Ettore Mutabito, J Cancer Sci Ther 2013, 5:10
http://dx.doi.org/10.4172/1948-5956.S1.029

OMICS Group Conferences
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3rd World Congress on
Cancer Science & Therapy

October 21-23, 2013 DoubleTree by Hilton Hotel San Francisco Airport, CA, USA

Targeting breast cancer: A metabolic control analysis approach

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In many diseases, such as cancer, cells show a specific metabolic shift from their normal physiological state. The differences between the normal and the altered metabolic phenotypes may be exploited to identify points of fragility characterising the disease, and hence to specifically target altered cells. The application of Metabolic Control Analysis (MCA) has been proposed as a possible way to identify such points of fragility at the metabolic level. Here we use an MCA approach to assess the suitability of different enzymes as molecular targets for drugs designed to attack breast cancer. We base our study on experimental data characterising the metabolic features of breast cancer, and make use, where possible, of actual kinetic equations in the attempt to provide the most realistic description of the system under study. Unknown metabolic and kinetic quantities are sampled randomly, providing us with a probabilistic assessment of the control profile of the system in the two metabolic phenotypes. The suitability of the different enzymes as molecular targets is subsequently assessed with respect to criteria of both high efficacy and low toxicity. The results obtained are in accordance with previous experimental work, highlighting the central role of certain enzymes such as GLT and G6PDH in controlling glycolysis and the pentose phosphate pathway respectively in some kinds of cancer.