Understanding DNA Repair and Cancer

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(PhysOrg.com) -- A protein that plays a key role in copying DNA also plays a vital role in repairing breaks in it, UC Davis scientists have found. The work is helping researchers understand how cancer cells can resist radiation and chemotherapy, as well as how cells become cancerous in the first place.

The protein, known as proliferating cell nuclear antigen, forms a ring that fits around the DNA double helix. This cuff-like ring helps to keep in place DNA polymerase, the enzyme that makes a copy of the DNA strand when cells divide into two new cells.

The new study, published Nov. 25 in the journal *Molecular Cell*, shows that PCNA performs a similar function during DNA recombination -- when pairs of chromosomes line up and exchange strands of DNA. Recombination occurs when cells divide to form eggs and sperm, and also when cells try to repair breaks that cross both strands of DNA.

"This is a new trick from an old horse," said Wolf-Dietrich Heyer, professor of microbiology at UC Davis and leader of the molecular oncology program at the UC Davis Cancer Center.

The system developed by Heyer and colleagues for their experiments, using defined DNA substrates and purified proteins in a test tube, can be used to investigate the behavior of other molecules involved in copying and repairing DNA as well, he said.

Heyer's lab works primarily with yeast. While yeast don't get cancer,

Heyer notes that their DNA recombination and repair machinery is essentially the same as in humans. This problem was solved by evolution a long time ago, he said.

Radiation therapy and cancer drugs both cause breaks in cancer cells' DNA. Create enough breaks, and the malignant cell dies -- but at the same time, the cell's repair machinery is at work patching and sealing the gaps.

Understanding how DNA recombination and repair work could open up ways to make tumors more vulnerable to treatment, or to predict how well patients will fare with a specific treatment. The research could also reveal genes that predispose some people to cancer. For example, the "breast cancer gene," BRCA-2, is involved in DNA repair.

"We now know a lot about the molecules involved in DNA repair; we're beginning to think about how they can be used in the clinic," Heyer said.

Provided by UC Davis (news : web)