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Proteins in DNA damage response network targeted for new therapies, Moffitt researchers say

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Researchers at Moffitt Cancer Center and colleagues at the University of South Florida; Duke University; Johns Hopkins University; the Brazilian National Cancer Institute; and the Rio de Janeiro Federal Institute of Education, Science and Technology have discovered that an intricate system to repair DNA damage called the "DNA damage response" (DDR) contains previously unknown components, including proteins that could be targeted as sensitizers for chemotherapy. Some of these targets may already have drugs available that have unrecognized uses in cancer therapy, said the researchers.

The study appears in the Sept. 18 issue of *Science Signaling*.

"A domain called BRCT is frequently present in proteins involved in the DDR network," said study lead author Alvaro N.A. Monteiro, Ph.D., senior member of Moffitt's Cancer Epidemiology Program. "We undertook a systematic analysis of the BRCT domain, a protein module that plays a critical role in the DDR, and found a large network of interacting proteins centered on BRCT-containing proteins. In doing so, we discovered new potential players in the DDR. These new players may constitute potential biomarkers for drug response or targets for treatment."

According to the authors, their data could be used to build a more comprehensive map of the components and interactions involved in the DDR, a system through which proteins detect DNA damage, promote repair and coordinate the cell cycle.

Because defects in the DDR can lead to cancer, the properly functioning network is considered to be a barrier against tumor growth. Chemotherapy regimens exploit weaknesses in the system to kill cancer cells. The new discoveries augment knowledge about the DDR by adding information on the function of specific proteins involved with BRCT-containing proteins.

"Our expectation is that the establishment of the BRCT-network will help identify potential sensitizers of therapy and accelerate the development of new therapeutic strategies," Monteiro said.

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About Moffitt Cancer Center

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Located in Tampa, Moffitt is one of only 41 National Cancer Institute-designated Comprehensive Cancer Centers, a distinction that recognizes Moffitt's excellence in research, its contributions to clinical trials, prevention and cancer control. Since 1999, Moffitt has been listed in U.S. News & World Report as one of "America's Best Hospitals" for cancer. With more than 4,200 employees, Moffitt has an economic impact on the state of nearly \$2 billion. For more information, visit MOFFITT.org, and follow the Moffitt momentum on Facebook, twitter and YouTube.

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