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Targeting Cancer Cells During Mitosis Using Novel S-Trityl-L-Cysteine (STLC) Analogs

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The design of synthetic small molecules that target cytoskeleton microtubule is important for the investigation of the mechanism of cell division and for the development of novel anti-tumor agents. Molecules targeting microtubule stability such as Taxanes and *Vinca* alkaloids are among the most successful anticancer agents. However, such molecules cause undesired side effects, including neurotoxicity, and are subject to acquired drug resistance. In 1999, researchers discovered a completely new target for anti-mitotic activity is the microtubule-associated kinesin Eg5 (kinesin spindle protein, KSP). Eg5 is a member of the kinesin-5 family and plays an important role in the early stages of mitosis. Specifically, kinesin Eg5 plays an important role in bipolar spindle formation. Inhibition of this motor protein leads to the formation of monopolar spindles, mitotic arrest, followed by cell apoptosis [1]. Molecules targeting KSP selectively act only on the cells undergoing cell division, making them mitosis-specific drugs. S-trityl-L-cysteine (STLC) is a potent allosteric inhibitor of kinesin spindle protein (KSP); however, this compound has limited potential use for cancer treatment due to its amphiphilic and poor drug-like characteristics [1].

Scientist from New Mexico synthesized small, flexible novel tritylthioethanamine derivatives by modifying the triphenylmethyl and cysteine groups in STLC guided by biochemical, cell-based assays, and have utilized molecular docking techniques. Several of these ethanamine derivaties show increased potency in both biochemical and cell-based assays [1]. Two of the active compounds were evaluated for anti-proliferative activity against the NCI60 tumor panel and showed a 143 and 35-fold average increase in potency over Monastrol and STLC, respectively. In addition, these analogs had activities over a broad range of tumor types, representing a significant increase in anti-proliferative potency. To understand the mechanism of action and live cell imaging applications they also synthesized a new class of fluorescent triaza-borolopyridinium compounds from hydrazones of 2-hydrazinylpyridine (HPY) as KSP targeting imaging agents. These dyes are small and have easily tunable absorption/emission properties through variation of pyridyl or hydrazone substituents. The stability, neutral charge, cell membrane permeability and relative water solubility of HPY conjugates offer advantages for the development of receptor-targeted small-molecule probes [2].

References

1 Delany R, Chinnasamy R, Lauren HH, Lori W, Bryantb BK, et al. (2011) Synthesis and characterization of tritylthioethanamine derivatives with potent KSP inhibitory activity. Bioorganic & Medicinal Chemistry 19: 5446-5545.

2 Sudath H, Gilbert M, Chinnasamy R, Rodriguez D, Lauren HH, et al. (2011) Design and Synthesis of a New Class of Membrane-Permeable Triazaborolopyridinium Fluorescent Probes. Journal of the American Chemical Society 133: 6780-6790.