

## Supplementary material

### Altered Expression of *ESR1*, *ESR2*, *PELP1* & *SRC* Genes is Associated with Ovarian Cancer Manifestation

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### Relationship between ER signaling and ovarian cancer

#### *Clinical data correlation*

The Spearman rank correlation test showed patient age positively and strongly correlated with BMI in controls (1<sup>st</sup> subgrouping) and non-cancerous benign ovarian changes (2<sup>nd</sup> subgrouping). None of the other analyzed clinical variables significantly correlated with age of the patients neither in the cancer patients nor in other distinguished groups (independent of 1<sup>st</sup> and 2<sup>nd</sup> subgrouping) (Figure S1).

#### *Gene expression level correlation*

Normalized concentration ratio data (referring to relative expression level) correlation results were presented in Figure S1. In case of the 1<sup>st</sup> subgrouping, in controls, *ESR1* Cr values were proportionally correlated with *PELP1* and *SRC* Cr (weak and moderately, respectively). None of the other correlations were significant in this group, for both gene expression and clinical data. In the ovarian cancer group (1<sup>st</sup> subgrouping), a moderate correlation was shown with *PELP1* with *ESR1* and *SRC* with both *ESR1* and *PELP1* normalized Crs. Taking into consideration the 2<sup>nd</sup> subgrouping, in tissues lacking any changes, a strong correlation was observed for BMI and *SRC* Cr as well as *ESR1* and *ESR2* Cr values. In benign changes of ovary tissue, the normalized Cr values strongly and positively correlated in the case of *SRC* and *PELP1* (Figure S1).

#### *Gene expression quotient ratio correlations*

In the 1<sup>st</sup> subgrouping, the controls, the *ESR1/ESR2* ratio correlated proportionally and very strongly with *ESR1* and moderately with *PELP1* Cr. The *ESR1/PELP1* ratio correlated positively and very strongly with *ESR1* Cr values and *ESR1/ESR2* ratio. Very strong and

proportional correlations were shown in the *ESR1/SRC* ratio and *ESR1* Cr and both *ESR1/ESR2* and *ESR1/PELP1* ratios. In turn, the *ESR2/PELP1* ratio was strongly and negatively correlated with *PELP1* Cr. The *ESR2/SRC* ratio was moderately and negatively correlated with BMI, *PELP1* Cr values, and weakly correlated with *ESR1/ESR2* ratio. A very strong negative correlation was shown with *SRC* Cr. *ESR2/SRC* ratio, only in the case of the *ESR2/PELP1* ratio, was moderately and positively correlated. In the case of the *PELP1/SRC* ratio, negative and strong correlations were shown with BMI and *ESR1/ESR2* and positive for the *ESR2/SRC* ratio (Figure S1).



**Figure S1.** Correlation coefficient plot of 1<sup>st</sup> subgrouping (controls and ovarian cancer patients), and 2<sup>nd</sup> subgrouping (ovarian tissue samples lack of any changes patients and females with beginning non-cancerous changes in the ovary). Designation: NS – not significant; numbers – Spearman rank correlation coefficients; green bars – proportional correlation; red bars – reverse proportional correlation. Green background – clinical data correlations; pink background – genes' expression correlations; yellow background – genes expression quotient ratio correlations.

In ovarian cancer patients of the 1<sup>st</sup> subgrouping, a moderate and negative correlation was shown for the *ESR1/SRC* ratio, *ESR2/SRC* and *ESR2/PELP1* vs. *ESR1* Cr values. Both *ESR1/ESR2* and *ESR1/PELP1* strongly and positively correlated with *ESR1* Cr while *ESR1/SRC* moderately correlated with *ESR1* Cr. The *ESR2* Cr values were negatively correlated at the moderate level with the *ESR1/ESR2* ratio and positively with the *ESR2/SRC* ratio. Strong and positive correlations were observed in case of *ESR2* Cr and the *ESR2/PELP1* ratio. None of the ratios correlated significantly with *PELP1* Cr. *SRC* Cr values obtained in the ovarian cancer patients correlated negatively with ratios of *ESR1/SRC* (moderately), *ESR2/PELP1* (weak), *ESR2/SRC* (strong), and *PELP1/SRC* ratio (very strong). The correlation of *ESR1/ESR2* with

*ESR1/PELP1* and *ESR1/SRC* ratios was proportional and very strong. In turn, *ESR1/ESR2* was strongly and moderately while being negatively correlated with *ESR2/PELP1* and *ESR2/SRC* ratios, respectively. Between *ESR1/PELP1* vs. *ESR1/SRC* ratios, strong positive correlations were shown and were negative moderate with *ESR2/PELP1* ratios. The *ESR1/SRC* ratio was moderately strong and positively correlated with *PELP1/SRC*. In case of both, *ESR2/PELP1* vs. *ESR2/SRC* and *ESR2/SRC* vs. *PELP1/SRC*, a positive Spearman rank correlation was found (Figure S1).

In the ovarian tissue without changes of the 2<sup>nd</sup> subgrouping, the *ESR1/ESR2* ratio was positively strong and very strongly correlated with BMI and *ESR1* Cr, respectively. Both ratios, *ESR1/PELP1* and *ESR1/SRC*, correlated positively very strong with *ESR1* Cr and *ESR1/ESR2* ratios and strongly with *ESR2* Cr. Additionally, *ESR1/SRC* was very strong positively correlated with the *ESR1/PELP1* ratio. The *ESR2/PELP1* ratio was moderately, reverse proportionally correlated with *PELP1* Cr. A negative correlation was also observed between *ESR2/SRC* vs. *PELP1* Cr (moderately strong), and *SRC* Cr (very strong). The *PELP1/SRC* ratio correlated negatively and very strong with *SRC* Cr but positively and very strong with *ESR2/SRC* ratio (Figure S1).

In the ovarian tissue with benign, non-cancerous changes of the 2<sup>nd</sup> subgrouping, *ESR1/ESR2* and *ESR1/PELP1* ratios both correlated positively very strong and *ESR1/SRC* was observed at a strong level with *ESR1* Cr. In turn, *ESR2/SRC* correlated negatively and moderately strong with *ESR1* Cr. *ESR2/PELP1* correlated negatively very strong with *PELP1* Cr, and *ESR2/SRC* was negatively strong with *SRC* Cr and moderately, negatively strong with the *ESR1/ESR2* ratio. *ESR1/PELP1* and *ESR1/SRC* ratios positively and very strong correlated with *ESR1/ESR2* ratios. No other correlations were statistically significant in this group (Figure S1).