs are able to induce the microtubule stabilization and to promote the soluble tubulin polymerization causing cell cycle arrest and apoptosis.
The peripheral neuropathy associated to tubulin polymerization is a major clinically-relevant side effect of these drugs thus the aim of this project is to study the peripheral neuropathy and the beta-tubulin polymerization in rats treated with paclitaxel and epothilones. Female Wistar rats were treated with different doses of these drugs and morphological and morphometrical changes in sciatic nerve as well as the tubulin polymerization in the protein extract were analyzed. In these models we observed a mild primary axonopathy and an increased beta-tubulin polymerization while we have different responses in morphometrical analysis. In fact we observed a g-ratio value decrease in the animals treated with paclitaxel and an increase of this value in the other models.

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