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Effect on Glycolysis and Glucose Transporters of Transplanted Isolated Normal Mitochondria from MCF-12A Cells into Breast Cancer Cells

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Otto Warburg postulated in the 1920s that tumor cells had altered metabolism with a defect in cellular respiration and a shift toward glycolysis (1). We reported on the Ultrastructural Observations of Mitochondria in Human Breast Carcinoma Cells describing three distinct groups based on grade of anaplasia (2). Then we demonstrated that JC-1 stained mitochondria of immortalized, untransformed mammary epithelial MCF-12A cells would enter into cultured cancer cells MCF-7, MDA-MB-231, and NCI/ADR-Res (3, 4, Fig. 1). Normal mitochondria of the MCF-12A cells suppressed proliferation of the MCF-7 and NCI/ADR-Res cells in a dose dependent pattern (Fig. 2); and also increased the drug sensitivity of the MCF-7 cells to doxorubicin, Abraxane, and carboplatin (Fig. 3). We postulated that these results were probably due to inhibition of glycolysis in the cancer cells; and thus prompted this study. Isolated normal MCF-12A mitochondria were cultured with the cancer cell lines MCF-7, T47D and MDA-MB-231, and the concentration of lactate in the media was measured by the Cayman Glycolysis Cell-Based Assay Kit. The uptake of normal mitochondria cancer cells caused a decrease of lactate production by MDA-MB-231 and T47D cancer cells and an inhibition of proliferation (Fig. 4). We also have preliminary RT-PCR evidence that uptake of normal mitochondria by cancer cells downgrades the plasma membrane glucose transporters (Fig. 5). Therefore, isolated normal mitochondria might be powerful biological nanoparticles that could significantly impact cancer therapy.

References:

[1] O. Warburg, K. Posener, and E. Negelein, Ueber den Stoffwechsel der Tumoren; *Biochemische Zeitschrift* 152 (1924) 319-344.

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[3] R. Elliott, X.P. Jiang, and J.F. Head, Introduction Of Normal Mammary Epithelial Mitochondria Into The MCF-7 Human Breast Cancer Cell Line Inhibits Proliferation And Increases Drug Sensitivity, Microsc. Microanal. 18 S2 (2012) 182-183.

[4] R. L. Elliott, X. P. Jiang, and J. F. Head, Mitochondria organelle transplantation: introduction of normal epithelial mitochondria into human cancer cells inhibits proliferation and increases drug sensitivity, Breast Cancer Res Treat. 136 (2012) 347-354.

Fig. 1

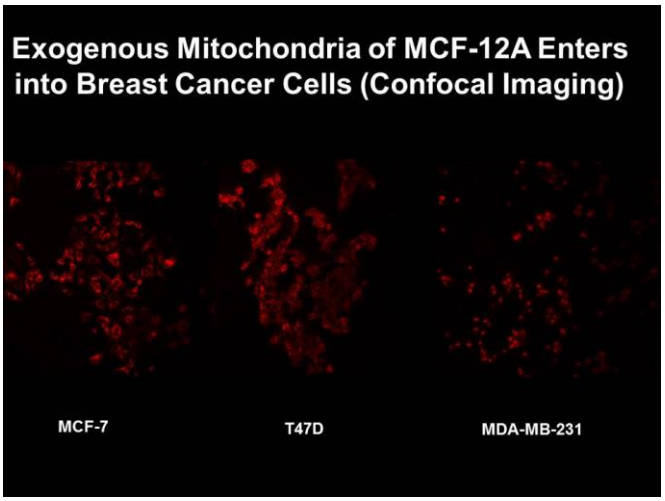


Fig. 2

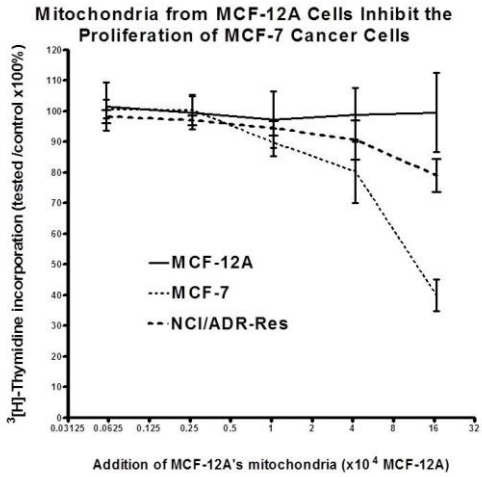


Fig. 3

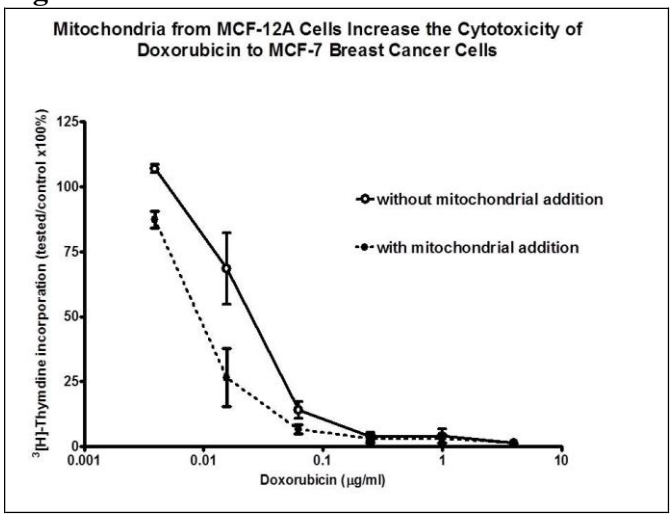


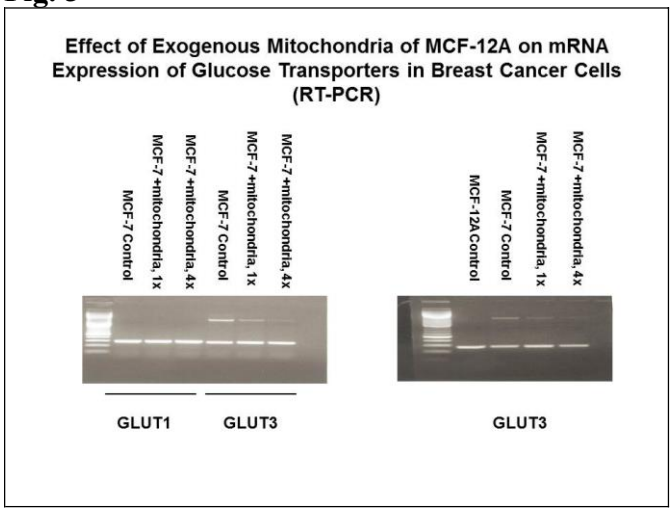
Fig. 4

Concentration of Lactate in Culture Media

Cell Line	Lactate (μm) mean ± SD (n)	P value
MCF-7 medium control	4894 ± 1105 (3)	
MCF-7 + mitochondria of MCF-12A	3635 ± 2358 (3)	0.22[1]
T47D medium control	5836 ± 712 (2)	
T47D + mitochondria of MCF-12A	2437 ± 512 (2)	<0.05, Significant
MDA-MB-231 medium control	2722 ± 767 (3)	
MDA-MB + mitochondria of MCF-12A	1838 ± 189 (3)	0.17

[1]Compare to control, paired t-test, p<0.05 is statistical significant

Fig. 5



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