PROJECT TITLE

Patient-specific prediction of fluoropyrimidine dose and toxicity risk based on circulating micro RNA and NextGen exome sequencing coupled to functional validation *in vitro* and *in vivo*

PRINCIPAL INVESTIGATOR
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SCIENTIFIC SUMMARY

Modern chemotherapy often includes 5-fluorouracil and capecitabine. These chemotherapies are effective and widely prescribed for the treatment of various cancers. However, patients are at high risk for experiencing severe, sometimes life-threatening toxicity during treatment with these chemotherapy medications. Genetic deficiency in the enzyme dihydropyrimidine dehydrogenase (DPD, gene name DPYD) has been recognized as an important cause of this toxicity. However, we now know that common genetic variations in DPYD identify only a subset of patients at risk for severe toxicity during this chemotherapy. To further enable individualized and precise dosing and treatment options for 5-fluorouracil and capecitabine chemotherapy, the Kim team has created a custom targeted NextGen (NGS) DNA sequencing panel that is capable of rapid identification of patient-specific rare genetic variants in DPYD. They are also able to measure circulating microRNA that regulate DPYD, from patient-derived blood samples. The team plans to demonstrate that integration of targeted NGS coupled with microRNA measurement from patient-derived blood samples prior to chemotherapy will result in more precise 5-fluorouracil and capecitabine dosing and less toxicity for patients.