Cell Division Cycle Protein 27 (CDC27) Is Down-Regulated In High Nitric Oxide-Adapted Breast Cancer Cell Lines

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INTRODUCTION

A key feature of cancer is the progression through the cell cycle in an uncontrolled manner. Adaptation to high NO levels results in an observed down-regulation of important genes that are involved in cell cycle regulation. Breast cancer cell lines were adapted to high NO (HNO cancer cells), and then compared to their corresponding parent cell lines. Expression of the CDC27 gene was observed to be down-regulated in HNO cancer cells from the breast cancer cell lines. CDC27 codes for a subunit of the anaphase-promoting complex/cyclosome (APC/C), which is an important regulator of the spindle checkpoint in cell division.

HYPOTHESIS

Adaptation of breast cancer cell lines to high nitric oxide (NO) will result in decreased expression levels of genes involved in the regulation of cell cycle arrest.

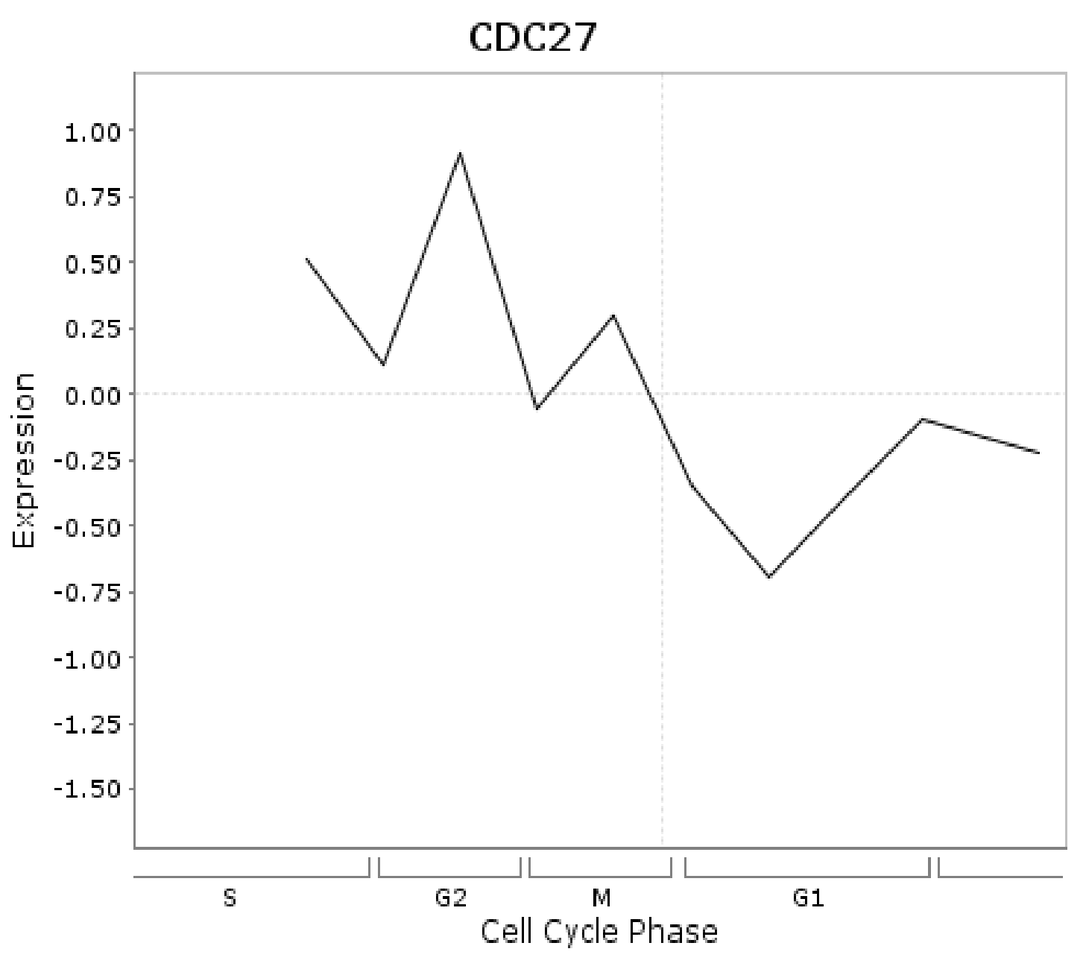
Methods

Three breast cell lines were studied: Hs578t, MCF7, T47D

DETA-NONOate: Using an NO donor, DETA-NONOate, the cell lines were adapted to high levels of NO.

Genome-wide gene chip experiment: A genome-wide gene chip experiment was used to assess the expression levels of genes between the HNO and corresponding parent cell lines.

Results



CDC27 is a component of the anaphase promoting complex (APC); a cell-cycle regulated E3 ubiquitin that controls progression through mitosis and the G phase of the cell cycle. The APC/C complex acts by mediating ubiquitination and the subsequent degradation of target proteins. This protein was shown to interact with mitotic checkpoint proteins including Mad2, p5CDC, and BYBR1, and might be involved in controlling the timing of mitosis. As shown in the graph, the gene expression falters during the M phase, leading to the down regulation of the gene.

The CDC27 gene was down-regulated in the HNO cancer cells of the Hs578t, MCF7, and T47D breast cancer cell lines.
The following data table provides the fold change for down regulated HNO cancer cells

Cell line	Log (HNO/P)	Fold Change	Gene info	Ensemble Gene
Hs578t	-0.957257159	-1.941614999	Cell division cycle protein 27 homolog (CDC27Hs)(H-NUC) [Source:UniProtKB/Swiss-Prot;Acc:P30260]	ENSG00000004897
MCF7	-1.312765275	-2.484172358	Cell division cycle protein 27 homolog (CDC27Hs)(H-NUC) [Source:UniProtKB/Swiss-Prot;Acc:P30260]	ENSG00000004897
T47D	-0.605652896	-1.521667233	Cell division cycle protein 27 homolog (CDC27Hs)(H-NUC) [Source:UniProtKB/Swiss-Prot;Acc:P30260]	ENSG00000004897

CONCLUSION

Exposure to high levels of NO results in down-regulation of the CDC27 gene in HNO cells of breast cancer compared to their parent cell lines. Further studies with varying expression levels of CDC27 may be helpful in understanding its impact on cell proliferation when comparing HNO cancer cells to their parent cells. It might also be helpful to search for expression levels of other genes that play an important role in cell cycle progression, and, thus, further explore the effects of nitric oxide on cell proliferation.

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References

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