UF scientists' offer perspective on need for new direction in cancer therapies

June 27, 2008

New cancer therapies must redirect their targets, University of Florida department of surgery researchers assert in the May issue of Science Signaling.

In "Focal Adhesion Kinase Versus p53: Apoptosis or Survival?" UF scientists William Cance, MD, a professor of surgical oncology, and Vita Golubovskaya, PhD, an assistant professor of surgery, say recent findings show the need for cancer drugs to now focus on destroying key protein interactions to effectively defeat aggressive cancer cells.

"Our perspective is the result of 16 years of research on focal adhesion kinase, which shows this protein plays a key role in making a number of types of cancers hard to destroy," said the paper's primary author, Cance, who also is president of the Society of Surgical Oncology. "New cancer drugs being developed should target protein interactions, instead of enzymes, to break down the protective barrier often found in more aggressive cancers."

In 2004, UF researchers found that a protein called p53 can regulate Focal Adhesion Kinase, or FAK, expression through binding to its regulatory DNA region. In 2005 in the Journal of Biological Chemistry, the UF group was the first to publish their findings on the direct binding of FAK and p53 proteins.

Earlier this year researchers from the Moores Cancer Center at the University of California, San Diego published findings in Molecular Cell confirming UF scientists' data on the binding of FAK and p53, and also showing that FAK degrades p53.

Both p53 and FAK are found in low levels in normal, healthy cells. The p53 protein ensures that cells strike a wholesome balance between growth and death. In its normal state, p53 suppresses the FAK protein and weakens the molecular force field around cancer cells. But mutations in the p53 protein can interfere with this regulatory function.

The Science Signaling journal, published by the world's largest scientific society, the American Association for the Advancement of Science, illustrated the breaking up of p53 on the cover of its May 20 issue.

Therapies have been focused on targeting enzymes, but these therapies have been largely ineffective in cancers such as melanoma, brain, breast, lung, colon and thyroid which seem to have a protective force field that deflects the drugs. It is the interaction between FAK and a mutated version of p53 that bolsters this shield.

Describing why the interaction strengthens the protective field, Golubovskaya said, "We propose it's a mechanism of signaling, where FAK sequesters, or removes, proteins such as p53 from its growth inhibitory function, resulting in increased survival signaling to the cells. The future drugs will be developed to disrupt this survival signaling."

Currently, UF researches have had success in finding drug therapies that are effective in blocking tumor growth in both cell and animal studies. The next step will be to test the drugs' efficacy in clinical trials.

UF researchers say it also must be determined whether there are any other tumor-suppressor proteins that can be sequestered and inhibited by FAK. They note in their perspective paper that it is possible there are other kinases that function like FAK and seize other proteins that regulate the balance between cell growth and death.

Science Signaling can be found at www.science.org.

###