

Anti-cancer agents grant: A Progress report from David Scheinberg, MD, PH.D

inhibition of A MITOCHONDRIAL ENZYME (peptide deformylase) DISRUPTS MITOCHONDRIAL FUNCTION AND KILLS CANCER CELLS SELECTIVELY

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Mitochondria are organelles in all human cells that are responsible for production of energy from glucose and oxygen. The mitochondria are also master controllers of cell death. The human mitochondrial protein, peptide deformylase, (PDF) is an enzyme that removes the ends of key proteins that are involved in the energy production process. We have shown that inhibition of PDF decreases human cancer cell growth in a

variety of human cancers in model systems. Similarly, pharmacologic inhibition of PDF with the antibiotic inhibitor actinonin results in mitochondrial dysfunction and promotes cell death or growth arrest in a wide variety of cancer cell lines.

The mechanism for how blocking PDF kills cancer cells more than normal cells is not known, but the understanding of this process would allow development of better anti-cancer drugs. We show that inhibition of PDF function in mitochondria of human cancer cell lines reduces accumulation of the key proteins that are involved in making energy for the cell; energy production by the mitochondria drops. We are in the process of trying to develop more potent inhibitors that might be used as drugs for human cancers.

