

New Publications from Agios Scientists and Collaborators Reveal Unexpected Regulation of Metabolic Pathways in Cancer

September 20, 2012 1:20 PM ET

Cambridge, Mass. – September 20, 2012 – Agios Pharmaceuticals, the leading biopharmaceutical company focused on discovering and developing novel drugs in the fields of cancer metabolism and rare metabolic genetic diseases, announced today two recent publications that provide important new validation for the emerging field of cancer metabolism. The article “Phosphofructokinase 1 Glycosylation Regulates Cell Growth and Metabolism” was published in the August 24, 2012 issue of the journal *Science*, and the article “Small molecule activation of PKM2 in cancer cells induces serine auxotrophy” will be published in the September 21, 2012 issue of the journal *Chemistry & Biology*.

"Alterations in metabolic pathways are a central recurring feature of cancer," said Scott Biller, Ph.D., chief scientific officer of Agios. "These studies establish new patterns of cell signaling, metabolic regulation and nutrient dependence in tumor cells that expand our understanding of cancer metabolism and could lead to promising new treatments for cancer patients."

The article in the journal *Science* identified a key response system in tumor cells that senses nutrient availability and oxidative stress and activates a signaling response that redirects cancer cell metabolism to promote growth. The findings show that altering the activity of the glycolytic enzyme phosphofructokinase 1 (PFK1) through O-glycosylation can control carbon flow through key central metabolic pathways. This alteration in PFK1 activity causes the re-routing of sugar carbon into pathways that protect cancer cells from oxidative damage and increase metabolite pools needed for rapid cell division. The research suggests that multiple cancer types hijack this mechanism to fuel rampant tumor growth. This publication arises from collaborative work conducted between Agios scientists and colleagues at the California Institute of Technology and the Genomics Institute of the Novartis Research Foundation.

Another publication in the journal *Chemistry & Biology* highlights the discovery of a novel chemical class of PKM2 activators and describes the impact of PKM2 activation on cancer cell metabolism. Findings from this publication were first highlighted earlier this year at the American Association for Cancer Research (AACR) Annual Meeting 2012. The findings published in *Chemistry & Biology* show that pharmacological activation of PKM2 in cancer cells makes those cells dependent on the availability of the amino acid serine for continued survival. Agios scientists discovered novel compounds that effectively increase activity of a cancer-associated isoform of pyruvate kinase (PKM2) in the glycolytic pathway, which is a conserved metabolic pathway that processes sugar to fuel cell growth. Unexpectedly, pharmacological activation of this enzyme induces certain cancer cell types to uniquely become highly dependent on serine—normally a non-essential amino acid—for cell proliferation.

Both papers further underscore the importance of in-depth understanding of metabolic networks to discover novel therapeutic modalities to treat cancer.

About Agios Pharmaceuticals

Agios is the leading biopharmaceutical company focused on discovering and developing novel drugs in the fields of cancer metabolism and rare metabolic genetic diseases. Agios has multiple first-in-class programs in cancer metabolism and inborn errors of metabolism advancing toward the clinic, in addition to an active research and discovery pipeline across both therapeutic areas. The company has a significant collaboration with Celgene focused on developing new treatments for cancer leveraging Agios' capabilities and insights into cancer metabolism. For more information, please visit our website at www.agios.com.