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New molecules discovered that block cancer cells from modifying cell DNA

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Researchers have discovered new small molecules that may prevent prostate cancer cells from turning off normal genes in a process that transforms normal cells into cancer cells. This significant discovery in the field of epigenetics has immediate implications in the development of new diagnostic tests and cancer medications. The findings were presented today at the Prostate Cancer Foundation's annual Scientific Retreat.

pigenetics refers to changes to genes other than changes to the DNA sequence itself, such as the addition of molecules to the DNA strand. While the development of cancer can arise from defective or mutated genes, it can also arise from these changes that can actually prevent a cell from acting as it should. Cancer cells exploit this process, putting some genes in "cold storage" or "turned off" by modifying the cell DNA in a process known as methylation.

Lead researcher William Nelson, M.D., Ph.D., Professor of Oncology and Urology at the Johns Hopkins Kimmel Cancer Center, explained the findings. "One of the proteins in the cell that triggers this process is called a methyl-CpG binding protein, or MBD. We have discovered an antagonist of MBD2 that keeps this protein from binding to methylated genes. If the protein can't bind to the gene, then it can't keep the gene 'turned off' and the gene is turned back on – able to act in the way it is supposed to."

Nelson noted that the discovery is particularly exciting because of

previous research that shows the importance of being able to alter the methylation process in DNA. When mice were developed without the gene that permits this process, they don't develop cancer. When the gene is removed from cancer cells, they "turn on" genes again in appropriate ways. "The small molecules that we've discovered mimic this process, so they may be very exciting lead candidates for the next generation of drugs that may help restore gene function in prostate cancer," said Nelson.

"This entire field of exploration has been tantalizing for a decade," said Nelson, "but has only begun to deliver fruit in just the past couple of years. This mechanism of action permits us to look for much more targeted therapies for prostate cancer, and for other cancers as well, such as breast cancer."

The promise of this field is evident in the current pipeline of diagnostic and therapeutic products in development. There are diagnostic tests being tested that focus on detecting the methylated DNA, which would permit prostate cancer diagnosis at an earlier stage and in a more precise manner. There is also a first generation of FDA-approved medications that work to reverse the methylation process in cancer cells. They include azacitine (Vidaza) and decitabine (Dacogen), both for the treatment of myelodysplastic syndrome, diseases in which the production of blood cells by the bone marrow is disrupted. Vorinostat (Zolinza) also works to turn back on silenced genes, and is approved for use in cutaneous T cell lymphomas.

Dr. Nelson noted that the Prostate Cancer Foundation funding was essential for the research that resulted in this discovery. "PCF supported our research at a time when it was a very new idea. Their investment permitted us to make critical discoveries that have not only put us along the pathway this field -- hopefully one day resulting in new drugs -- but that also allowed us to secure competitive research funding from the

National Cancer Institute," explained Nelson.

Source: GYMR