Fundamental breast and ovarian cancer protein isolated

17:49 23 August 2010 by **Jessica Hamzelou**
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Three separate groups have isolated the BRCA2 protein that is involved in inherited cases of breast and ovarian cancer. The researchers hope that better understanding of the protein and how it works will aid the development of new cancer therapies.

The BRCA2 protein is known to protect cells from damage that can occur during cell division. Mutations in the *BRCA2* gene result in DNA damage that can turn a cell cancerous.

The protein has been notoriously difficult to isolate until now. As one of the largest proteins in a cell, it can't be expressed in bacteria in order to be isolated like other proteins – it is three to four times too big, says Stephen West at Cancer Research UK's London Research Institute. "It's impossible, it just doesn't work," he says. As a result, researchers have so far been using fragments of the protein to understand its function.

Virus to kidney

But now three teams have managed to isolate BRCA2. One, led by Stephen Kowalczykowski at the University of California, Davis, have found a way to isolate the protein by inserting its gene into a human virus which they then used to infect human embryonic kidney cells, which subsequently expressed the desired protein.

The group then looked at how BRCA2 interacted with RAD-51, another protein known to be involved in repairing DNA damage. The group found that around six RAD-51 proteins bind to each BRCA2, and identified some of the conditions in which BRCA2 works.

A separate team at the university led by Wolf-Dietrich Heyer took a different approach but came to the same conclusions. The group expressed the *BRCA2* gene in yeast and then looked at how it interacted with RAD-51. They agree that around six RAD-51 molecules bind to each BRCA2 protein to enable it to repair chromosomal damage.

Meanwhile, West and his colleagues also studied this interaction, and found that BRCA2 takes RAD-51 to where it is needed at sites of DNA damage. This would explain why BRCA2 mutations restrict a cell's ability to repair damage.

The groups hope that by understanding how these proteins function, others can work out how to sensitise cancerous cells to certain drug treatments.

Journal references: Kowalczykowski, *Nature*, DOI: 10.1038/nature09399; Heyer, *Nature Structural and Molecular Biology*, DOI: 10.1038/nsmb.1904; West, *Nature Structural and Molecular Biology*, DOI: 10.1038/nsmb.1905

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