

Rictor protein offers scientists a new molecular target for cancer therapies

October 28 2010

The discovery that a protein called Rictor plays a key role in destroying a close cousin of the AKT oncogene could provide scientists with a new molecular target for treating certain cancers, including breast cancer. Described in the September 2010 issue of the journal *Molecular Cell*, the study was led by scientists at Beth Israel Deaconess Medical Center (BIDMC).

The oncogenic cousin, known as SGK1, resembles the widely known AKT [oncogene](#) in structure, according to the study's senior author Wenyi Wei, PhD, of the Department of Pathology at BIDMC and Assistant Professor of Pathology at Harvard Medical School (HMS).

"If we put the two proteins together, they are very similar," explains Wei. "But in one important way they are very different. AKT is stable, it lives for a long time. But SGK1 has a very short lifespan, and proteins with short lifespans tend to be powerful. Everybody's eye [has been] on AKT, but you have to wonder if this little cousin of AKT can do all the things AKT does." Wei and his team, therefore, set out to better understand how cells control SGK1.

Previous research showed that the [protein](#) Rictor forms a multi-protein complex called mTORC2 that activates both AKT and SGK1. Wei's team cultured cells lacking Rictor to observe the effect on SGK1. Surprisingly, they found that SGK1 levels increased.

"We said, that cannot be," notes Wei. "How could we get rid of the

protein kinase that activates SGK1 and still have the SGK1 levels be heightened?"

They found their answer when they observed that the cells weren't producing more SGK1; rather, SGK1 was living longer. This suggested to the scientists that Rictor might be playing a role in the destruction of SGK1. And, in subsequent experiments, Wei found that SGK1 is indeed held in check by a protein complex made up of Rictor, Cullin-1, Rbx1, and possibly other components. The protein complex forms a cellular garbage collector called an E3 ligase that degrades SGK1 so it cannot build up.

"The protein Rictor is modular and multifunctional," said Wei. "Its function depends on its partners." This observation suggests that some proteins may act like a central machine that can work with a variety of attachments, the same way a construction vehicle can change its function depending on whether it's wielding a bulldozer or a crane. "With further study," he adds, "we may find more proteins [like Rictor] that have multiple functions. When a cell makes a protein this big, isn't it a waste of energy to have only one function?"

Wei's team further observed that once SGK1 begins to accumulate, it turns right around and interrupts the Rictor-Cullin1 complex, stifling its garbage collection activities. "It looks like a positive feedback loop that serves to increase SGK1," says Wei.

"The novelty and significance of this work lies in the discovery of a role for Rictor in destroying SGK1, a key regulator of cell growth and cell death that is frequently associated with human cancers," said Marion Zatz, PhD, who manages cell cycle grants at the National Institutes of Health (NIH). "The finding suggests that faulty regulation of Rictor may play a part in some forms of cancer, and could offer us a new target for treating the disease."

While the exact role of SGK1 in tumor growth isn't yet clear, Wei speculates that SGK1 may play a role in [cancer](#) by hijacking a cell's metabolism, just as its close cousin AKT does. "This mechanism we discovered may be part of what drives overexpression of SGK1," he adds.

Provided by Beth Israel Deaconess Medical Center

Citation: Rictor protein offers scientists a new molecular target for cancer therapies (2010, October 28) retrieved 5 May 2024 from <https://phys.org/news/2010-10-rictor-protein-scientists-molecular-cancer.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
