New study points to novel mechanism by which tumors escape recognition by the immune system

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Potential Role of Reata's Antioxidant Inflammation Modulators in Cancer Prevention and Treatment Highlighted in Report

IRVING, Texas, Nov. 29, 2011 – A new study in *The Journal of Clinical Investigation* (JCI) has uncovered a novel mechanism that cancer cells may use to escape detection by the body's immune system. The study, "Tumor-infiltrating myeloid cells induce tumor cell resistance to cytotoxic T cells in mice," led by researchers at the H. Lee Moffitt Cancer Center in Tampa, Fla., shows that a specific type of immature white blood cells (myeloid derived suppressor cells or "MDSCs") are recruited to tumors where they modify tumor cells so that they are no longer recognized by the immune system's cells (cytotoxic T cells) that fight cancer. The study also suggested that bardoxolone methyl, the lead compound in a new class of molecules called antioxidant inflammation modulators (AIMs), may have the ability to prevent these modifications and thereby boost the immune system's ability to detect and fight cancer.

In previous studies, the authors, Dr. Dmitry Gabrilovich and colleagues, showed that oxidative stress produced by MDSCs inhibited tumor recognition by the immune system (*Nature Medicine*, 2007). The findings in the new study demonstrate how this occurs. Oxidative stress produced by MDSCs alters the surface proteins on tumor cells so that cytotoxic T cells can no longer recognize the tumor. The authors hypothesized that reducing oxidative stress in the tumor microenvironment would prevent alteration of tumor surface proteins and thereby restore the immune system's ability to recognize the tumor. The authors chose to use one of Reata's AIM class compounds to lower oxidative stress because it is a potent activator of Nrf2 and inhibitor of NFκB, thereby reducing oxidative stress and suppressing inflammation. In mice with lung cancer or melanoma, treatment with the AIM improved the ability of cytotoxic T cells to recognize tumor cells and significantly slowed tumor growth. This approach may be important in addressing other tumor types because MDSC activity has been shown in numerous cancers, including pancreatic cancer, breast cancer, lung cancer and melanoma.

Commenting on the study results, Dr. Gabrilovich said, "Our study not only demonstrated a novel mechanism by which the tumor escapes recognition by the immune system but also suggested a potential approach to its correction, which may improve the clinical outcomes associated with current immune therapeutics."

"We are very impressed by the data from this recent study," said Colin Meyer, M.D., Vice President of Product Development at Reata Pharmaceuticals, Inc. "These findings are a significant advance in our understanding of the fundamental basis by which tumors escape immune surveillance, and these preclinical data with one of our AIM class compounds are highly encouraging."

About Reata Pharmaceuticals

Reata Pharmaceuticals is the leader in discovering and developing novel, oral anti-inflammatory drugs that activate Nrf2, the primary regulator of cellular antioxidant and detoxification enzymes. Activation of this important biological target is thought to protect against a broad range of diseases associated with inflammation and oxidative stress. Reata's lead product candidate, bardoxolone methyl, was initially studied in cancer patients. In these studies, cancer patients with moderate to severe chronic kidney disease (CKD) demonstrated marked improvement in a key measure of kidney function. On the basis of these observations, Reata initiated development of bardoxolone methyl in patients with advanced CKD, and the drug is currently in a global Phase 3 clinical trial. Reata is advancing a second generation AIM to be used in clinical development for the treatment of cancer patients.

For more information, please visit the company's Web site at www.reatapharma.com.

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