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Study identifies gastric cancer biomarker and possible treatment

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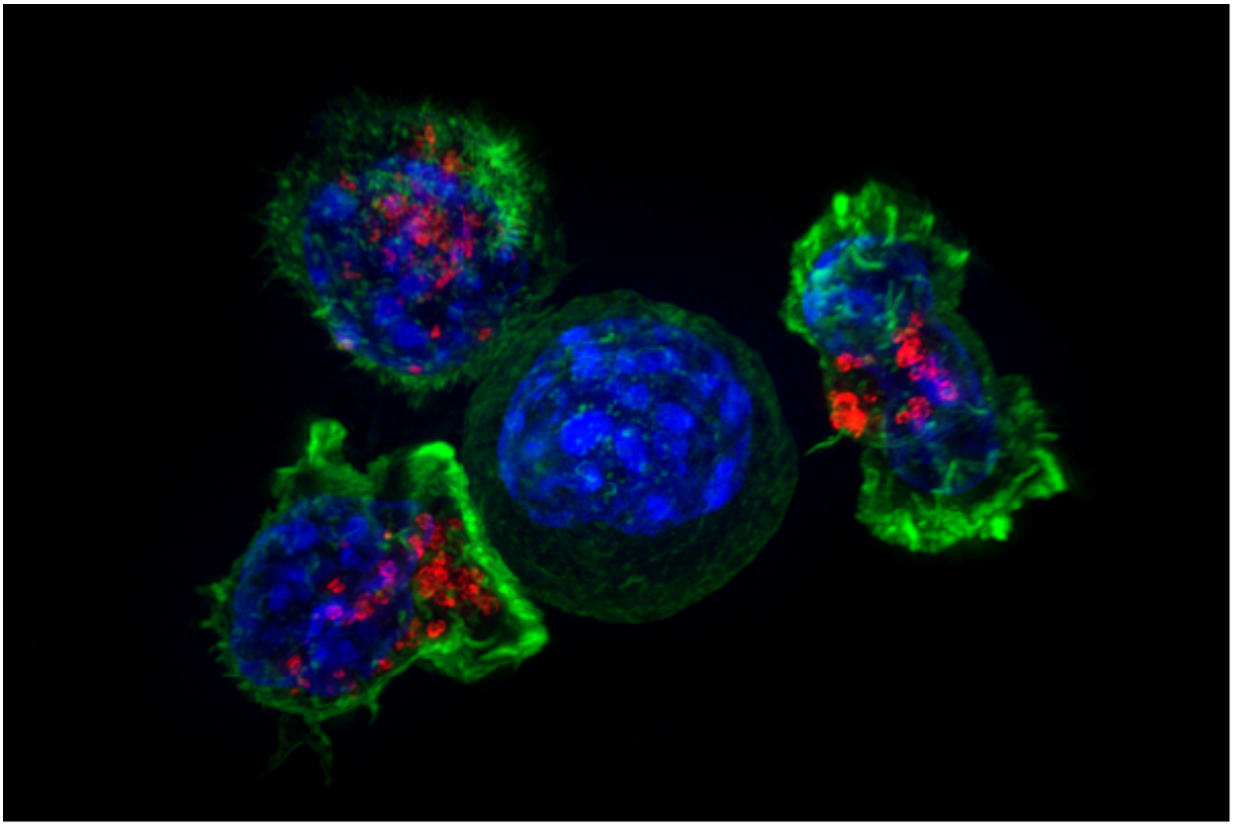

Killer T cells surround a cancer cell. Credit: NIH

Scientists at Sylvester Comprehensive Cancer Center at the University of Miami Miller School of Medicine, the Veterans Affairs Medical Center in Miami, and Shantou University Medical College in China, have shown

that the hormone receptor GHRH-R could be a potential biomarker for gastric cancer, enabling earlier diagnoses and better staging. In addition, the team found that the GHRH-R antagonist MIA-602 inhibited gastric cancer in both cell lines and human xenografts. The research was recently published in the journal *PNAS*.

"The GHRH receptor is both a biomarker that can confirm prognosis and a therapeutic target," said Andrew V. Schally, Ph.D., M.D.h.c., D.Sc.h.c., cancer researcher at Sylvester, professor of pathology at the Miller School, distinguished medical research investigator at the Veterans Affairs Medical Center in Miami, and a Nobel Prize in Physiology or Medicine recipient. "Gastric cancer is the second deadliest in the world - we need new approaches."

Though occurring less frequently than other cancers in the United States, gastric cancer kills around 700,000 people worldwide each year, second only to lung cancer. The problem is two-fold: Diagnoses are often delayed, allowing the cancer to spread, and there are few effective treatments. Chemotherapy is often ineffective and surgery works best when the disease is caught early.

The two-pronged study combined epidemiology and lab work. The researchers studied nearly 1,000 tumors from patients in China and other parts of the world. They linked the prevalence of GHRH receptors with larger, more-aggressive tumors and lower overall survival.

"We found that measuring GHRH receptor overexpression could be very useful, both for prognosis and identifying the stage of the cancer," said Schally.

The GHRH receptor also offers a potential therapeutic target. The receptor helps drive the aberrant growth associated with gastric and other cancers. Schally and his collaborators have been working for many

years to develop an inhibitor that will reduce or eliminate these signals, culminating in the peptide drug candidate MIA-602.

In the study, MIA-602 inhibited gastric cancer growth in cell lines and human tumor xenografts, decreasing both tumor size and weight. Further research showed that MIA-602 works by mitigating a network of proteins controlled by PAK1, ultimately inhibiting the well-known inflammatory proteins STAT and NF-κB. In addition, MIA-602 showed no evidence of side effects.

While developing an effective agent against gastric cancer would be an enormous advance, MIA-602 may also benefit other patients.

"This compound is an efficient inhibitor for a variety of cancers," noted Schally, "including lung, prostate, breast and brain."

Schally hopes the therapy will soon move forward into clinical trials.

More information: Jinfeng Gan et al. Growth hormone-releasing hormone receptor antagonists inhibit human gastric cancer through downregulation of PAK1–STAT3/NF-κB signaling, *Proceedings of the National Academy of Sciences* (2016). DOI: 10.1073/pnas.1618582114

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