

Results and discussions We compared invasion rate of control OAW42 and SKOV3 cells with that of isogenic cell lines containing *ITGBL1* construct. The results indicate that *ITGBL1* overexpression increases invasiveness of ovarian cancer cells.

Conclusion Our results indicate that *ITGBL1* may increase ovarian cancer cell invasion rate. Along with our previous reported results that overexpression of *ITGBL1* may increase migration, decrease adhesion³ and has no effect on proliferation rate,⁴ this results suggests that *ITGBL1* may play an important role in ovarian cancer progression enabling easier spreading of the cells within peritoneal cavity.

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HUMAN LIGASE PROFILING TO PREDICT PLATINUM SENSITIVITY AND CLINICAL OUTCOME IN PRIMARY EPITHELIAL OVARIAN CANCERS

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Introduction Ovarian cancer (OC) is the third most common gynaecological cancer among women worldwide. In Europe, OC is the main cause of death among all the gynaecological tumours. DNA ligases play an essential role in maintaining genomic integrity by joining DNA breaks generated during replication and recombination. The human ligases, *LIG I*, *LIG III* and *LIG IV* are ATP-dependent DNA ligases. Our objective was to evaluate if ligases expressions could predict platinum sensitivity and clinical outcome in epithelial ovarian cancers.

Material and methods Investigation of *LIG I*, *LIG III* and *LIG IV* expression in ovarian epithelial cancer was carried out in 525 consecutive ovarian epithelial cancer cases treated at Nottingham University Hospitals (NUH) between 1997 and 2010. Ligase expression was correlated to clinicopathological features, recurrence free survival (RFS) and ovarian cancer specific survival (OCSS).

Results and discussions High expression of *LIG I* was significantly associated with serous carcinoma ($p < 0.0001$), higher FIGO stage at presentation ($p < 0.0001$), higher tumour grade ($p < 0.0001$), non-optimal surgical tumour de-bulking ($p = 0.004$). High cytoplasmic ligase III expression was significantly associated with higher FIGO stage ($p = 0.002$), higher histology grade ($p = 0.028$), residual tumour following surgery ($p = 0.001$), measurable disease before chemotherapy ($p = 0.006$) and platinum resistance ($p = 0.025$). High *LIG IV* expression was significantly associated with less residual tumour following surgical excision ($p = 0.006$) and better response to platinum based chemotherapy ($p = 0.049$). High *LIG I* and *LIG III* protein expressions were correlated with poor survival outcome. However, *LIG IV* was correlated with favourable outcome. *LIG I* expression was independently associated with poor outcome in cox multivariate model.

Conclusion Human Ligases are promising predictive biomarkers of platinum response and clinical outcome in epithelial ovarian cancer.

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NEUTRALISING EXTRACELLULAR MORGANA IMPAIRS BREAST TUMOUR GROWTH AND MIGRATION

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Introduction Morgana is a ubiquitously expressed protein with chaperone activity *per se* and HSP90 co-chaperone function. High Morgana expression correlates with high tumour grade, mitosis number, and lymph node positivity in different breast cancer subtypes. Several chaperones are overexpressed in a wide range of human cancers and are implicated in tumour progression. Moreover, it has become evident that also from the extracellular compartment, where surprisingly chaperones and co-chaperones are actively released by cancer and immune cells, they favour tumour progression. If, the cytoplasmic role of Morgana has been well characterised in tumorigenesis and metastasis formation of Triple-Negative Breast Cancer (TNBC), nothing is known about extracellular Morgana (eMorgana).

Material and methods Conditioned medium from human and murine TNBCs cell lines were analysed for Morgana presence. To address the role of eMorgana, a Maltose Binding Protein (MBP) fused recombinant protein was produced in ClearColi BL21 and used to evaluate eMorgana role in migration, treating MDA-231 and BT-549. The identification of Morgana receptor was performed indirectly, through the inhibition of Toll-like 2 and Toll-like 4 receptors (TLR2, TLR4). The activity of extracellular Morgana was inhibited, in mice injected with the syngenic cancer cell line E0771, using the homemade blocking antibody 5B11.

Results and discussions Morgana is secreted by TNBC cell lines and as for other chaperones and co-chaperones, Morgana reaches the outside with an unconventional mechanism. From the extracellular compartment Morgana is able to induce cell migration, through the TLR2 and TLR4. Blocking of eMorgana with 5B11 inhibits migration *in vitro* and proliferation *in vivo*. Different efforts are needed to understand if Morgana binds to TLRs alone or through HSP90 and the consequently downstream signalling pathway. Moreover since TLR are prevalently expressed by immune cells it is important to address the role of eMorgana in this context and the possible cross-talk between the tumour and microenvironment.

Conclusion Since TNBCs have an high rate of recurrence and poor prognosis, the identification of innovative treatments is an urgent need. In this view, although many other studies are required, eMorgana in serum patients could represent a new biomarker and its targeting a possible clinical approach in breast cancers.

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CLINICOPATHOLOGICAL SIGNIFICANCE OF EMT MARKERS IN THYMIC EPITHELIAL TUMOURS

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Introduction Thymic epithelial tumours (TETs) are the relatively rare tumours originated from thymus. TETs are histologically categorised according to the WHO classification based on the morphology of epithelial tumour cells and proportion of lymphocytic involvement. Epithelio-mesenchymal transition (EMT) has reported to play pivotal roles in tumour