SFM as Predictive Biomarker for Determining Response to TOP1-Directed Chemotherapy

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Accumulation of DNA damages by Camptothecin/Topotecan-type chemotherapy drugs

Topoisomerase 1 and Camptothecin (CPT)-type chemotherapy drugs

- As DNA is unwound, it becomes necessary to reverse the supercoiling effects
- TOP1 induces single-strand breakage and DNA strand unwinding
- CPT-type drugs halt the re-ligation process, resulting in ds breaks during DNA replication and transcription.

Yves Pommier, Nat. Rev. 2006

SFM-deficiency increased the susceptibility of breast cancer cells to Camptothecin-induced DNA damage

A

CPT (2 μM) 0 hr + 1 hr + 2 hr + 3 hr +
shCtrl shSFM

γH2AX TBP

B

-CPT +CPT

shCtrl shSFM

SFM-deficiency sensitized breast cancer cells to Camptothecin-induced apoptosis

A

CPT cell cycle

shCtrl shSFM

C

Campera 3 Chopped Campera 3

PARP Cleaved PARP s-fubulin

Suppression of SFM sensitizes xenograft tumors to chemotherapeutic agents

A

shCtrl/IBT474-nuc shSFM/IBT474-nuc

Day 4

Day 24

SFM inactivation has no effect on the growth rate of BT474 xenograft tumors

A

shCtrl shCon-E3 shSFM

B

Day (h)

Current clinical choice of FOLFIRI or FOLFOX regimen for metastatic colorectal cancer

- FOLFIRI (irinotecan+5-FU+leucovorin): irinotecan is an analogue of CPT
- FOLFOX (Oxaliplatin+5-FU+leucovorin)

Potential Commercial Applications

- Predictive biomarker to determine patient response to TOP1-directed chemotherapy (e.g. FOLFIRI vs FOLFOX for colorectal cancer patients).
- Predictive biomarker for selecting patients in clinical trials with new TOP1-directed chemotherapy drugs

Licensing Contact

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