Cancer is not a disease of individual cells, but principally a failure of cells and tissues to communicate properly.

- Key to understanding breast cancer is understanding basic mammary biology.
- Research focused on critical developmental factors will improve understanding of the possible effects of environmental agents.
2D breast cell cultures on plastic do not organize and communicate correctly
3D organotypic cultures retain the ability to organize and communicate correctly
Human mammary cell culture models

<table>
<thead>
<tr>
<th>Culture</th>
<th>ERα(+)</th>
<th>Organization</th>
<th>Secretion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor cell lines (e.g., MCF7, T47D)</td>
<td>+++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Immortal cell lines (e.g., MCF10A)</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Primary cells</td>
<td>+</td>
<td>+/- *</td>
<td>+</td>
</tr>
<tr>
<td>HMSC-derived cells</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

* Although primary cells exhibit organization, it is heterogeneous and unpredictable.
Stem cells and their progeny in adult breast tissue

Primary cultures vs. HMSC-generated cultures

Primary cultures prepared directly from tissue
- Cells in various states of repair and remodeling
- Variable stem and progenitor cell content
- Variable ERα and PGR expression
- No control of developmental staging

Secondary cultures prepared from HMSCs
- Synchronous growth and structure formation
- Consistent stem and progenitor cell content
- Consistent ERα and PGR expression
- Temporal control of developmental stages
  subject to environmental perturbations
Can we generate homogeneous yet representative 3D organotypic cultures?

Fournier et al., 2006

Yaswen lab, unpublished
3D Breast Cell Culture Objectives

Normal breast tissue

Digest w/collagenase

Heterog. organoids

Expansion in growth medium/ECM

Dissociate

Adult stem cells

Assays of growth, differentiation, organization

Chemical exposure

Homogenous organoids

Gene expression profiling

Genetic manipulation*