Exposure to high levels of Nitric Oxide (NO) showed transmembrane glycoprotein NMB (GPNMB) over expression and Cadherin-1, Type-1 (CDH1) downregulation, in head and neck Squamous Cell Carcinomas (SCC)

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Hypothesis: Exposing SCC cell lines to increasing levels of NO can result in the increased expression of Transmembrane Glycoprotein NMB (GPNMB) and down regulation of Cadherin-1, Type-1 (CDH1) that contribute to the progression of metastasis.

Objective: Nitric Oxide is a free radical molecule which communicate and transmit signals throughout the body. Recent studies have shown that exposure to Nitric Oxide (NO) results in stem cell-like properties of cancer cells. Cancer metastasis is a complex process involving a number of highly regulated steps, such as, cell invasion, proliferation and migration. Overexposure of HNO levels in cells cause protein coding genes to be down regulated that play a key role in cell adhesion, cell signaling and cell communication. To study the relationship between HNO Levels and metastatic potential, High Nitric levels were presented in four H&N SCC cell lines. HNO adapted cell lines caused down regulation of CDH1 and up regulation of GPNMB in all four cell lines. One of the causes of carcinogenesis is due to abnormalities in tumor suppressor protein coding genes. In this case, CDH1 was found to be down regulated. CDH1 gene provide manuals for producing a protein that codes for Epithelial Cadherin or E-Cadherin. E-Cadherin regulate cell-cell adhesion, cell proliferation which plays an important role as tumor suppressor genes In similar studies, it was also found that cancer cells overexpress the GPNMB gene, which is believed to have a role in metastasis. GPNMB is a type I transmembrane glycoprotein protein that has been found to be up-regulated in various cancers. A key feature of GPNMB is its tripeptide (Arg-Gly-Asp) RGD motif, which is capable of integrin binding. This activity is important when it comes to the regulation of cell migration, cell adhesion, and other vital processes of metastasis.

Methods: GPNMB type I transmembrane glycoprotein protein and Cadherin-1 Type-1 (CDH1) were observed in all H&N SCC cell lines. SCC016, SCC040, SCC056, SCC114, and SCC116. The cell lines were subjected to increased levels of NO by DETA-NONOate until a maximum concentration of 600 mM was reached. RNAs were isolated from these cell lines and their respective parent cell lines. The gene level expression of these NO exposed cell lines were then compared to their individual parent cell lines using DNA microarrays. 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: It was observed that along with GPNMB being commonly overexpressed and CDH1 genes to be down regulated, in all five SCC cell lines (SCC016, SCC040, SCC056, SCC114, SCC116) that were exposed to increased levels of NO, they also appeared to be the most consistently up-regulated genes. 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.

Conclusions: Exposure to high levels of NO is correlated with an increase in the expression levels of genes that enhance metastatic potential. NO cancer cells were found to overexpress the GPNMB gene and downregulate CDH1 gene. Down regulation of CDH1 means that the gene expression is reduced or decreased. Therefore, causing it to be increase in metastatic potential. Further study is required to understand the mechanism by which GPNMB and CDH1 contributes to the progression of metastasis. Additional studies with varying concentrations of NO and its effect on GPNMB expression may also be useful in determining the genes significance.

Biography
Juel Chowdhury began his professional education at the Gulf Medical University where he received his Bachelor of Medicine and Bachelor of Surgery. Since then, his works have led him to partner and study with Nobel laureate Dr. Ferid Murad and many well-known scientists such as Dr. Robert Winn Director of UI Health. He is the founder and president of Oncomarks.org an online professional network with an open access journal for the oncologist. His innovative iGenX lab is a genetical research lab based on data-mining and data analysis of the gene-chip experiment. Editorial Board for many international journals like Tumor Biology, JCMT, JUMD, and many professional societies like ASCO and ISOBM. He was the director of ISOBM (International society of oncology and biomarkers) 2016 congress held in Chicago and also the upcoming ISOBM 2017 congress in Brazil. Expert in Botulinum Toxin and Dermal Fillers, facial reconstruction and hair transplant procedures. Faculty member of National College of Health. research interests are as follows: head & neck cancer, lung & upper aero digestive tumors, human tumor stem cells. Nitric oxide in tumor environment.