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Heat helps cancer drugs battle cancer

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(PhysOrg.com) -- Localized hyperthermia has been used occasionally with cancer drugs for some time, but until now, the reason it helps has been a mystery. In a report in the *Proceedings of the National Academy of Sciences*, scientists have discovered that the addition of heat inhibits homologous recombination so the cancer cells are unable to repair DNA damage caused by the cancer treatments.

Originally used in the 70s and 80s, hyperthermia showed promise in inhibiting the tumor cells repair mechanism, though clinical trials at the time were unable to establish a definitive connection and interest in the combination diminished. However, new technology and clinical trials have brought it back into the spotlight, and this new study may just give it the fuel it needs.

Przemek Krawczyk from the University of Amsterdam and his team studied tumor cells both in a Petri dish and those injected into rats. They discovered that when the cells were heated to 106-109 degrees Fahrenheit, the protein BRCA2 (essential for repair pathway) was degraded and thus blocked homologous recombination.

This new finding opens up the possibility for a new type of drug, called PARP, to have a wider range of possible cancer treating options. PARP is currently under clinical trials to treat a certain type of hereditary breast cancer. In this particular cancer, BRCA1 is mutated and already unable to repair DNA damage. PARP is specifically designed to attack these already mutated tumor cells.

If hyperthermia is able to cause the same type of defect in cancer cells, the door could be opened for PARP to be used to treat many other cancers. PARP has shown to be well tolerated by many patients with very few side effects compared to current chemotherapy treatments.

More information: Mild hyperthermia inhibits homologous recombination, induces BRCA2 degradation, and sensitizes cancer cells to poly (ADP-ribose) polymerase-1 inhibition, *PNAS*, Published online before print May 9, 2011, doi: 10.1073/pnas.1101053108

Abstract

Defective homologous recombination (HR) DNA repair imposed by BRCA1 or BRCA2 deficiency sensitizes cells to poly (ADP-ribose) polymerase (PARP)-1 inhibition and is currently exploited in clinical treatment of HR-deficient tumors. Here we show that mild hyperthermia (41–42.5 °C) induces degradation of BRCA2 and inhibits HR. We demonstrate that hyperthermia can be used to sensitize innately HR-proficient tumor cells to PARP-1 inhibitors and that this effect can be enhanced by heat shock protein inhibition. Our results, obtained from cell lines and in vivo tumor models, enable the design of unique therapeutic strategies involving localized on-demand induction of HR deficiency, an approach that we term induced synthetic lethality.