

November 01, 2016 | By Jackie Carr

## Researchers Identify New Drug Target for Gastrointestinal Stromal Tumors

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



*Jason Sicklick, MD, surgical oncologist at Moores Cancer Center at UC San Diego Health.*

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.

Moore's Cancer Center is the region's only NCI-designated comprehensive cancer center. It is also the first and only San Diego-based member of the National Comprehensive Cancer Network, an alliance of the world's leading cancer centers. Moore's Cancer Center currently operates more than 170 open treatment trials. These investigational therapies include advanced, highly personalized stem cell-based approaches and immunotherapies that leverage the inherent healing powers of the human body.

To learn more about the treatment of GIST at Moore's Cancer Center, visit:

<https://health.ucsd.edu/specialties/cancer/programs/gastrointestinal/Pages/gist.aspx>

Contributors to this paper include: Chih-Min Tang, Tracy E. Lee, Adam M. Burgoyne, Stephanie Y. Leonard, Jonathan C. Chan, Eileen Shi, Martina De Siena, and Olivier Harismendy from UC San Diego; Sabriya A. Syed, Fei Gao, Michael L. Kendrick, and Michael R. Bardsley from Mayo Clinic; Junhao Mao from University of Massachusetts, Worcester, Massachusetts; and Juliann Chmielecki, Deborah Morosini, Kai Wang, and Jeffrey S. Ross from Foundation Medicine Inc.

Support for this study came from the National Institutes of Health (K08 CA168999, R01 DK058185, R21 CA191186, P30 DK084567, P30 CA015083), SSAT Career Development Award, the UCSD GIST Research Fund, UCSD Academic Senate Health Sciences Research Grant, The Life Raft Group, and the Mayo Clinic Center for Individualized Medicine.

---

## MEDIA CONTACT

**Jackie Carr**, 858-249-0456, [jcarr@ucsd.edu](mailto:jcarr@ucsd.edu)

Colette Gallagher, Mayo Clinic, 507-284-5005 [newsbureau@mayo.edu](mailto:newsbureau@mayo.edu)

UC San Diego's [Studio Ten 300](#) offers radio and television connections for media interviews with our faculty, which can be coordinated via [studio@ucsd.edu](mailto:studio@ucsd.edu). To connect with a UC San Diego faculty expert on relevant issues and trending news stories, visit <https://ucsdnews.ucsd.edu/media-resources/faculty-experts>.