The cancer 'TRAP'

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Current research suggests that TNF-receptor associated protein-1 (TRAP-1) may prevent cancer cell death. The related report by Leav et al, "Cytoprotective Mitochondrial Chaperone TRAP-1 as a Novel Molecular Target in Localized and Metastatic Prostate Cancer," appears in the January 2010 issue of the *American Journal of Pathology*.

Prostate cancer is the most common type of cancer and is the second leading cause of cancer deaths among men in the United States, following lung cancer. Prostate cancer most commonly develops in men over the age of 50 and is slow-growing; however, it may metastasize to other organs, particular to the bones and lymph nodes. Metastatic phase prostate cancer claims over 30,000 deaths per year in the United States alone.

Prostate cancer cells are often resistant to cell death. Researchers led by Dr. Dario C. Altieri of the University of Massachusetts Medical School, therefore, explored the role of TRAP-1, a protein thought to regulate cell death, in prostate cancer survival. TRAP-1 was highly expressed in both high-grade human prostate cancer lesions and mouse models of prostate cancer, but not in benign or normal prostate tissue. In addition, TRAP-1 overexpression in non-cancer prostate cells inhibited cell death, whereas TRAP-1-deficient prostate cancer cells had enhanced levels of cell death. Moreover, treatment with Gamitrinib, which inhibits TRAP-1, resulted in prostate cancer cell death, but not death of non-cancerous prostate cells. Therefore, targeting TRAP-1 via Gamitrinib treatment may be a viable therapeutic strategy for patients with advanced prostate cancer.

Leav et al suggest that "TRAP-1 [is] a novel marker of localized and metastatic prostate cancer, but not normal glands, required for prostate cancer cell viability, in vivo. Taken together with the preliminary safety of Gamitrinibs in preclinical studies, these data suggest that targeting mitochondrial TRAP-1 may provide a novel therapeutic approach for patients with advanced and metastatic prostate cancer" A similar approach may be also suitable for other types of cancer, as TRAP-1 is broadly expressed in disparate human malignancies. In future studies, Dr. Altieri and colleagues plan to "further dissect the biology of TRAP-1 cytoprotection in cancer cells, and test whether disabling its function may overcome drug resistance, the most common reason of treatment failure and dismal outcome in patients with advanced prostate cancer."

More information: Leav I, Plescia J, Goel HL, Li J, Jiang Z, Cohen RJ, Languino LR, Altieri DC: Cytoprotective Mitochondrial Chaperone TRAP-1 as a Novel Molecular Target in Localized and Metastatic Prostate Cancer. Am J Pathol 175: 393-401

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