
GEN news highlights : Aug 23 2010

Researchers Succeed in Purifying Protein Expressed by BRCA2

A protein called DSS1 stimulates the oncogene to assemble functional RAD51/DNA complexes, which aid DNA repair.

Scientists at the [University of California, Davis](#) have purified the protein produced by the breast cancer susceptibility gene BRCA2. The researchers were also able to leverage the protein to study the oncogene's role in DNA repair.

BRCA2 is known to be involved in repairing damaged DNA, but exactly how it works with other molecules has been unclear, points out Stephen Kowalczykowski, Ph.D., distinguished professor of microbiology in the UC Davis College of Biological Sciences and UC Davis Cancer Center member.

Dr. Kowalczykowski's group purified the protein from human cells and published its findings in *Nature*. Another group led by Wolf-Dietrich Heyer, Ph.D., used genetic engineering techniques to manufacture the human protein in yeast. Dr. Heyer is in the UC Davis department of microbiology and is leader of the Cancer Center's molecular oncology program. His team's work is published in *Nature Structural and Molecular Biology*.

Experiments with the BRCA2 protein confirm that it plays a role in repairing damaged DNA. It helps a protein called RAD51 to associate with a single strand of DNA and stimulate its activity. One BRCA2 molecule can bind up to six molecules of RAD51.

The RAD51/DNA complex then looks for the matching strand of DNA from the other chromosome to make an exact repair. If the BRCA2/RAD51 DNA repair system is not working, the cell resorts to other, more error-prone methods.

While the BRCA2 gene was discovered in 1994, purifying the protein made by the gene has proved difficult. "It's very large, it does not express well, and it degrades easily," Dr. Kowalczykowski explains. Ryan Jensen, Ph.D., a postdoctoral researcher in Dr. Kowalczykowski's lab, after testing many different cell lines, succeeded in introducing a BRCA2 gene into a human cell line and expressing it as a whole protein. Dr. Jensen and another postdoc, Aura Carreira, Ph.D., tested the purified protein for its function in repairing damaged DNA.

Jie Liu, Ph.D., a postdoctoral researcher in Dr. Heyer's lab, found that a much smaller protein called DSS1 stimulated BRCA2 to assemble functional RAD51/DNA complexes. Together with Dr. Liu, staff research associate Tammy Doty and UC Davis undergraduate student Bryan Gibson (now a doctoral student at Cornell University) purified the human BRCA2 and DSS1 proteins from yeast.