

# 27P - Search for markers of breast carcinogenesis associated with ER status

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## INTRODUCTION

Advances in cancer therapy and diagnosis have led to an increase in the survival rate of women with breast cancer (BC). However, for metastatic BC, the 5-year relative survival rate remains about 30%. Previously, we identified miRNAs potentially regulated by estrogen, progesterone, or androgen receptors (ER, PR, and AR), the change in the level of which was associated with the presence of lymph nodes metastases (LNM) in patients with BC (miR-193b, -190a, -190b, -21) [Table 1].

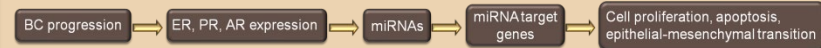


Table 1. Association between the level of miRNAs and the presence of metastases in the lymph nodes in BC.

miR-190a	miR-190b	miR-193b	miR-21
<b>Luminal A</b>			
-	-	Decreased level in tumors of patients with metastases	-
<b>Luminal B (HER2-positive)</b>			
Decreased level of miRNAs in tumors of patients with metastases as compared to cases without.			

The most common method for cancer diagnosis is immunohistochemical analysis. Therefore, the search for protein markers is an urgent task. We identified putative target genes for the above miRNAs that are expressed predominantly in breast tissue according to The Human Protein Atlas. We analyzed the expression of selected genes in BC samples.

### Aim of this research:

Search for genes, changes in expression of which are associated with metastasis to lymph nodes in BC.

This is necessary because:

- understanding of mechanisms of BC progression
- creation of new diagnostic methods

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## RESULTS

• The expression of *OXTR*, *TRPS1*, *STC2*, and *AKR1C2* in MCF-7 cells changed under the influence of hormones (Table 2). *OXTR* mRNA level increased in cells after incubation with all hormones. The most significant increase was in cells treated with E2 for 48 h. *TRPS1* mRNA level increased in cells treated with E2 for 48 h. *STC2* mRNA level increased in cells treated with E2 or T for 6 h. *AKR1C2* mRNA level decreased in cells treated with T for 24 and 48 h.

Table 2. The relative level of mRNA of *OXTR*, *TRPS1*, *STC2*, and *AKR1C2* in MCF-7 cells treated with 100 nM of estradiol, testosterone, or progesterone.

		E2	T	P4	
<i>OXTR</i>	6h	1.01	1.02	<b>0.71*</b>	* The statistically significant difference compared with DMSO-treated cells).
	24h	<b>1.30*</b>	<b>1.73*</b>	1.00	
	48h	<b>2.38*</b>	<b>1.26*</b>	<b>1.33*</b>	
<i>AKR1C2</i>	6h	1.09	1.12	0.83	
	24h	0.90	<b>0.71*</b>	0.94	
	48h	1.23	<b>0.65*</b>	0.90	
<i>TRPS1</i>	6h	1.11	1.11	0.97	
	24h	0.99	1.09	1.02	
	48h	<b>1.62*</b>	<b>1.33*</b>	1.12	
<i>STC2</i>	6h	<b>1.42*</b>	<b>1.40*</b>	0.96	
	24h	0.91	0.99	1.05	
	48h	1.02	<b>0.78*</b>	0.89	

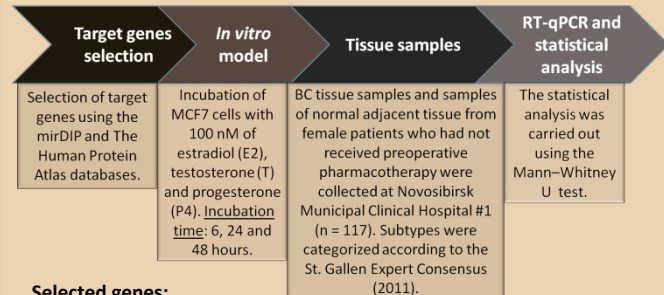
• Expression of E2-sensitive *OXTR*, *STC2*, and *TRPS1* Increased in ER- and/or PR-positive tumors as compared to ER- and PR-negative tumors (Table 3).

Table 3. Association of *OXTR*, *STC2*, and *TRPS1* mRNA levels with ER status of BC.

ER and PR status	n	Relative Level * of mRNA and p-Value					
		<i>OXTR</i>	p-value	<i>STC2</i>	p-value	<i>TRPS1</i>	p-value
ER+ and/or PR+	87	0.09	0.003	0.76	< 0.001	1.66	< 0.001
ER- and PR-	30	0.03		0.12		0.63	

\* Median of differences in mRNA levels between BC tissue and normal adjacent tissue (control) samples; the results were normalized to the control.

## METHODS



### Selected genes:

Gene	miRNAs predicted to target a gene
<i>OXTR</i>	miR-21
<i>TRPS1</i>	miR-190a/b, miR-193b, miR-21
<i>STC2</i>	miR-190a/b, miR-21
<i>AKR1C2</i>	miR-190a/b, miR-193b, miR-21

• *OXTR* and *TRPS1* (higher level of mRNA in tumors of patients with LNM) were found to be associated with presence of LNM in luminal tumors not expressing HER2 (Figure 1).

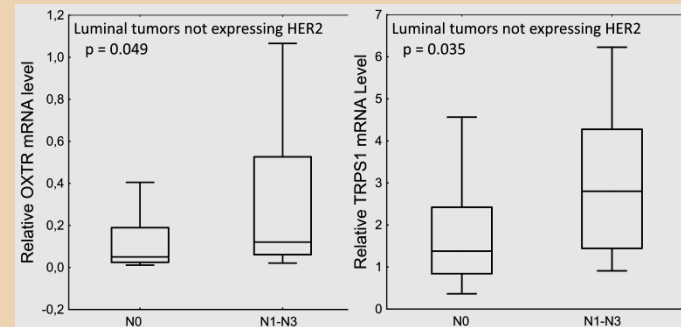


Figure 1. *OXTR* and *TRPS1* mRNA levels in luminal HER2- breast tumors. The upper and lower bounds of boxes denote 75th and 25th percentiles. The horizontal line is the median of changes in the mRNA level in tumor samples relative to paired normal (adjacent) tissue (the results are normalized to control—normal tissue). The whiskers represent a range of values.

Our study indicates the association between the expression of *OXTR*, *STC2*, *TRPS1* and ER expression in BC. We discovered that increased *OXTR* and *TRPS1* mRNA level is a potential marker of LNM in ER- and/or PR-positive tumors with HER2 IHC score 0.