

Researchers demonstrate RAS dimers are essential for cancer

January 11 2018, by Cathy Frisinger



RAS oncogenes work in pairs, known as "dimers." Credit: UT Southwestern



Mutated RAS genes are some of the most common genetic drivers of cancer, especially in aggressive cancers like pancreatic and lung cancer, but no medicines that target RAS are available despite decades of effort.

Researchers at UT Southwestern's Simmons Cancer Center have shown that RAS molecules act in pairs, known as dimers, to cause cancer, findings that could help guide them to a treatment.

"RAS mutations are one of the most common causes of cancer and there are no options for attacking them. The dimerization activity of RAS gives us a solid lead for moving forward," said Dr. Kenneth Westover, Assistant Professor of Radiation Oncology and Biochemistry with the Harold C. Simmons Comprehensive Cancer Center at UT Southwestern Medical Center, which is recognizing its 75th anniversary this year.

The question of RAS dimerization has been hotly debated, he said, but researchers previously haven't been able to prove what RAS dimers look like, limiting the ability to design experiments that assess their importance in normal physiology and cancer. The UT Southwestern team led by Dr. Westover used X-ray crystallography data to predict what a RAS dimer might look like, then tested the model in cells using a method called fluorescence resonance energy transfer (FRET) to show when RAS forms dimers and when it does not.

The study, published in the journal *Cell*, provides a foundation for further studies that delve into RAS biology and could potentially pave the way to develop new cancer drugs that target RAS dimerization.

"The primary function of RAS is to transmit signals that tell a cell to grow and divide, a pathway commonly hijacked in cancer. What became clear in our studies is that RAS needs to dimerize to efficiently pass signals in <u>cells</u>. Moreover, RAS dimerization appears to be a crucial event for mutated forms of RAS to cause cancer," said Dr. Westover,



part of the Simmons Lung Cancer Team.

Members of the Westover research lab teamed up with researchers from the Dana Farber Cancer Institute to show that RAS dimers are essential in a number of cancer cell systems and animal models of <u>cancer</u>.

Provided by UT Southwestern Medical Center

Citation: Researchers demonstrate RAS dimers are essential for cancer (2018, January 11) retrieved 4 May 2024 from https://medicalxpress.com/news/2018-01-ras-dimers-essential-cancer.html

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