Loss of ERbeta expression as a common step in estrogen-dependent tumor progression.
Allison Bardin, Nathalie Boulle, Gwendal Lazennec, Françoise Vignon, Pascal Pujol

To cite this version:
Table 1: Relative expression of ERα and ERβ in breast tumor progression.

<table>
<thead>
<tr>
<th>Studies</th>
<th>Tissues</th>
<th>Number</th>
<th>Methods</th>
<th>ERα</th>
<th>ERβ</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Roger et al.</td>
<td>Normal</td>
<td>118</td>
<td></td>
<td>+</td>
<td>+++</td>
<td><a href="#">NR</a></td>
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<td>(2001)</td>
<td>NP-BBD</td>
<td>18</td>
<td></td>
<td>+</td>
<td>++</td>
<td><a href="#">NR</a></td>
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<td></td>
<td>P-BBD</td>
<td>37</td>
<td>IHC</td>
<td>++</td>
<td>++</td>
<td><a href="#">NR</a> cells decrease during pre-invasive tumor progression</td>
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<td></td>
<td>P-BBDWA</td>
<td>13</td>
<td>IHC</td>
<td>++</td>
<td>+</td>
<td><a href="#">NR</a></td>
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<td></td>
<td>CIS</td>
<td>25</td>
<td>IHC</td>
<td>++</td>
<td>+</td>
<td><a href="#">NR</a></td>
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<td></td>
<td>High grade CIS</td>
<td>35</td>
<td>IHC</td>
<td>++</td>
<td>-</td>
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<tr>
<td>Iwao et al.</td>
<td>Normal</td>
<td>11</td>
<td>Real Time-PCR</td>
<td>++</td>
<td>+++</td>
<td>Changes in ERβ1 and ERβ2 mRNA levels in breast cancer.</td>
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<tr>
<td>(2000)</td>
<td>Cancer</td>
<td>112</td>
<td>Real Time-PCR</td>
<td>+++</td>
<td>++</td>
<td><a href="#">NR</a></td>
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<td></td>
<td>Normal</td>
<td>89</td>
<td>ISH</td>
<td>+++</td>
<td><a href="#">NR</a></td>
<td><a href="#">NR</a></td>
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<td>Breast Cancer</td>
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<td>Met. lymph node</td>
<td>85</td>
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<td>++</td>
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<td></td>
<td>Met. lymph node recurrences</td>
<td>10</td>
<td>ISH</td>
<td>+</td>
<td><a href="#">NR</a></td>
<td><a href="#">NR</a></td>
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<tr>
<td>Skliris et al.</td>
<td>Normal</td>
<td>138</td>
<td></td>
<td>+++</td>
<td>+++</td>
<td>Reduced expression of ERβ in invasive breast cancer.</td>
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<td>(2003)</td>
<td>PDCIS</td>
<td>16</td>
<td></td>
<td>+++</td>
<td><a href="#">NR</a></td>
<td><a href="#">NR</a></td>
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<td>Invasive cancers</td>
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<td>Met. lymph node recurrences</td>
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<td>IHC</td>
<td>-</td>
<td><a href="#">NR</a></td>
<td><a href="#">NR</a></td>
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<tr>
<td>Speirs et al.</td>
<td>Normal</td>
<td>23</td>
<td>RT-PCR</td>
<td>+</td>
<td>+++</td>
<td>22% of normal breast expressing exclusively ERβ mRNA.</td>
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<td>(1999)</td>
<td>Cancer</td>
<td>60</td>
<td>RT-PCR</td>
<td>+++</td>
<td>+</td>
<td>50% of breast tumours coexpressing ERα and ERβ.</td>
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<tr>
<td>Leygue et al.</td>
<td>Normal (adjacent tissues)</td>
<td>18</td>
<td>Multiplex RT-PCR</td>
<td>+</td>
<td>++</td>
<td>Increase in ERα and decrease in ERβ during tumor progression.</td>
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<tr>
<td></td>
<td>(7ER-/11ER+)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><a href="#">NR</a></td>
</tr>
<tr>
<td>Gustafsson et al.</td>
<td>Normal</td>
<td>Total of 30 samples</td>
<td>RT-PCR Western-Blot, IHC</td>
<td><a href="#">NR</a></td>
<td><a href="#">NR</a></td>
<td>ERβ is the predominant form in normal mammary gland.</td>
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<tr>
<td>(2000)</td>
<td>BBD</td>
<td></td>
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<td></td>
<td><a href="#">NR</a></td>
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<td></td>
<td>Cancer</td>
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<td></td>
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Table 2: Relative expression of ERα and ERβ in ovarian tumor progression

<table>
<thead>
<tr>
<th>References</th>
<th>Tissues</th>
<th>Number</th>
<th>Methods</th>
<th>ERα SQ Ov.</th>
<th>ERβ SQ Ov.</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>Pujol et al. (1998)</td>
<td>Normal Cysts</td>
<td>24</td>
<td></td>
<td>+</td>
<td>+</td>
<td>ERα/ERβ mRNA ratio increase during tumor progression</td>
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<td></td>
<td>Borderline tumors Cancers</td>
<td>3</td>
<td>Competitive RT-PCR</td>
<td>++</td>
<td>++</td>
<td></td>
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<td></td>
<td></td>
<td>10</td>
<td>RT-PCR</td>
<td>++</td>
<td>+</td>
<td></td>
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<tr>
<td>Brandenberger et al. (1998)</td>
<td>Normal Cancer</td>
<td>10</td>
<td>Northern RT-PCR</td>
<td>+++</td>
<td>++</td>
<td>ERβ mRNA level decreases in cancer</td>
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<tr>
<td>Rutherford et al. (2000)</td>
<td>Normal Primary cancer</td>
<td>9</td>
<td>RT-PCR</td>
<td>++</td>
<td>++</td>
<td>ERβ mRNA and protein levels decrease in ovarian cancer and metastases</td>
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<tr>
<td></td>
<td>Met cancer</td>
<td>8</td>
<td>Western Blot</td>
<td>+++</td>
<td>-</td>
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Table 3: Relative expression of ERα and ERβ in prostate tumor progression

<table>
<thead>
<tr>
<th>References</th>
<th>Tissues</th>
<th>Number</th>
<th>Methods</th>
<th>ERα SQ Ov.</th>
<th>ERβ SQ Ov.</th>
<th>Comments</th>
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<tr>
<td>Latil et al. (2001)</td>
<td>Normal Cancer</td>
<td>4/23</td>
<td>Real-Time RT-PCR</td>
<td>++</td>
<td>+</td>
<td>Decreased expression of ERβ mRNA in the hormone-resistant group</td>
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<tr>
<td>Pasquali et al. (2001a)</td>
<td>Normal Cancer</td>
<td>5/10</td>
<td>IHC</td>
<td>+++</td>
<td>+</td>
<td>ERβ protein expression decreases in cancer</td>
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<td>Pasquali et al. (2001b)</td>
<td>Normal Cancer</td>
<td>6/5</td>
<td>RT-PCR</td>
<td>++</td>
<td>+</td>
<td>ERβ mRNA expression decreases in cancer</td>
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<tr>
<td>Horvath et al. (2001)</td>
<td>Normal Hyperplasia Cancer</td>
<td>5/157</td>
<td>IHC</td>
<td>+++</td>
<td>- or +</td>
<td>Loss of ERβ protein expression during tumor progression</td>
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<td></td>
<td>Moderate grade Dysplasia</td>
<td></td>
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<td></td>
<td>High grade Carcinoma - grade III</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>High grade Carcinoma - grade IV/V</td>
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<td></td>
<td>Metastasis</td>
<td></td>
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<td>Leav et al. (2001)</td>
<td>Total of 50 samples HGPIN</td>
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<td>IHC</td>
<td>-</td>
<td>-</td>
<td>Decrease in ERβ protein and mRNA expression in high grade dysplasia and carcinoma.</td>
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<td>Adenocarcinoma Gleason grade:</td>
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<td>RT-PCR</td>
<td>+/+</td>
<td>+/+</td>
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<td>Fixemer et al. (2003)</td>
<td>HGPIN Adenocarcinoma Gleason grade: III</td>
<td>47</td>
<td>IHC monoclonal antibody</td>
<td>+++</td>
<td>+</td>
<td>ERβ protein expression decreases during tumor progression. ERβ expression higher in Gleason grade IV than in grade III and V</td>
</tr>
</tbody>
</table>
Table 4: Relative expression of ER\( \alpha \) and ER\( \beta \) in colon tumor progression

<table>
<thead>
<tr>
<th>References</th>
<th>Tissues</th>
<th>Number</th>
<th>Methods</th>
<th>ER( \alpha )</th>
<th>ER( \beta )</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Campbell-Thompson et al. (2001)</td>
<td>Normal cancer</td>
<td>26</td>
<td>RT-PCR</td>
<td>+</td>
<td>+</td>
<td>ER( \beta 1 ) and ER( \beta 2 ) mRNA expressions decrease in cancer</td>
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<td></td>
<td>26</td>
<td>Southern</td>
<td>+</td>
<td>+</td>
<td>++</td>
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<tr>
<td>Foley et al. (2000)</td>
<td>Normal Cancer</td>
<td>11</td>
<td>RT-PCR</td>
<td>+</td>
<td>+</td>
<td>Decrease ER( \beta ) protein but not mRNA expression in cancer.</td>
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<tr>
<td></td>
<td>11</td>
<td>Western</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Post-transcriptional mechanism?</td>
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</table>

The number of + indicates the ERs relative expression. The arrows indicate a decrease (↓), an increase (↑) or no variations in expression (↔) between normal and cancer tissues. SQ= semiquantitative, Ov= overall trends, BBD= Benign Breast Disease, NP-BBD= Non Proliferative BBD, P-BBD= Proliferative BBD, P-BBDWA= Proliferative BBD with atypia, BBT= Benign Breast Tumors, CIS= carcinoma in situ, HGPIN= High grade prostatic intraepithelial neoplasia, IHS= in situ hybridization, IHC= immunohistochemistry, Met= metastatic, RT-PCR= reverse transcription polymerase chain reaction.
Figure 1 Schematic representation of the structure of human ERα and ERβ nuclear receptors. The A/B domain at the NH-2 terminal contains the ligand independent transcriptional-activation function AF-1, the C domain represents the DNA-binding-domain, D corresponds to the hinge region, E domain contains the hormone binding domain and the hormone-dependent transcriptional-activation function AF-2. Numbers outside each box refer to amino acid number whereas the number inside each box of ERβ refers to the percentage of amino acid identity. The arrow indicates the translation starting site in ER cDNA.
Figure 2 Schematic representation of ERα and ERβ imbalance in estrogen dependent tumor progression
Figure 3 Hypothetical mode of ERβ action on cell proliferation pathways.