

Thyroid Hormone Receptor (TR) Expression in Malignant Breast Tumors

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Background

- Association of breast cancer and thyroid disorders (hyperthyroidism, hypothyroidism or thyroiditis)¹
- Hormonal regulation of the mammary gland²
- Similarity of Thyroid Hormone Receptor (TR) and Estrogen- /Progesterone (ER/PR)-Receptor

➡ Analysis of TR as a marker in breast cancer

Thyroid receptor (TR)

- Nuclear receptor activated by binding thyroid hormone
- ligand-activated transcription factor¹
- 3 major isoforms: TRalpha1 and 2 and TRbeta1

➡ Immunohistochemistry for TRalpha and TRbeta expression in breast cancer tissue

Study population

- 181 patients with sporadic breast cancer
- clinical and histopathological parameters: age, tumor size, histopathological type, axillary lymph node involvement, grading, ER/PR and Her-2/neu
- follow-up data: relapse, metastases

Immunohistochemistry

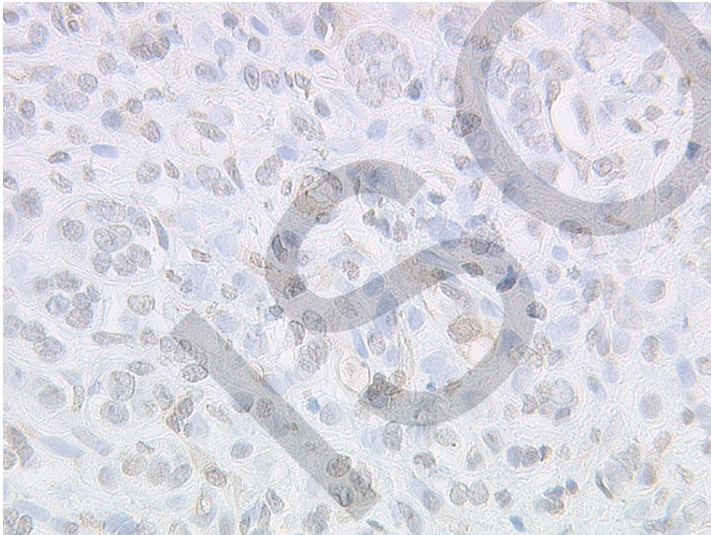
Antibody	Clone (Isotype)	Concentration	Source
TRalpha1/2	polyclonal Rabbit IgG	1:200 (0.2mg/ml)	abcam
TRalpha2	Monoclonal Rabbit IgG	1:200 (1ml)	AbDSerotec
TRbeta1/2	Polyclonal Rabbit IgG	1:200 (200yg/ml)	Zytomed
TRbeta1	Polyclonal Rabbit IgG	1:200 (1.66mg/ml)	Novus Biologicals

- Immunoreactive score (IRS) according to Remmele and Stegner: receptor-positive in case of >10% positive staining

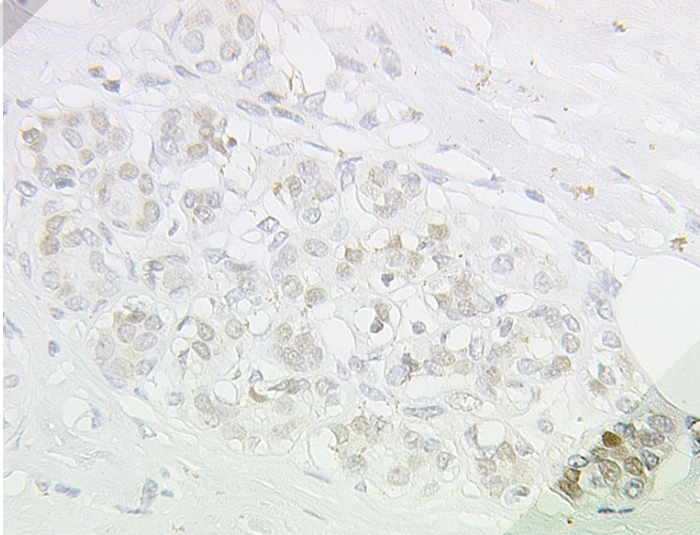
Results

- mean age: 68±13.6 a
- Histological type:
 - Invasive ductal carcinoma: 80%
 - Invasive lobular carcinoma: 8%
 - Invasive medullary carcinoma: 7%
 - others: 5%
- pT1a: 1.7%, pT1b: 11%, pT1c: 36.5, pT2: 35%, pT3: 5%, pT4: 8.4, unknown: 4%
- Axillary lymph node involvement: N0 40%
- Grading: G2/3 92%
- ER/PR-positive: 61%

Results: Immunohistochemical staining



TRalpha1/2: IRS positive



TRbeta1/2: IRS positive

Results

- TRalpha1/2:
57% receptor positive, low scores (median IRS 1)
 - TRalpha2: high scores (median IRS 6)
- TRbeta1/2:
60% receptor positive, low scores (median IRS 1)
 - TRbeta1: low scores (median IRS 0.5)

Results TRalpha

Significant positive correlation of *TRalpha1/2* expression and

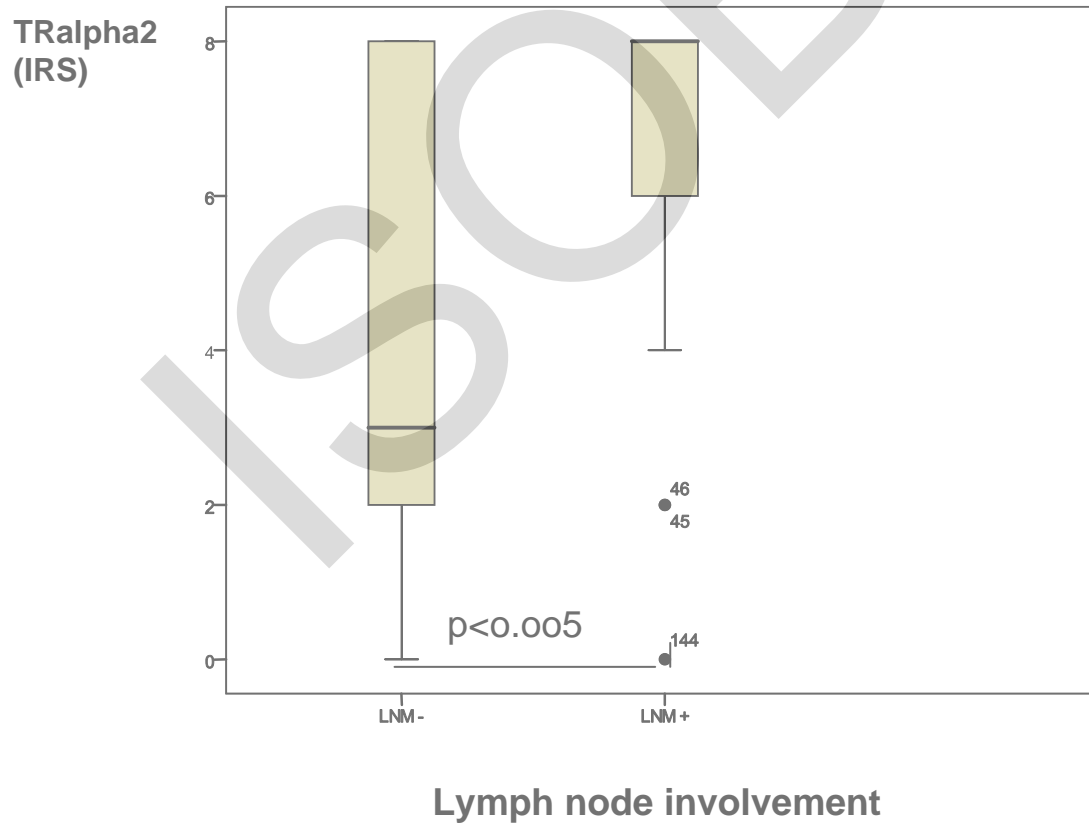
- tumour size (pT) (p=0.002)
- metastatic disease (p=0.017)

Significant positive correlation of *TRalpha2* expression and

- histopathological type (p=0.016)
- positive axillary lymph node (p=0.002)

Results TRalpha

Boxplot for TRalpha2 expression in pts. with or without positive lymph nodes



Results TRbeta

TRbeta1/2

- Significant *negative* correlation with ER expression (ρ -0.277; $p=0.011$)

TRbeta1

- Significant *negative* correlation with tumor size (ρ -0.588; $p=0.006$)

Summary

- Thyroid hormone receptor often expressed in breast cancer
- Low median IRS seen for TRalpha1/2, TRbeta1/2 and TRbeta1, but high median IRS for TRalpha2
- Significant positive correlation of TRalpha and negative correlation of TRbeta with clinical and histopath. parameters (tumor size, histological type, nodal status, metastases, ER)

Conclusion

- The thyroid hormone receptor seems to be relevant in the pathophysiology of breast cancer.
- The thyroid hormone receptor might be a prognostic marker e.g. TR α 2 indicating risk for distant spread.
- Further studies on thyroid hormone receptor expression and prognosis in breast cancer patients are needed.