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Energy restriction synergizes doxorubicin activity via targeting breast cancer stem cells

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Unlike normal cells, cancer cells often shift their metabolism from oxidative phosphorylation to aerobic glycolysis as an adaptive response to intermittent hypoxia and the robust demand for energy production. However, the high need of glucose and the lack of flexibility in modifying energy resources make cancer cells extremely vulnerable to glucose starvation and energy restriction. Breast cancer stem cells (BCSCs) are known to mediate metastasis, resistance to radiation and chemotherapy, and contribute to relapse. The aim of the current work was to study to effect of energy-restriction mimetic agents (ERMAs) such as resveratrol and 2-deoxyglucose on the anticancer activity of doxorubicin in breast cancer cells. Methods: The antitumor effects of ERMAs and/or doxorubicin and the therapeutic combination were assessed by MTT assay, caspase activation, PARP cleavage, colony formation assay, immunofluorescence, and Western blot analysis. Percentage of ALDH1⁺/CD44⁺/CD24^{-/low} in MDA-MB-231 cells was assessed by flow cytometry. Treatment with doxorubicin, while inhibited the cell viability, increased breast cancer ALDH1⁺/CD44⁺/CD24^{-/low} cells. This stem cell-enriched population was declined and the anticancer effect of doxorubicin was significantly synergized by its combination with resveratrol or 2-deoxyglucose, suggesting that ERMAs preferentially inhibit stem/progenitors in breast cancer cells. Together, our results suggest that the targeting BCSCs population by ERMAs could be a rational strategy to minimize the resistance to doxorubicin.

Biography

Hany A. Omar holds a Bachelor's degree in Pharmaceutical Sciences (1998) and a Master's degree in Pharmacology and Toxicology (2005) from Faculty of Pharmacy, Cairo University, Egypt. He completed his Ph.D. degrees in molecular biology at The Ohio State University, Columbus, Ohio (2010). After post-doctoral studies at The Ohio State University (2011), he led cancer cell molecular biology research in different places. He is now an assistant professor of Molecular Pharmacology and Therapeutics, University of Sharjah, United Arab Emirates & Beni-Suef University, Beni-Suef, Egypt. Dr. Omar has published close to 35 scientific reports, including many in the most respected professional journals on molecular oncology and anti-cancer drugs.

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