# The expression of Prolactin receptor and its ligands in ovarian epithelial tumours

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## Background

Accumulating evidence suggests a role for Prolactin receptor (PRL-R) signaling in ovarian cancer and in the development of chemoresistance. PRL-R functions mainly through binding to Prolactin (PRL), however, both Growth Hormone (GH) and Placental Lactinogen (PL) can also bind to PRL-R, activating the same signaling cascades with no difference in activation based on which ligand binds to the PRL-R.

The aim of this study is to investigate the profile and significance of expression of PRL-R, PRL, GH and PL in ovarian epithelial tumours.

## Material and Methods

We studied the expression of PRL-R, PRL, GH and PL in 503 ovarian epithelial tumours (431 carcinomas, 46 borderline and 26 benign tumours) using immunohistochemistry.

## Results

All tumours expressed PRL-R in epithelial cells. Benign tumours showed significantly stronger expression than other categories ($p<0.001$). PRL-R expression in malignant tumours was significantly stronger in lower grade and higher stage ($p=0.013$ *and* $p=0.037$).

At least one of the three ligands (PRL, GH or PL) was expressed in 92.4% of the studied cases, either in tumour epithelial cells, stroma or both and they tend to be expressed together. In tumour epithelial cells, PRL expression showed positively significant correlation with the expression of both PL ($p=0.009$) and GH ($p<0.001$) while in tumour stromal cells, PRL expression was significantly and positively correlated with GH ($p<0.001$) expression.

**PRL** was expressed in tumour epithelial cells and/or stroma. Stromal expression was significantly higher in borderline tumours compared to other categories ($p<0.001$). PRL epithelial expression in malignant tumours was significantly correlated with shorter patient overall survival ($p= 0.033$).

**GH** was expressed in tumour epithelial cells and/or stroma. Stromal expression was significantly higher in borderline tumours as compared to other categories ($p<0.001$). GH epithelial expression was significantly higher in malignant tumours as compared to other categories ($p<0.001$).

**PL** was expressed in tumour epithelial cells in 50 % of cases. No stromal expression was detected in any of the cases. PL expression was significantly higher in benign tumours compared to other categories ($p<0.001$). PL expression in malignant tumours was significantly higher in low grade ones ($p=0.002$).

None of the three ligands expression was significantly correlated with the response to chemotherapy.

## Conclusions

The expression of PRL-R in 100% of the studied ovarian tumours and the expression of at least one of its ligands in 92.4% of the same tumours confirm the presence of an autocrine loop of PRL-R signaling pathway. It also highlights the potential of PRL-R and its ligands as therapeutic targets in ovarian tumours and in particular borderline and low grade tumours.