PROJECT TITLE

Unique and Selective Targeting of Cdk Activity in Aggressive Carcinomas

PRINCIPAL INVESTIGATOR

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PROJECT SUMMARY

Combination chemotherapy focuses on targeting one of hallmarks of cancer, rapidly growing cells, and for many forms of cancer this remains the only available treatment. Following or during treatment cancer cells that are not effectively removed by chemotherapy will accumulate mutations making them increasingly aggressive and eventually they will evolve to a drug resistant state. Many of these mutations help the cancer cell by crippling the normal protective cellular mechanisms that trigger the death of cells with damaged DNA. Reinstalling these protective pathways represents an attractive mechanism to sensitize some of the most aggressive cancer cells to treatment.

One family of protective proteins lost or blocked by aggressive cancers are Cyclin Dependent Kinase Inhibitors (CKIs). Basic research and pharma development have led to synthetic CKIs, which have met with variable success in the clinic. One issue not considered by these drugs, is the existence of a family of proteins called the Speedy/Ringo family. These proteins can override CKI activity, rendering synthetic and natural CKIs less effective. These proteins are elevated in several forms of cancer and pre-clinical data in-cells and animals supports our contention that developing drugs to block this family of proteins is a novel and promising therapeutic approach.

This OICR funded project supports an interdisciplinary team of researchers with expertise in cancer cell biology and chemistry/drug development who are making significant progress in developing compounds to block this novel mechanism. This team has established tools that are not available elsewhere in the world to test the effectiveness of new classes of drugs. The overall goal of this work is to develop very selective drugs that will block action of the Speedy/RINGO family of proteins and render drug resistant cells sensitive to standard of care therapies and natural cellular processes of eliminating damaged cells. Ultimately this work aims to improve outcomes for patients with some of the most aggressive forms of cancer.