Research pinpoints action of protein linked to key molecular switch

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Rho proteins have been described as "molecular switches" and play a role in cell migration, cell proliferation, cell death, gene expression, and multiple other common cellular functions.

Understanding the actions of Rho proteins is important to illuminating cellular mechanisms related to cancer, which is fundamentally a disease of cell misbehavior. When cells multiply too rapidly, multiply and migrate into inappropriate places in the body, do not die after their natural lifespan or create networks of blood vessels where they should not, cancer results.

A study led by Keith Burridge, PhD, professor of cell and developmental biology, published online April 18 in the journal Nature Cell Biology, demonstrates that a protein called Rho GDI1 is a key to maintaining a balance of Rho proteins that allow optimal cellular functioning.

Traditionally scientists have understood the regulation of these proteins to be a function of "on" or "off" switching and that Rho GDI was a passive player in this process. This study demonstrates that the mechanism is more subtle, like a dimmer switch on a lighting panel that allows for a spectrum of levels. Rho proteins are inherently unstable because they are partially made up of a lipid (or fat). RhoGDI contains a "pocket" that can bind this lipid, thus protecting it.

One of the most important findings from this study is that changes in the expression level of one Rho protein can affect the expression levels and

activities of other members of the family. In cells there is a limited amount of RhoGDI, and many different Rho proteins compete for binding to RhoGDI. The authors show that, when the protein levels of a particular Rho protein are artificially increased, the other Rho proteins are displaced from RhoGDI and degraded. Notably, previous studies have shown that many cancers exhibit altered levels of Rho proteins, raising the possibility that RhoGDI may be playing an important role in the biology of these cancer cells.

The authors hope that their work will help scientists better understand the subtle balancing mechanism that keeps cells functioning optimally, eventually leading to therapies that might target the balance of these proteins to prevent the cellular misbehavior that leads to cancers. The authors present preliminary results with two different cancer cell lines showing a correlation between the expression levels of RhoGDI and the levels and activities of Rho proteins.

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