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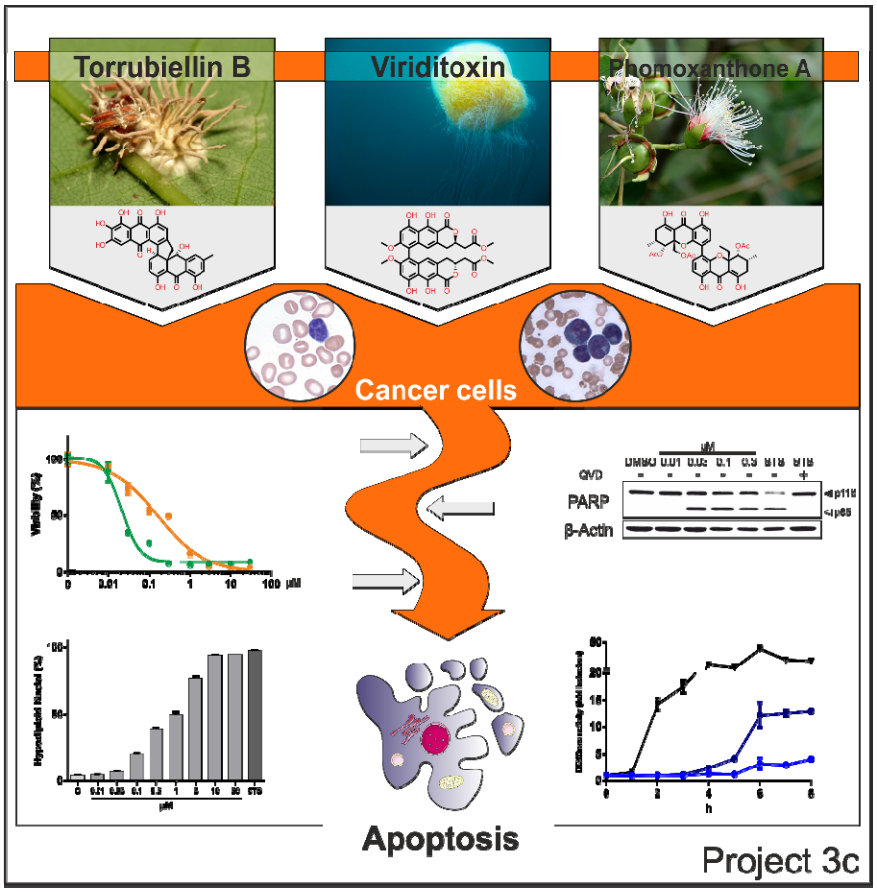
Identification of novel signaling pathways in apoptosis and autophagy for the elimination of anticancer drug resistant tumors



Inactivation of the canonical mitochondrial apoptosis pathway in tumor cells is a common mechanism of therapy resistance. Therefore the identification of new lead compounds, which are able to target novel apoptosis signaling pathways, is mandatory. Our approach to find suitable structures consists of a multi-staged screening of natural products. In the first step, natural products are screened for their cytotoxicity. Subsequently, we analyze the affected signaling pathways and search for molecular targets. So far, a number of promising natural product drugs – such as phomoxanthone A (PXA) and viriditoxin (VT) – have been identified. Thus, we could show that both compounds induce apoptosis in different tumor cell lines in rapid kinetics and effectively at low EC50 values. Moreover, we could show that leukemia cells are remarkably more susceptible to apoptosis induced by VT than healthy hematopoietic stem cells. The focus of the project is the further characterization of the involved signaling pathways as well as of further bioactive natural product drugs.

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