

Einladung zum Vortrag von

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„Trick and treating drug-resistant cancer: Development of the clinically trialled anti-cancer drug, DpC”

Cancer is a disease that is a "moving target", since as the condition progresses, the molecular targets change and evolve. Moreover, due to clonal selection, a specific anti-cancer drug with one molecular target may only be effective for a limited time period before drug resistance results and the agent becomes ineffective. Hence, the concept of an anti-tumor therapeutic exhibiting poly-pharmacology can be highly advantageous, rather than a therapeutic obstacle.

A novel class of agents possessing these desirable properties are the di-2-pyridylketone thiosemicarbazones, which bind iron and copper to affect a variety of critical molecular targets in tumors. In fact, these compounds possess multiple properties that enable them to overcome the "triad of death" in cancer, namely: primary tumor growth, drug resistance and metastasis.

In fact, at the molecular level, their potent anti-oncogenic activity includes: up-regulation of the metastasis suppressor, N-myc downstream regulated gene 1; overcoming drug resistance mediated by P-glycoprotein; up-regulation of the tumor suppressor, PTEN; down-regulation of the proto-oncogene, cyclin D1; inhibition of the rate-limiting step in DNA synthesis catalyzed by ribonucleotide reductase; and the inhibition of multiple oncogenic signaling pathways, e.g., Ras/MAPK signaling, protein kinase B (AKT)/phosphatidylinositol-3-kinase, ROCK/pMLC2, etc.

The lead agent of this class of di-2-pyridylketone thiosemicarbazones, namely di-2-pyridylketone 4-cyclohexyl-4-methyl-3-thiosemicarbazone (DpC), demonstrates pronounced anti-tumour activity by both the oral and intravenous routes and has recently entered multi-centre, Phase I clinical trials for advanced and resistant cancer.

Freitag, 31. März 2017, 15:30 Uhr
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