Genetic biomarker may help identify neuroblastomas vulnerable to novel class of drugs

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An irregularity within many neuroblastoma cells may indicate whether a neuroblastoma tumor, a difficult-to-treat, early childhood cancer, is vulnerable to a new class of anti-cancer drugs known as BET bromodomain inhibitors, Dana-Farber/Children's Hospital Cancer Center scientists will report at the annual meeting of the American Association for Cancer Research in Washington, April 6-10.

The findings (abstract 4622) will be discussed in a minisymposium on Tuesday, April 9, 3:50 - 4:05 p.m., ET, in Room 147, in the Washington Convention Center. The work was published in *Cancer Discovery*, a journal of the American Association of Cancer Research, on Feb. 21, 2013.

In studies with laboratory samples of neuroblastoma cells and mice with the disease, the researchers found that tumors with excess copies, or "amplification," of the gene MYCN were highly sensitive to BET bromodomain inhibitors. The findings may lead to clinical trials of the drugs in patients whose neuroblastoma tumors carry this amplification.

"BET bromodomain inhibitors are a class of drugs that, many researchers hope, may offer a new therapeutic option for treating patients with certain cancers," says Dana-Farber/Children's Hospital Cancer Center researcher and clinician Kimberly Stegmaier, MD, who will be presenting the research. "The challenge has been identifying biomarkers that can help direct clinical translation of these drugs by pinpointing those patients with the highest likelihood of response."

Stegmaier and her colleagues screened more than 600 cancer cell lines, each with a known set of genetic abnormalities, to see which would succumb to a prototype BET bromodomain inhibitor. They found the most susceptible cells were those with a MYCN amplification.

"Neuroblastoma is a devastating childhood cancer – the most common extracranial tumor of early childhood – and only a minority of children with aggressive forms of the disease are cured with currently available treatments," Stegmaier remarks. "Although prior research has shown that MYCN amplification is common in neuroblastoma, it has been an elusive drug target."

Working with Dana-Farber's James Bradner, MD, Stegmaier found that the BET bromodomain inhibitor reduced the levels of MYCN protein in lab-grown neuroblastoma cells, resulting in impaired cell growth and induction of cell death. In studies of mice with MYCN-amplified neuroblastoma – including animals with a form of the disease that doesn't respond to many standard therapies – the drug had anti-tumor effects and prolonged survival.

Provided by Dana-Farber Cancer Institute