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Gene expression changes in metabolic and hypoxic related genes in response to long term hypoxia in MCF7 breast cancer cell line

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Hypoxia is a feature of most tumors and consider as a negative prognostic and predictive factor because of its role in the chemoresistance, radioresistance, angiogenesis, invasiveness, metastasis and resistance to cell death. Around 40% of all breast cancer and half of the locally advanced breast cancers include regions affected by hypoxia. This study was designed to simulate real hypoxic conditions as much as possible with the aim of characterizing the gene expression changes in metabolic and hypoxic related genes in response to long term hypoxia in MCF7 breast cancer cell line. The MCF7 breast cancer cells were exposed to hypoxia episodes (1% oxygen) in two different patterns. The first was to expose the cells to 8 hours of hypoxia every other day with a total of 60 eposides and the second was to expose the cells to 72 hours of hypoxia every week for a total of 20 weeks. RNA was extracted at different intervals in the two patterns and gene expression level was determined for the targeted genes. Regarding the hypoxic pathway genes, marked changes were identified after both patterns of hypoxia. Half of the genes (12 genes) that shown remarkable changes were common to both conditions. Those common genes include the insulin-like growth factor binding protein 3, tumor protein p53 and endothelin-1. However, there was a very interesting observation regarding the gene expression of a gene called the hepatocyte nuclear factor 4, alpha (*HNF4A*) gene that was the most up-regulated genes in both cases scoring 32 folds after 60 hypoxic shots and 14 folds after 10 shots of 72 hypoxic shots. Such changes in HNF4 were confirmed using western blotting. Regarding the metabolic pathway changes, again some changes were observed giving a clear indication for switch from using glucose pathway as a scours of power toward using a different pathway called pentose phosphate pathway. In conclusion, a collective gene expression data on different long term hypoxic pattern firstly proposed *HNF4A* as a potential biomarker in tumor hypoxia and a major player in MCF7 breast cancer cell response to chronic hypoxia and secondly, indicate a switch in the normal metabolic pathway toward a new adapted pentose phosphate pathway.

Biography

Malek Zihlif has completed his PhD from University of New South Wales, Post-doctoral studies from Stanford University School of Medicine. He is the Head of Pharmacology department at the School of Medicine, University of Jordan. He has published more than 25 papers in reputed journals. His research focuses on "How cells adapt to different condition and how cells overcome harsh condition such as hypoxia and drug assault".

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