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Tumor cells adapted to high nitric oxide ensure survival by up or down regulating specific genes within the apoptosis pathway

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Hypothesis: High nitric oxide (HNO) adapted squamous, lung, breast tumor cells show up or down regulation in multiple steps of apoptosis pathway and prevent apoptosis from occurring.

Objectives: Apoptosis is an ATP dependent programmed cell death through which our bodies remove damaged cells. One of the pathways of apoptosis involves apoptosis-inducing factor (AIF), a protein that triggers chromatin condensation and DNA fragmentation in a cell in order to induce programmed cell death. It has been observed that nitric oxide (NO) plays a significant role in a patient's clinical outcome where patients with lower NO levels have a better clinical outcome compared with higher levels. This may be explained by the role of the AIF gene in suspension of the apoptosis pathway. The IκBα gene which is found in the apoptosis pathway regulates the NF-κB gene and this allows for generation of anti-oxidants. NF-κB gene activation can also play a role in furthering the expression of high nitric oxide cells. To better understand the effects of NO, our laboratory studied a cell line system of both HNO-adapted and parent cell lines via a gene chip analysis.

Methods: In human breast adenocarcinoma, four pairs of parent/HNO cell lines (MCF7, Hs578t, T47D, BT20) and five parent/HNO pairs (SCC016, SCC040, SCC056, SCC114, and SCC116) of squamous cell carcinoma cell lines, and one pair (A549) of human lung adenocarcinoma cell lines were tested in a gene chip experiment. This experiment involved dying cell lines green, the HNO cell lines, or red, the parent cell lines, within a microarray plate. The cell lines showed a magnitude of up-regulation (green) or down-regulation (red) of all genes in the human genome in these tumor cells.

Results: In squamous cell carcinoma cell lines (SCC016, SCC040, SCC056, SCC114, and SCC116), it was discovered that the Apoptosis Inducing Factor (AIF) gene was commonly down-regulated. Additionally, the IκBα gene was found to be commonly up-regulated in all the adenocarcinoma cell lines (MCF7, Hs578t, T47D, BT20, and A549).

Conclusions: These results suggest that the adaptation of squamous carcinoma cells to increased levels of NO leads to down regulation of the AIF flavoprotein thus prolonging the lifespan of the malignant cell and allowing further damage. In addition, the up-regulation of the IκBα gene deactivates the NF-κB gene and prevents the formation of anti-oxidants that reduce the damage caused by high levels of Nitric Oxide.

Biography

Karla Licona is an MPH and MD student. She received her Bachelor's in Science with a major in Health Education and Nutrition from California State University of Northridge. After graduating, she attended Saint James School of Medicine and is now currently completing her MPH degree with two certificates in Epidemiology and Healthcare Management and Policies from Benedictine University, Chicago. She completed research on the topic of HPV Vaccine Gardasil which has been lagging usage in the United States among college students. This year she participated as Organizing Committee Member for International Society of Oncology and Biomarkers (ISOBM)-2016 which was held in Chicago. Currently, she is a Board Member for Oncomarks.org, an online professional network which allows open access to journals for students and those interested in research. Her research interests are: HPV related cancers (cervical, penile, vulvar, anal and oropharyngeal cancers) and nitric oxide effects in the tumor environment.

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