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## Exposure to high levels of Nitric Oxide (NO) showed transmembrane Glycoprotein NMB (GPNMB) over expression in Head & Neck (H&N) Squamous Cell Carcinomas (SCC)

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**Hypothesis:** Increasing levels of NO can result in the increased expression of genes that contribute to the progression of metastasis of SCC cell lines.

**Objective:** Cancer metastasis involves an intricate series of events influenced by myriad of regulatory and proliferative factors. Recent research has shown that exposure to high levels of NO induces stem cell like properties in cancer cells resulting in a more aggressive phenotype and worse prognosis. This is mediated through the increase in metastatic potential observed in cancerous cells after exposure to high levels of NO when compared to their parent cell lines. In this study, it was found that cancer cells with high levels of NO exposure tend to over-express the GPNMB gene. This type I transmembrane glycoprotein is up-regulated in various cancers and believed to play a role in metastasis through regulation of cell migration and adhesion using its tripeptide (Arg-Gly-Asp) RGD motif, which is capable of integrin binding. When it comes to the regulation of cell migration, this activity is important in cell adhesion, and other vital processes of metastasis.

**Methods:** In this study, five H&N cell SCC cell lines were used: SCC016 (tongue), SCC040 (tongue), SCC056 (tongue), SCC114 (floor of mouth), and SCC116 (alveolar ridge). The cell lines were subjected to increased levels of NO by DETA-NONOate until a maximum concentration of 600 mM was reached. In these cell lines, RNAs was isolated from and their respective parent cell lines. Using DNA microarrays, the gene level expression of these NO exposed cell lines were then compared to their individual parent cell lines. This data was further compared to a UniProt-GOA association file (Human) by a program, in order to find genes belonging to certain Gene Ontology (GO) terms. The GO term used was GO:0005178, which contains genes related to the molecular function of integrin binding.

**Results:** GPNMB was overexpressed in all the five SCC cell lines (SCC016, SCC040, SCC056, SCC114, SCC116). These cell lines which were exposed to high levels of NO appeared to be the most consistently up-regulated. GPNMB contains an RGD motif in its extracellular domain region, which is recognized by many members of the integrin family. Binding of this ligand motif to integrins can lead to important cell adhesion interactions and other metastatic processes.

**Conclusion:** High levels of Nitric Oxide exposure correlate with an increased metastatic potential through over expression of genes such GPNMB. However, the exact mechanism by which GPNMB contributes to the progression of metastasis is yet to be understood. Additional studies examining GPNMB expression under varying concentrations of NO may aid better understanding of this gene's significance in the cancer process.

### Biography

Khatja Batool graduated with her Bachelor of Medicine and Bachelor of Surgery degree from Gulf Medical University, UAE. She started her research at UIC-Chicago, IL where she studied the effects of nitric oxide in cancer stem-cell lines. Additionally, she is a certified expert in Botulinum Toxin, Dermal Fillers and Facial reconstruction. Her distinguished efforts led her to be a part of the Organizing Committee at the 43rd ISOBM Annual Conference in Chicago, IL which was attended by Nobel laureate Dr. Ferid Murad and other well-known scientists. She has her works published in research journals such as Tumor Biology. Furthermore, she is on the Editorial Board for international journals like Tumor Biology and JCMT, Board member at Oncomarks.org and a member of professional societies like ASCO and ISOBM. She has an active interest in oncology research especially in the studies of nitric oxide and telomerase shortening in cancer stem cells.

### Notes:

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