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Targeting the reprogrammed energy generation system of metastatic cancer cells-A therapeutic approach

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The aspiration to achieve efficacious cancer targeted therapy involves intense global R&D efforts. Blockage of fundamental processes like the unique reprogramed 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 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 enables the survival of cancer cells under harsh conditions which are prevalent in solid tumors and during metastatic dessimination. 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 compound 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 and very efficiently perturbs mitochondrial functioning in non-metastatic and metastatic malignant cells, thereby imposing evoking energy crisis and consequent necrotic death in cancer, but not in normal cells. The anti- cancer therapeutic potency of the E260 formulation is also manifested in-vivo, against metastatic human tumors derived-xenografts, elicited in mice, thus portraying it as a new potential anti-cancer drug.

Accordingly, E260 is now being progressed toward FDA approval for human clinical trials.

Biography

Uri Nir leads the "Cancer metabolism" research lab in the Faculty of Life-Sciences at Bar-Ilan University, Israel. Between the years 2010-2014 he served as the dean of the Faculty. Nir gained his PhD degree from the Weizmann Institute of Sciences in Israel. He then went for a post-doctoral training in the "Hormone-Research Institute" at the University of California San-Francisco, CA., USA. Since 1988 Nir is a faculty member in the Mina and Everard Faculty of Life-Sciences at Bar-Ilan University. The main research interest of the Nir's group is: Identification of key regulators of the reprogrammed energy-generation system of cancer cells and the development of new anti-cancer compounds.

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