Agios Announces Cancer Cell Publication of Research Illuminating Link between Cancer Metabolism and Epigenetics

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Study provides insight into role of IDH1 and IDH2 mutations in AML

Cambridge, Mass. December 14, 2010 - Agios Pharmaceuticals, the leading biopharmaceutical company focused on discovering and developing novel drugs in the rapidly emerging field of cancer metabolism, today announced the publication of a paper in Cancer Cell that illuminates the mechanism by which 2-hydroxyglutarate (2HG), and the mutations in the metabolic genes IDH1 and IDH2 that produce it, may be driving the growth of tumors in patients with acute myeloid leukemia (AML). This research was conducted as a collaboration between Weill Cornell Medical College, Memorial Sloan Kettering Cancer Center, the University of Pennsylvania and Agios.

IDH1 and IDH2 are normal metabolic enzymes that are mutated in several forms of cancer, including AML. In a 2009 publication in Nature, Agios researchers previously established that mutated IDH1 and IDH2 have novel enzyme activity (consistent with a cancer-causing gene or oncogene) producing high levels of 2HG in cancer cells with IDH mutations. This new research suggests that high 2HG levels may trigger epigenetic changes within the cells ??? a known cancer-causing mechanism ??? thus strengthening the biological link between IDH mutations, 2HG and the development of cancer.

"This study broadens our understanding of the role of IDH1 and IDH2 mutations in AML, where novel therapies are desperately needed," said David Schenkein, M.D., chief executive officer of Agios. "These unique insights will help in the development of programs directed towards finding therapies for AML, and other IDH associated diseases. More broadly, this finding further validates the field of cancer metabolism by demonstrating how altered metabolic processes can cause cancer-related changes in tumors."

In this study, researchers conducted DNA sequencing and DNA methylation analysis for AML-associated recurrent mutations, including IDH1 and IDH2. Specimens were taken from 385 patients with AML less than 60 years of age who are enrolled in a Phase 3 multicenter Eastern Cooperative Oncology Group clinical trial.

The study found that IDH mutations induce DNA hypermethylation, an epigenetic phenomenon noted in many cancer cells, and impair differentiation in hematopoietic cells. Similar DNA hypermethylation effects are caused through the loss of function of TET2, a demethylase enzyme that is also mutated in leukemia. This study supports IDH-mutant and TET2-mutant leukemias as biologically distinct disease subtypes and links cancer metabolism with epigenetic control of gene expression.

"Earlier research about the role of mutant IDH and the discovery of 2HG was very exciting, but until now, we haven't really understood the relationship between 2HG and cancer," said Ari Melnick, M.D., associate professor of medicine, co-director, medical research track at Weill Cornell Medical College. "This study broadens and contextualizes our understanding of the biology of IDH mutations. These findings are meaningful not just for researchers in AML and gliomas, who have historically been interested in IDH, but also for scientists working more broadly in both cancer metabolism and epigenetics."

About Cancer Metabolism
Cancer metabolism is a new and exciting field of biology that provides a novel approach to treating cancer. Cancer cell metabolism is marked by profound changes in nutrient requirements and usage to ensure cell proliferation and survival. Research in the field has demonstrated that cancer cells become addicted to certain fuel sources and metabolic pathways. In cancer, this metabolic reprogramming is coordinated with proliferative signaling and regulated by the same oncogenes and tumor suppressor genes to ensure efficient proliferation. Glycolysis (sugar metabolism), fatty acid metabolism and autophagy (self metabolism) are three pathways shown to play a critical role in cancer metabolism. Identifying and disrupting certain enzymes in these, and perhaps other, metabolic pathways provides a powerful intervention point for discovery and development of cancer therapeutics.

About Agios Pharmaceuticals
Agios Pharmaceuticals is the first biopharmaceutical company dedicated to the discovery and development of novel therapeutics in the emerging field of cancer metabolism. To support and drive these efforts, Agios is building a robust platform integrating cancer biology, metabolomics, biochemistry and informatics to enable target and biomarker identification. Agios' capabilities to interrogate differential cellular metabolism of diseased cells relative to normal cells may also be applicable to other therapeutics

areas including autoimmune, inflammatory and neurological diseases. To date, Agios has put in place a world-class scientific team of more than 60 people, built a fully integrated cell metabolism platform within the largest research laboratory dedicated to cancer metabolism, and created an emerging product development pipeline of novel cancer therapeutics. The company's founders represent the core thought leaders in the field of cancer metabolism, responsible for key advances, insights and discoveries in the field. Agios Pharmaceuticals is located in Cambridge, Massachusetts. For more information, please visit the company's website at www.agios.com.

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