SFM as Predictive Biomarker for Determining Response to TOP1-Directed Chemotherapy
Pengbo Zhou, Department of Pathology and Laboratory Medicine, Weill Cornell Medical College, New York, NY 10065

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.

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

CPT-induced TOP1 degradation and cytotoxicity are dependent on the SFM E3 ligase

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

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

Suppression of SFM sensitizes xenograft tumors to chemotherapeutic agents

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

Except Luminal-A subtype, SFM staining in breast cancer tissues is statistically significantly different from the staining in normal mammary epithelial tissues

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)
- Current decision on regimen is based on potential side effects and other non-therapeutic parameters, not on therapeutic efficacy
- The choice of second-line treatment typically depends on what was given originally

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
Brian Kelly, Director, Technology Commercialization & Liaison/WCMC Office, (212)746-6189, bjk44@cornell.edu

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

**CPT-induced TOP1 degradation and cytotoxicity are dependent on the SFM E3 ligase**

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

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

**Suppression of SFM sensitizes xenograft tumors to chemotherapeutic agents**

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

**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)
- Current decision on regimen is based on potential side effects and other non-therapeutic parameters, not on therapeutic efficacy
- The choice of second-line treatment typically depends on what was given originally

**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**
Brian Kelly, Director, Technology Commercialization & Liaison/WCMC Office, (212)746-6189, bjk44@cornell.edu