Role of Arylamine N-acetyltransferase 1 (NAT1) in Breast Cancer Growth and Metastasis

Andrew R. Ray, M.S.¹,³, Mark A. Doll, M.S.¹,³, Kyung U. Hong, Ph.D.¹, Raúl A. Salazar-González, Ph.D.¹,³, Daniel Hodge, M.Eng.¹,³, Levi J. Beverly, Ph.D.¹,²,³, David W. Hein, Ph.D.¹,³

¹Department of Pharmacology/Toxicology, ²Department of Medicine, ³James Graham Brown Cancer Center, University of Louisville, Louisville, Kentucky

Introduction

1. Metastasis from the primary solid tumor site is the leading cause of mortality in breast cancer patients.
2. In order for cancer cells to metastasize, they must undergo a complex process known as epithelial-to-mesenchymal transition (EMT).

Hypothesis

Knockout of NAT1 was expected to decrease the anchorage independent growth, metastatic potential, and markers of epithelial-to-mesenchymal transition (EMT) in MDA-MB-231 (ER+/PR-/Her2-), MCF-7 (ER+/PR+/Her2-), and ZR-75 (ER+/PR+/Her2-) breast cancer cell lines.

Experimental Scheme

Results

1. NAT1 knockout drastically decreases the ability of breast cancer cells to grow in an anchorage-independent manner (soft agar). However, does not effect growth in polyHEMA or hanging drop assays.
2. NAT1 knockout decreases expression of vimentin - a key marker of epithelial-to-mesenchymal transition.
3. NAT1 knockout results in impaired in vivo growth of MDA-MB-231 breast cancer in NRGs mice.

Conclusions

These studies suggest that arylamine N-acetyltransferase 1 (NAT1) may contribute to cancer metastasis and EMT and would potentially serve as an effective target for the treatment of metastatic breast cancer.

Clinical Significance

Further study is necessary to understand the role of NAT1 on metastatic behavior of MCF-7 and ZR-75 cells injected into NRGs mice (experiments in progress).

Future Work

Table 1 – NAT1 Knockout Cell Growth Assay Characteristics

<table>
<thead>
<tr>
<th>Assay</th>
<th>Cells Attached?</th>
<th>Cells Alone?</th>
<th>Cells Forced Together?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doubling Time</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Plastic/Colony Formation</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Soft Agar</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PolyHEMA</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Hanging Drop</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

References


Acknowledgements

Research was supported by generous funding from the National Cancer Institute’s Cancer Education Program (R25-CA134283).