# Farnesoid X receptor (FXR) status complements the evaluation of estrogen receptor alpha (ER) in breast cancer (BC) patients and predicts poor response to tamoxifen

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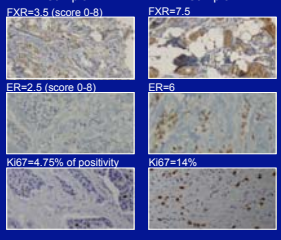
## Farnesoid X receptor (FXR, NR1H4)

- Bile acids are physiological ligands of FXR, a nuclear receptor with a ligand-dependent transcriptional activity
- Metabolic nuclear receptor normally produced in the liver and the gastrointestinal tract
- FXR controls lipid metabolism
- FXR has been demonstrated in breast cancer (Journe et al 2008)

## Bile acids in breast cancer

- Accumulation of bile acids from serum has been reported in breast cyst fluid and has been proposed as a potential risk factor for developing breast cancer
- High plasma levels of deoxycholic acid have been detected in postmenopausal breast cancer patients
- Bile acids are lipids which can accumulate in bone tissue from serum and which may promote breast cancer cell migration

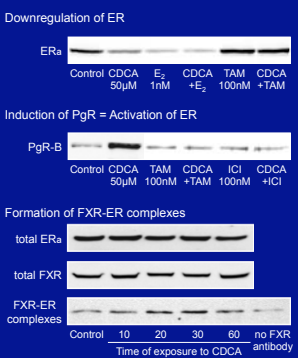
## Significant correlations between FXR and proliferation markers in the ER+/postMP breast cancer patients



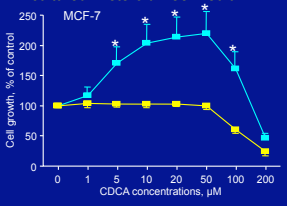

Significant correlations (Spearman's rho) between the expression of FXR and:

- those of ER and PgR in total population (n=204)
- that of Ki-67 in the ER+ subgroup, especially in postMP patients
- no correlation in the ER- subgroup

## Crosstalk between FXR and ER may account for FXR-mediated ER activation in MCF-7 cells




## Mitogenic effects of FXR agonist in MCF-7 cells cultured in steroid-free-medium




## Relationship between FXR expression in primary breast cancer and the propensity to develop bone metastasis

| Metastasis sites | Primary tumors | | |
|---|---|---|---|
| | n | Median score (0-8) | % of FXR-positive tumors |
| Bone | 30 | 5 | 97 |
| Visceral | 20 | 3 | 55 |

## Objectives

To assess the prognostic value of FXR expression in BC by retrospectively analyzing microarray data in a population of 2473 patients

## Methods

- Evaluation of patient overall survival and distant metastasis-free survival in the total population and in subgroups characterized by ER, node and menopausal status
- Comparison of the prognostic value of FXR with that of Ki-67
- Determination of the predictive value of FXR with regard to response to TAM

## FXR / ER crosstabulation

FXR0/ER0 = 420
FXR0/ER1 = 1401
} 75%

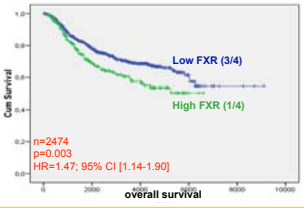
FXR1/ER0 = 151
FXR1/ER1 = 450
} 25%

↓

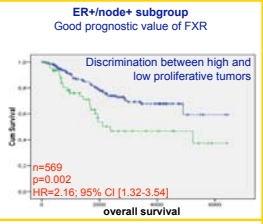
ER0 = 25%
ER1 = 75%

## Total population

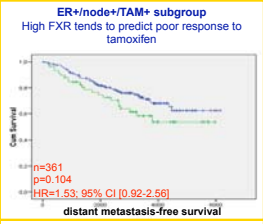
High FXR was significantly associated with shorter overall survival



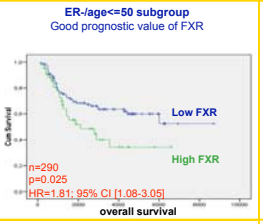

**ER+/node+ subgroup**
Good prognostic value of FXR



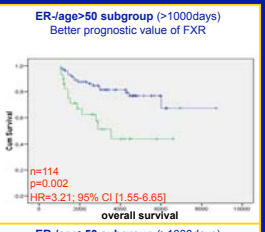

**ER+/node+/TAM+ subgroup**
High FXR tends to predict poor response to tamoxifen



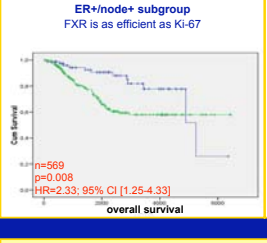

**ER-/age<=50 subgroup**
Good prognostic value of FXR



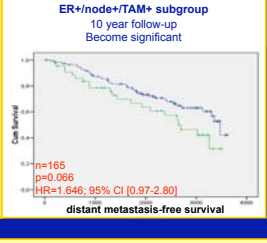

**ER-/age>50 subgroup** (>1000days)
Better prognostic value of FXR



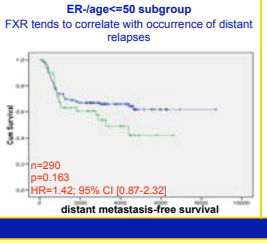

**ER+/node+ subgroup**
FXR is as efficient as Ki-67



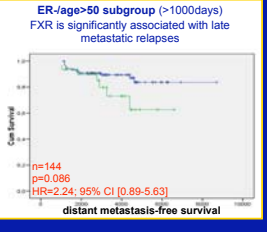

**ER+/node+/TAM+ subgroup**
10 year follow-up
Become significant




**ER-/age<=50 subgroup**
FXR tends to correlate with occurrence of distant relapses




**ER-/age>50 subgroup** (>1000days)
FXR is significantly associated with late metastatic relapses




## Conclusions

- Microarray database analyses confirm the expression of FXR in breast cancer specimens
- In total population, FXR brings forth a significant prognostic information
- In ER+/node+ subgroup, high FXR is associated with poor survival, similar to Ki-67 marker
- In ER+/node+ subgroup, high FXR tends to predict poor response to tamoxifen, especially in a 10 year follow-up
- In ER-/age<50 subgroup, high FXR is of poor prognosis, particularly in long-term follow-up, and it seems related to the occurrence of distant relapses