

Researchers identify new drug target for gastrointestinal stromal tumors

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Researchers at University of California San Diego School of Medicine and Mayo Clinic provide the first evidence that the Hedgehog signaling pathway is central to the formation of gastrointestinal stromal tumors (GIST), which are frequently driven by the KIT oncogene. Results of the human study were recently published online in *Oncotarget*.

"Our new finding is a step forward in overcoming [tyrosine kinase inhibitor](#) resistance, a clinically significant problem in the management of GIST," said Jason Sicklick, MD, associate professor of surgery at UC San Diego School of Medicine and surgical oncologist at Moores Cancer Center at UC San Diego Health. "By knowing that Hedgehog signaling is altered in human GIST, and that it controls KIT expression, we may have found a way to turn the cancer off."

GISTs eventually become highly resistant to current drug therapies. Clinicians fight the growth with progressively aggressive drugs, the downside being that each later line of therapy has diminishing effectiveness and higher toxicity for patients. More than 95 percent of patients eventually succumb to drug-resistant GIST, necessitating the search for alternative therapeutic targets.

"We may have found this cancer's 'on' switch," said Sicklick. "We are flipping the switch 'off' with arsenic, a drug that is already in clinical practice. With this drug, we are able to kill multidrug-resistant cell lines, offering a new approach to treatment."

GIST is the most common sarcoma with an estimated annual incidence of 6.8 cases per million people in the United States. These tumors start in special cells found in the wall of the GI tract, called the interstitial cells of Cajal (ICCs). ICCs are sometimes called the "pacemakers" of the GI tract because they signal the muscles in the digestive system to contract to move food and liquid through the GI tract.

Sicklick was recently named by The Life Raft Group, a national advocacy group that supports research and treatment of GIST, as their Clinician-of-the-Year for 2016. As a physician-scientist, Sicklick is dedicated to understanding GIST at the basic science level while finding treatments for GIST that are best for adult, adolescent and pediatric patients. Tamas Ordog, MD, co-senior author of the paper, is a basic scientist known for his research on ICCs. He is affiliated with the Mayo Clinic Center for Individualized Medicine and he is a member of the Life Raft Group Research Team.

More information: Chih-Min Tang et al, Hedgehog pathway dysregulation contributes to the pathogenesis of human gastrointestinal stromal tumors *via* GLI-mediated activation of *KIT* expression, *Oncotarget* (2016). [DOI: 10.18632/oncotarget.12909](https://doi.org/10.18632/oncotarget.12909)

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