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TITLE

HOPEFUL TRIP FROM HERBS TO HUMANS

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It was Meadow Saffron (genus-*Colchicum*) that was toxic to animals that ate it. Chemists then isolated the toxic compound, colchicine, and its high affinity cellular receptor, tubulin, turned out to be the major protein that assembles into cellular microtubules (MTs). MTs make many cellular machineries, the most notable one is the mitotic spindle, responsible for maintaining fidelity of chromosome segregation during cell division. Colchicine disassembles these machines causing havoc in the life of a cell. Thus, a small molecule resulted in the fundamental understanding of several vital cellular processes. Using a chemical-genetic approach, we have screened structurally similar compounds with minor variations (mutant molecules) in the pursuit of finding chemicals that can alter only subtle Mt-behaviors (e.g., polymerization/depolymerization dynamics). The hope is to find small molecular tools to study nuances of mitosis in normal cells as well as in diseased cancer cells. Our screens have led to a battery of compounds that mitigate Mt dynamics enough to activate cell cycle checkpoints that halt the progression of cell cycle in normal cells. Owing to the mutational lesions in the genome of cancer cells, their checkpoint mechanisms result in gain or loss of many chromosomes, a prelude to cellular self-destruction. We will present the behavior of prostate cancer cells under compromised Mt-dynamics by novel class of chemicals. The following collage is an example of natural small molecules leading to discovery of functionally important cellular proteins, which in turn, serve as targets for novel chemotherapeutic intervention of disease.