Renewed hope in a once-abandoned cancer drug class

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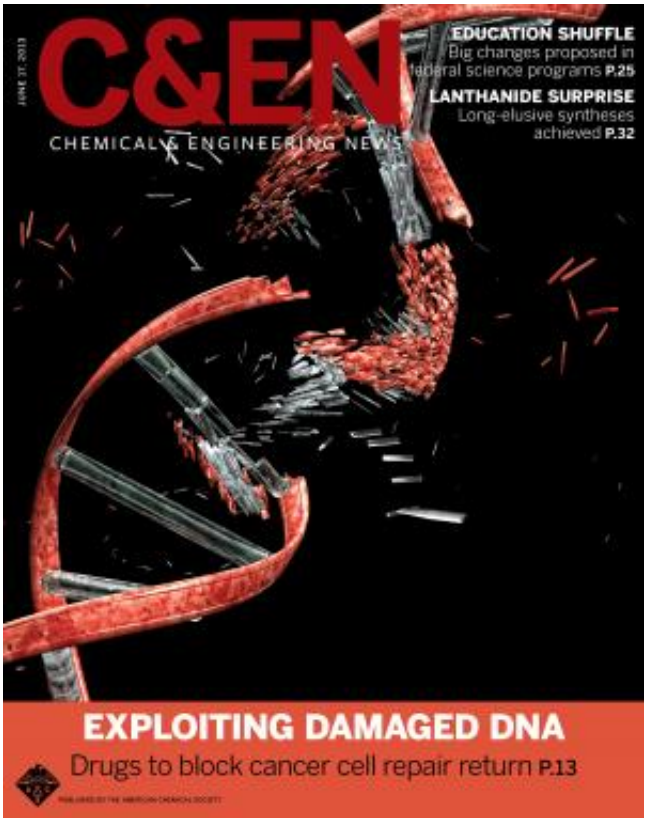

Could drugs that block the body's system for repairing damage to the genetic material DNA become a boon to health? As unlikely as it may seem, those compounds are sparking optimism as potential treatments for ovarian and breast cancers driven by a mutation in BRCA, a gene

that made headlines when actress Angelina Jolie revealed she carries the mutation. The compounds, termed PARP inhibitors, are the topic of the cover story in the current edition of *Chemical & Engineering News*. *C&EN* is the weekly newsmagazine of the American Chemical Society, the world's largest scientific society.

Lisa Jarvis, *C&EN* senior editor, explains that some members of the family of enzymes known as PARP, which stands for poly(ADP-ribose) polymerase, help fix damaged DNA. When DNA is broken, PARP moves in and signals other enzymes to repair the break so the cell can live. As early as the 1980s, scientists looked seriously at stopping PARP from working in cancer cells. If they could damage cancer cells' DNA with chemotherapy and then block PARP from fixing it, the cancer cells would die. By the 2000s, scientists identified BRCA-positive cancer patients, whose cells' ability to repair double-stranded DNA damage is already compromised, as good candidates for treatment with PARP inhibitors.

The story describes how PARP inhibitors held great promise. But a couple of years ago, momentum came to a screeching halt when one drug candidate, which had advanced to a Phase III clinical trial, failed to prolong patients' survival. More recently, researchers realized that the drug was not a PARP inhibitor. Soon after, an in-depth look at a previous study showed that a different drug candidate did in fact help some ovarian cancer patients. The findings breathed new life into PARP inhibitor research. Now, four drug candidates in this family are ready to enter Phase III clinical studies for breast and ovarian cancer.

More information: Pushing Cancer over the Edge, *Chemical & Engineering News*. cen.acs.org/articles/91/i24/Pu … ancer-Over-Edge.html