

## **High Throughput Screen for siRNA Modulators of Non-homologous End Joining**

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The repair of double strand breaks (DSBs) plays a crucial role in cancer predisposition and cancer therapy. Transient inhibition of DSB repair might be useful as a method for sensitizing tumors to radiotherapy ("radiosensitization"), allowing the dose of radiation to the patient to be minimized. This could benefit specific cancer patients of all ages, including a subset of children with curable cancers. DSB repair entails two major pathways: homologous recombination (HR) and non-homologous end joining (NHEJ). Of these, the most potent radiosensitization comes from inhibition of NHEJ. NHEJ inhibition might have additional value for cancer treatment independent of radiation therapy. Germ line mutations in NHEJ genes can also cause rare recessive human immunodeficiency syndromes. Although the "core" human NHEJ genes are known, we believe that additional NHEJ genes remain to be discovered, some of which may be human disease genes. Thus, there is a compelling rationale for identifying the full spectrum of human genes that mediate NHEJ. Our goal here is to work with the ICCB-Longwood screening facility to conduct a high-throughput screen for small interfering RNAs that modulate NHEJ in human cells, with the aim of identifying new human NHEJ genes.