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Targeting the reprogrammed energy generation system of cancer cells


The aspiration to achieve efficacious cancer targeted therapy involves intense global R&D efforts. Blockage of fundamental processes like the unique reprogrammed energy generation system of malignant cells, combined with a nano-technology approach, should offer new tools for efficient interference with cancer progression. While deciphering the energy generation systems of cancer cells, we found that two related enzymes (kinases), termed Fer and FerT, which normally reside in the cell energy power-station-mitochondria of sperm cells, are harnessed to the reprogrammed mitochondria of cancer cells. Both enzymes potentiate the generation of energy by mitochondria in cancer cells subjected to stress conditions like nutrient and oxygen deprivation. This enabled the survival of cancer cells under harsh conditions which are prevalent in solid tumors. To translate these findings into a novel anti-cancer therapy we have combined, synthetic-chemistry, robotic, and high throughput screening approaches, for

the development of a synthetic low molecular weight compounds which binds and inhibit the kinase activity of both Fer and FerT. Such a compound termed E260 was then formulated and incorporated into nano-micelles to selectively target Fer and FerT in the mitochondria of malignant cells. Notably, the formulated E260 compound selectively perturbs mitochondrial functioning in malignant cells thereby imposing energy crisis and consequent necrotic death in cancer but not in normal cells. The anti-cancer potency of the E260 formulation is also manifested using human tumors derived-xenografts models in mice, thus portraying it as a new potential anti-cancer drug.

Biography

Uri Nir leads the cancer and inflammatory diseases research lab in the Faculty of Life- Sciences at Bar-Ilan University, Israel. He completed his PhD degree from Weizmann Institute of Sciences in Israel. He then went for a Post-doctoral training at Hormone-Research Institute, University of California San-Francisco, USA. Since 1988, he is a faculty member at Bar-Ilan University.

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