Distribution of hormone receptors (Estrogen Receptor, Progesterone Receptor and Androgen Receptor) in epithelial malignancies

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Abstract #3152

The importance of steroid hormone receptors to the biology of breast cancer was recognized over 40 years ago. New insights into hormone receptor biology and the increasing array of proteins that can modify their function have already translated into better therapies for breast cancer. The responsiveness of a tumor to hormone therapy is an important parameter in cancer management. Besides breast cancer, other cancers also express estrogen and androgen receptors. Hence, the purpose of this study was to capture the relative distribution of hormone receptors in all types of cancer including breast cancer.

In a total cohort of 9,491 patient samples, hormone receptors ER, PR and AR were assayed by immunohistochemistry on a Ventana platform using antibodies (ER SP 1, PR (IE 2) and AR (AR 2)). The slides were scored manually by pathologists using the cutoff of ≥1% and >10% as positive for AR, PR and ER. Based on these cutoffs, samples were deemed positive or negative.

Our preliminary observations indicate that the frequency of AR was highest in prostate (82%), followed by breast (36%) and ovary (21%). Low expression of AR was most often found in appendiceal (9%), colon (8%) and gallbladder (9%). The frequency of ER was highest in fibroadenoma (81%) followed by endometrium (69%), uterus (69%), breast (52%) and male reproductive system (51%). The frequency of PR was highest in endometrium (81%), ovary (71%), breast (69%), cervix (69%) and salivary gland (67%). The frequency of PR was lowest in colon (3%), breast (0%) and liver (1%). The frequency of PR was highest in endometrium (81%), ovary (71%), breast (69%), cervix (69%) and liver (1%). The frequency of PR was lowest in colon (3%), breast (0%) and liver (1%).

The examination of steroid hormone receptors is pivotal to the understanding of endocrine sensitivity and therefore our study summarizes the frequency distribution of these biomarkers in a large cohort of different cancer lineages.

Conclusions

- The examination of steroid hormone receptors is pivotal to the understanding of endocrine sensitivity and therefore our study summarizes the frequency distribution of these biomarkers in a large cohort of different cancer lineages.
- Expression of AR was highest in prostate, breast, ovary, bladder and other male salivary gland tumors. The expression of AR was lowest in appendix, colorectal, pancreas, and gallbladder cancers.
- Expression of ER was highest in gynecologic cancers and breast cancer and was lowest in brain, appendix, colorectal, bones, joint and kidney cancers.
- Expression of PR was highest in gynecologic cancers and breast cancer and was lowest in brain, appendix, colorectal, bones, joint and kidney cancers.
- Our study provides frequency distribution of hormone receptors in both expected and unexpected lineages which might be useful in evaluating new therapies, determining prognosis and assessing outcome of patients on endocrine therapy. Further, our data may be of value in exploring molecular target driven therapy in cancer particularly to research involving endocrine therapy and androgen deprivation therapy in non breast and non prostatic lineages.

Introduction

Steroid hormones are lipophilic molecules derived from cholesterol and synthesized in the adrenal cortex, the testis, the ovary and placenta. Steroid hormones reach their target cells via the blood, where they are bound to carrier proteins. Within the target cells, steroid hormones bind to steroid hormone receptors which are the key mediators of steroid hormone action like cell proliferation, cell death, secretion and cellular mobility. This ability of steroid hormones is retained in many diseases including cancers originating in steroid hormone sensitive tissues including breast, genital tract, gastrointestinal tract, pancreas, lung and intracranial tumors.

The human estrogen receptor (ER) is a steroid hormone receptor which exists in the nucleus of the cells and a transactivation following the binding of a ligand (estrogen) and subsequently forms dimers within the nucleus as specific estrogen response elements in DNA upsignature of estrogen regulated genes. Many of the genes regulated by estrogen are important for cell proliferation, survival, metastasis and angiogenesis. Tamoxifen, a selective estrogen receptor modulator (SERM) functions as an estrogen antagonist. Therapies designed to reduce the level of estrogen in patients such as ovarian ablation or aromatase inhibitors reduce the synthesis of estrogens from their androgenic precursors. JOHNSTON 924 et al. Aromatase inhibitors for breast cancer lesions from the laboratory. Nature Rev Cancer. 2003; 3: 621-631.

Classical model of estrogenic signaling and its deprivation by endocrine therapy

Hormone receptor expression in epithelial cancers

Distribution of PR

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>Frequency of PR expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenocarcin (98)</td>
<td>95.40%</td>
</tr>
<tr>
<td>Gastrbladder (62)</td>
<td>88.70%</td>
</tr>
<tr>
<td>Bladder (150)</td>
<td>88.30%</td>
</tr>
<tr>
<td>Small intestine (64)</td>
<td>79.90%</td>
</tr>
</tbody>
</table>

Representative images of immunohistochemical staining of hormone receptor expression in breast, endometroid, and head and neck cancers.

The top three panels show representative images of ER in breast, ER expression in endometrioid cancer, followed by PR expression in breast cancer. The bottom two panels show AR expression in normal prostate, followed by AR expression in head and neck carcinoma and breast cancer. Magnification 200x 40x.