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Targeting energy metabolism in cancer cells

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Abstract

Kinetic modeling and elasticity analysis show that tumor glycolysis is controlled by several steps (hexokinase, glucose transporter, glycogen degradation) under a variety of experimental conditions (normoxia/ hypoxia; normoglycemia/ hypoglycemia), and that partial inhibition of the controlling steps may have significant impact on the glycolytic flux under hypoxia/hypoglycemia, where glycolysis is the main ATP producer. Vast recent data also show that the ATP supply in many cancer cells is mainly provided by mitochondria, with glycolysis playing a minor role. Thus, mitochondria and the mitochondrial functions have emerged as intriguing novel targets for anti-cancer therapy and hence it is proposed that energy metabolism may be an alternative therapeutic target for both glycolytic and oxidative cell populations within solid tumors. This proposal requires the development of anti-cancer drugs that may selectively target cancer cells and mitochondria. Here, the challenge is to move away from the design of drugs that specifically inhibit a single gene/protein target towards drugs that may have multiple target sites in the most exacerbated, unique and controlling pathways in cancer cells. Several mitochondrially targeted drugs induce apoptosis, OxPhos inhibition, ROS generation and ATP depletion in human cancer cells more potently than in normal cells, by acting as uncouplers and/or respiratory inhibitors. These encouraging results indicate that tumor cells and mitochondria can be specifically targeted by these drugs, highlighting their potential clinical relevance.

Biography

Rafael Moreno-Sánchez received his Ph. D. from the National Autonomous University of México (UNAM) and made postdoctoral stays at NIH/NIA/GRC in Baltimore, MD and Hahnemann University in Philadelphia, PA. He is currently the biochemistry department head at the Instituto Nacional de Cardiologia de México. He has published over 140 papers in reputed journals, has a Hirsch index of 30 and serves as an editorial board member of Plos One. Thirteen researchers have been trained under his advice and supervision to get their Ph. D. from Mexican universities, some of which are now working in USA institutions as independent scientists

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