The Cadherin-1, Type-1 (CDH1) Gene is Down Regulated by High Nitric Oxide Levels in Head & Neck Squamous Cell Carcinomas (SCC)

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ABSTRACT

Patients with high levels of Nitric Oxide (NO) have lower survival rates compared to those with lower levels of NO. Moreover, it has been shown that exposure to high levels of NO results in increased potential for metastasis. A key step in the progression of metastasis is the modification of cell adhesion. To further study the observed increase in metastatic potential, four head and neck (H&N) SCC cell lines have been adapted to high levels of NO (HNO cancer cells). When comparing the expression of genes, Cadherin-1, Type-1 (CDH1) was found to be down-regulated in the HNO cancer cells of all four SCC cell lines. CDH1 codes E-Cadherin, which plays an important role in cellular adhesion.

HYPOTHESIS/OBJECTIVE

Exposing H&N SCC cancer cells to high levels of nitric oxide (NO) will result in down-regulation of genes coding for proteins involved in cell adhesion, thus increasing metastatic potential.

METHODS

Cell Lines: Four H&N SCC cell lines were studied: SCC016, SCC040, SCC056, and SCC114.

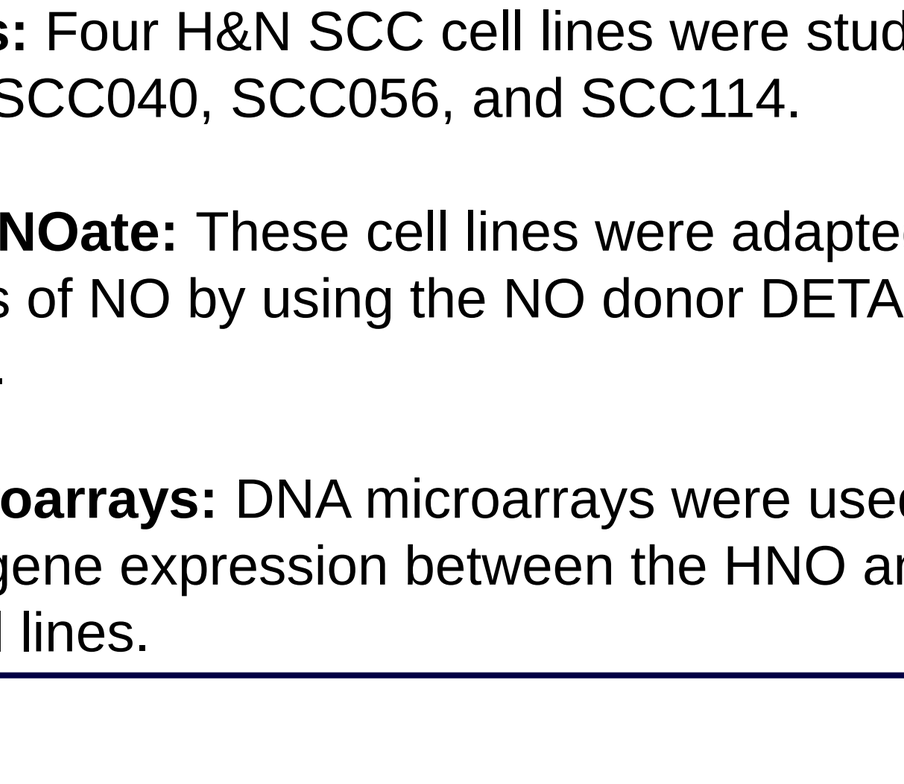
DETA-NONOate: These cell lines were adapted to high levels of NO by using the NO donor DETA-NONOate.

DNA microarrays: DNA microarrays were used to compare gene expression between the HNO and parent cell lines.

RESULTS

Cadherin-1, Type-1 (CDH1) was consistently down-regulated in the HNO cancer cells of the four H&N SCC cell lines studied.

Cell Line	Fold Change	Cell Line Info Cancer (Squamous Cell Carcinoma)
SCC016 P-SCC016 HNO	-1.72923307	head and neck (tongue)
SCC040P -SCC040 HNO	-1.5559588	head and neck (tongue)
SCC056P-SCC056 HNO	-2.67676276	head and neck (tongue)
SCC114P-SCC114 HNO	-1.4732179	head and neck (floor of mouth)

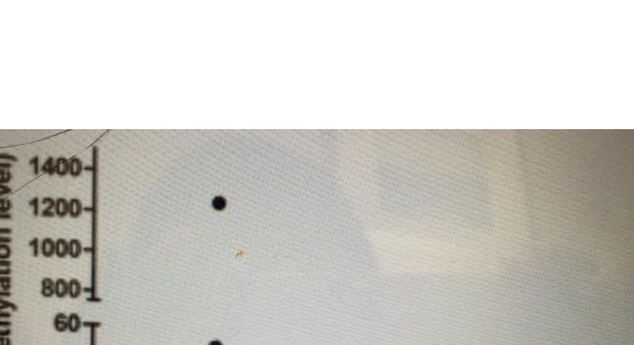


This graph above shows methylation rates of CDH1 oral squamous cell carcinoma (OSCC) tissue samples and saliva from controls.

How does CDH1 relate to tumor Biology?

Loss of CDH1 gene function may lead to progression of tumor by increasing proliferation, invasion or metastasis.

Loss of CDH1 gene expression may also lead to cancer progression by adjusting or altering pathways that regulate processes such as cell metabolism , immune evasion or oxidative stress.



CDH1 gene is located on chromosome 16 at position 22.1

CONCLUSION

Exposure to high levels of NO results in a down-regulation of the CDH1 gene in all four H&N SCC cell lines. The loss of E-Cadherin gene expression needs to be further explored at the protein and cell surface levels. The HNO cells have properties that are consistent with previously reported data that suggest they are highly metastatic. Studies involving varying expression levels of CDH1 in the presence and absence of NO may also be helpful in understanding the impact of CDH1 on metastatic potential.

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