Characterization of GAGE antigen expression in thirteen common breast cancer cell lines

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Why is Breast Cancer Research Important?

- Over the course of a lifetime 1 in 8 women will be diagnosed with breast cancer.
- Estimates: 200,000 women are diagnosed per year, along with 1,700 men. Approximately 40,000 women and 450 men die annually from breast cancer.
- In the USA women have a 12% chance of developing invasive breast cancer at some point in their lives.
- BRCA1 and BRCA2 genes are linked to a high susceptibility of breast cancer but occur in only 5% of breast cancer patients.
- In 2006 the cost of breast cancer treatment in the US was estimated to be $13.9 billion dollars.
- Further research may provide insight into breast cancer pathways involved in disease progression.
GAGE Antigens

- Chosen for investigation based on previous microarray results and subsequent investigation conducted at the University of North Dakota.
- Microarray data indicated that they were differentially regulated based on the presence or absence of the N- and C-terminal of MT-3.
- The goal of this research is to characterize the expression of GAGE family antigens across several ER receptor positive and negative breast cancer cell lines.
What are GAGE Antigens?

- Belong to a group of cancer/testis antigens normally expressed in human germline cells.
- Also found to be expressed in several tumor types.
- GAGE antigens fall into three groups.
- GAGE-1 has a unique C-terminal sequence no other member has.
- GAGEs 2 through 8 amino acid sequences are 98% identical.
- GAGE antigens may direct cell proliferation, differentiation, and the survival of germline cells.
- Normally expressed in adult male germ cells, and a subset of oocytes in the adult ovary.
GAGE Antigens and Cancer

- Present in 26% of breast cancers.
- Also expressed in stomach cancer, neuroblastoma, and esophageal cancer.
- Expression is correlated to a poor prognosis and aggressive tumor type.
- Normal expression is limited to immune privileged sites making them useful targets for prognostic indicators.
- Potential targets for immunotherapy.
<table>
<thead>
<tr>
<th>Cell Line</th>
<th>Characteristics</th>
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<tbody>
<tr>
<td>MCF7</td>
<td>No MT-3 expression, ER+</td>
</tr>
<tr>
<td>T47D</td>
<td>ER+</td>
</tr>
<tr>
<td>MDA-MB-157</td>
<td>Triple negative (No ER, PR, or HER2 receptors)</td>
</tr>
<tr>
<td>MDA-MB-231</td>
<td>Triple negative (No ER, PR, or HER2 receptors)</td>
</tr>
<tr>
<td>MDA-MB-361</td>
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<tr>
<td>1-7HB2</td>
<td>Immortalized non-tumor forming cell line.</td>
</tr>
<tr>
<td>ZR-75-1</td>
<td>ER+</td>
</tr>
<tr>
<td>ZR-75-30</td>
<td>ER+</td>
</tr>
<tr>
<td>VP267</td>
<td>ER-</td>
</tr>
<tr>
<td>VP303</td>
<td>ER+ but progesterone receptor negative</td>
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<tr>
<td>SVCT</td>
<td>SV40 Transformed human breast epithelial cells. Non-tumorigenic.</td>
</tr>
<tr>
<td>HS578T</td>
<td>Triple negative.</td>
</tr>
<tr>
<td>MT-M223</td>
<td>High androgen receptor/low estrogen and progesterone receptor expression. Dihydrotestosterone inhibits proliferation.</td>
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</tbody>
</table>
T47D cell line shows consistently high expression.

Note: Statistics were not performed at this point. There is no single control group.
GAGE12B was only expressed in the T47D cell line. The expression was also lower than other GAGE antigen expression in T47D cell lines.
GAGE12J has the highest expression levels in ZR-75-1 cells
GAGE13 has the highest expression levels in VP303 AND MT-M223 cells
GAGE06 is expressed at a very low copy number in T47D, MDA-MD-361 and ZR-75-01 cell lines.
Conclusions

- GAGE antigen expression is highly variable amongst the cell lines tested.
- There is no clear correlation between GAGE antigen expression and estrogen receptor status.
- Expression of GAGE2B, 2C, 12C, and 12D were highly expressed in T47D cells.
- Expression is variable amongst the GAGE antigens in the cell lines tested.
Research at Cankdeska

- Made possible by three grants (NARCH, INBRE, ICE-TI)
- All grants function to hire STEM faculty, and to conduct student driven research.
- NARCH and INBRE support a ten week summer research internship.
- ICE-Ti supports faculty teaching and research in STEM.
- Since 2014 Cankdeska has added $250,000 worth of research equipment.
- Cankdeska is looking to expand its research facilities even further.
- Local research done by local students.