Medical Xpress

Researchers identify new therapeutic target for cancer

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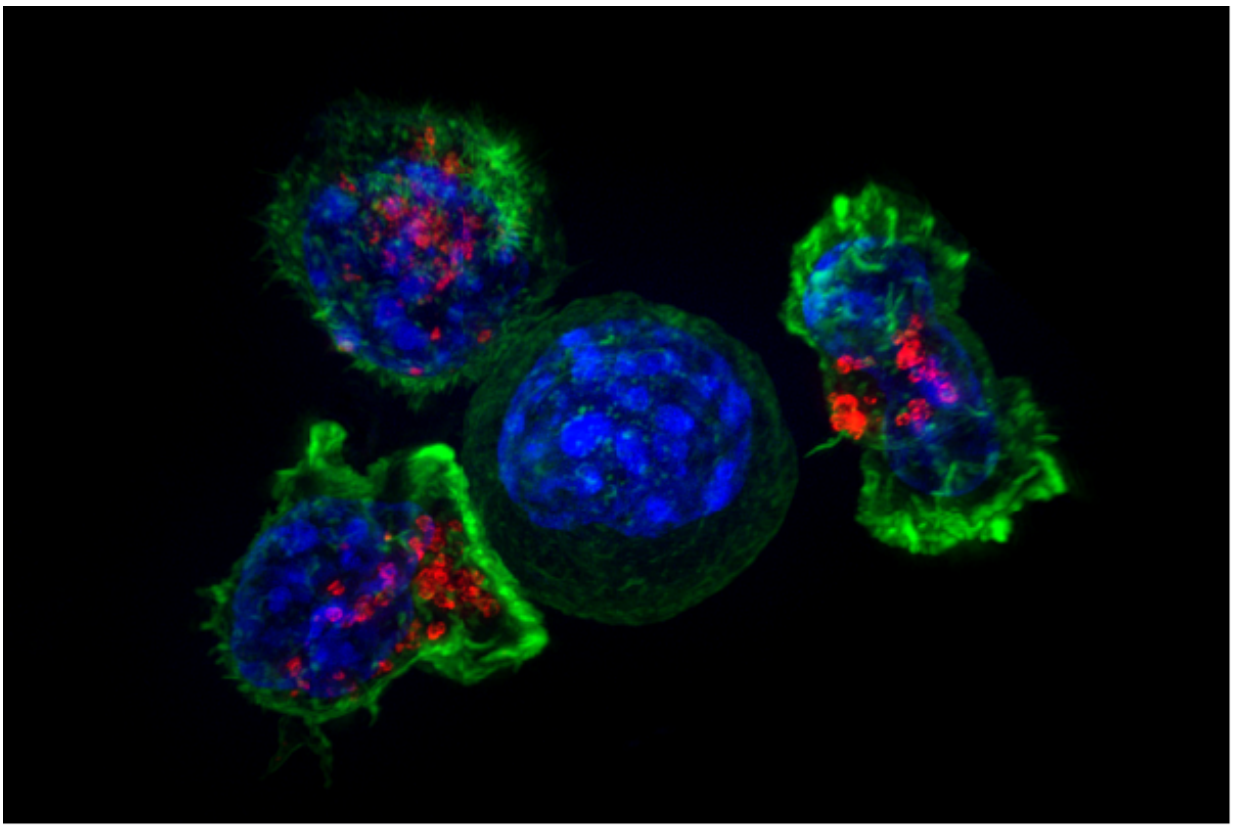

Killer T cells surround a cancer cell. Credit: NIH

New research from The Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai identifies a protein that may be an unexplored target to develop new cancer therapies. The protein, known as kinase

suppressor of Ras, or KSR, is a pseudoenzyme that plays a critical role in the transmission of signals in the cell determining whether cells grow, divide, or die. The findings, published in the September issue of the journal *Nature*, show that targeting KSR could have important therapeutic implications, potentially improving outcomes in many aggressing cancers such as lung and pancreatic cancer.

Ras is the most frequently mutated human cancer gene (oncogene), yet despite recent breakthroughs, therapeutic options to target Ras-dependent cancers remain limited. Previous studies had supported the possibility of targeting oncogenic forms of Ras via KSR, but no pharmacological approaches had been reported until now.

"New drug targets for Ras-dependent cancers have long been sought," said Arvin Dar, PhD, Assistant Professor of Oncological Sciences and Pharmacological Sciences at The Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai and lead researcher on the study. "We used data on known genetic variants in KSR that suppress mutant Ras signaling to guide the development of novel compounds. In this way our study took a very different approach as we have used chemistry to mimic genetic mechanisms that are able to block the development of Ras-dependent cancers."

The lead compound reported in the study, APS-2-79, was shown to modulate Ras signaling and increased the potency of several other cancer drugs within RAS-mutant cell lines. "KSR belongs to a large class of proteins that are not only implicated in the development of cancer, but also other diseases as well," Dr. Dar explained. "No one has really figured out how to exploit these important drug targets. Our study opens the possibility of modulating KSR as a new cancer therapy and also potentially an entirely new class of interventions."

More information: Neil S. Dhawan et al. Small molecule stabilization

of the KSR inactive state antagonizes oncogenic Ras signalling, *Nature* (2016). DOI: 10.1038/nature19327

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