

From Undruggable to Unstoppable: A New Cancer Cure Target Emerges

Researchers have produced the world's first drugs that target the KRAS gene, which causes about 25% of all cancerous tumors.

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Roughly a quarter of all cancerous tumors are caused by mutations in the KRAS gene, which fosters cell growth. For more than three decades, scientists believed these mutations were impervious to treatment. Today, National Institutes of Health (NIH)-funded discoveries by UC San Francisco Professor of Cellular Molecular Pharmacology [Kevan Shokat, PhD](#) have produced the world's first drugs that target KRAS.

What they found

The KRAS gene is present in nearly all of our cells and provides the blueprint for a protein called K-Ras that helps signal to cells to divide and grow. Some mutations in the KRAS gene cause this signal to get stuck in the “on” position and cells divide uncontrollably, while additional mutations occur to create cancerous tumors. Some of the deadliest cancers are the result, including lung, pancreatic, and colorectal.

In 2013, Shokat and his team became the first to discover a tiny “pocket” on the mutated K-Ras’ surface that would finally prove to be the protein’s Achilles’ heel. Shokat’s lab developed drugs that could snuggle into the pocket and bind to the protein, weakening and killing the cancerous cells.

Why it matters

Shokat and his team at UCSF proved the K-Ras protein was “druggable” and could be targeted with medicine. Their discovery and subsequent drug development led the Food and Drug Administration to recently approve the world's first two KRAS-targeting cancer treatments, sotorasib and adagrasib. Similar treatments are now in late-stage clinical trials, ushering in a new era in cancer treatment. The work has also inspired Shokat and others to explore new ways to target enzymes whose dysfunction can lead to Parkinson's and other diseases.

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