## Technology Brief: Small Molecule Inhibitors of Nuclear Export of Topoisomerase II Alpha for Multiple Myeloma Treatment

**Summary**
- Inhibitors of topoisomerase II, such as doxorubicin, are effective chemotherapy for multiple myeloma.
- Resistance to these agents may arise when cancer cells export topoisomerase II alpha from the nucleus to the cytoplasm.
- Scientists at Moffitt Cancer Center have identified small molecules that inhibit nuclear export of topoisomerase II alpha and sensitize human myeloma cells to topoisomerase II inhibitors such as doxorubicin.
- These newly identified export inhibitors may be useful as agents for treating multiple myeloma and other hematologic cancers, either alone or in combination with topoisomerase II inhibitors.

## Features and Benefits
- The two nuclear export signals in topoisomerase II alpha were targeted by in silico screening against a library of drug-like molecules.
- The 20 top-scoring compounds were assayed for inducing cell death in human multiple myeloma cell lines NCI-H929 and RPMI 8226, both as single agents and in combination with topoisomerase II inhibitors.
- Two inhibitors have IC\(_{50}\) values in the low micromolar range as single agents.
- Nuclear export inhibitors are synergistic in combination with inhibitors of topoisomerase II in inducing death of human multiple myeloma cells.
- These newly identified inhibitors may be useful as single agents in treatment of multiple myeloma, or in combinations to overcome resistance to topoisomerase II inhibitors.

## Stage of Development
Proof of concept in human multiple myeloma cell lines. Testing planned in patient cell samples.

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## Patent Status
PCT patent application filed.

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