NEIs have revealed that CRM1 is a novel target for the treatment of cancer. NEIs cause the rapid nuclear accumulation of CRM1 cargo proteins, which function to induce cell cycle arrest or apoptosis. Activation of many CRM1 cargo proteins in the nucleus can lead to inhibition of proliferation; treated cells arrest in the G2 and/or G1 phase of the cell cycle.

NEI treatment rapidly induces apoptosis in leukemia cells. NEIs are synergistic with many chemotherapeutic agents in vitro and in vivo.

Conclusions:
- Nuclear export is a novel target for cancer therapy.
- KOSan’s lead nuclear export inhibitors show efficacy in vitro and in vivo.
- Targeting CRM1 leads to a rapid and prolonged block of nuclear export.
- Nuclear export inhibition induces apoptosis in cancer cells but not normal cells.
- NEIs are synergistic when combined with a broad spectrum of cancer therapeutics in vitro and in vivo experiments.
- Nuclear export inhibition is observed in multiple in vivo models (mouse xenografts; xenografts; mouse Yang et al., Poster # 5597, this session).