Survival of the healthiest: Selective eradication of malignant cells

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The ultimate goal in cancer research, a treatment that kills cancer cells whilst leaving healthy cells untouched, is brought nearer by the success of a new therapeutic approach. The potential therapy, published in BioMed Central's open access journal *Breast Cancer Research*, targets proliferation of cancer, but not normal, cells.

An international research team led by Professor Cohen-Armon of Tel-Aviv University found that potent phenanthridine derived polyADP-ribose polymerase (PARP) inhibitors that were originally designed to protect cells from cell-death under stress conditions (e.g. stroke or inflammation), efficiently eradicate MCF-7 and MDA231 breast cancer cells without impairing normal proliferating cells, such as human epithelial cells (MCF-10A), nor normal non-proliferating cells, such as neurons and cardiomyocytes.

Human cancers depending on a constitutive activity of externally regulated kinase (ERK) were examined. The rationale for testing PARP inhibitors in these cancers was the recently disclosed up-regulation of ERK signals in the nucleus by activated PARP-1. However, other mechanisms are apparently involved. The phenanthridine PJ-34 caused a permanent G2/M cell-cycle arrest and cell death within 48-72 hours in breast cancer MCF-7 and MDA231 cells. In contrast, normal proliferating cells overcame the imposed G2/M cell-cycle arrest within 12 hours, survived and continued to proliferate.

In vivo, PJ-34 prevented the development of MCF-7 and MDA231

xenotransplants in nude mice without affecting their growth, development or behaviour.

Other PARP inhibitors were recently proved efficient only for treating relatively rare hereditary human cancers developed in individuals with an impaired DNA repair (BRCA gene mutation). However, in the current research, breast cancer cells lacking the BRCA mutation were efficiently eradicated.

According to Professor Cohen-Armon, "This research provides a new therapeutic approach for a selective eradication of abundant human cancers."

More information: A selective eradication of human non-hereditary breast cancer cells by phenanthridine derived polyADP-ribose polymerase inhibitors, Dana Inbar-Rozensal, Asher Castiel, Leonid Visochek, David Castel, Francoise Dantzer, Shai Izraeli and Malka Cohen-Armon, Breast Cancer *Research* (in press), breast-cancer-research.com/

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