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 impair ovarian cancer cell invasion rate. Along with our previous reported results that overexpression of ITGBL1 may increase migration, decrease adhesion and has no effect on proliferation rate, 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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PO-236 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.

PO-237 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 theTLR2 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 prevalenty 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.

PO-238 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...
TOWARDS IDENTIFYING KEY DRIVERS OF BREAST CANCER METASTASIS TO THE BONE

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Introduction Metastasis is the cause of death of most cancer patients and approximately 70 percent of metastatic breast cancer patients develop bone lesions. The establishment and growth of metastasis at distant sites is dependent on critical interactions between the tumour cells and the host microenvironment. Our aim is to decipher this process at the molecular level and identify factors that influence migration and invasion of breast cancer cells in the bone.

Material and methods To investigate this mechanism we cultured breast cancer cells with conditioned media derived from bone cells in culture. To best mimic in-vivo conditions, we mechanically stimulated the bone cells to release essential factors that could potentially play significant role in metastasis. As a second approach, we used Chipster software1 to integrate and analyse publicly available gene expression repositories to identify a set of highly dysregulated genes in breast cancer patients who are highly likely to develop bone metastasis.

Results and discussions Having optimised the mechanical stimulation process and identified the best suitable media for the study, our results show that there is a significant increase in the proliferation and migration of breast cancer cells when they are maintained in media derived from mechanically stimulated bone cells. We are currently using cytokine arrays to specifically elucidate the factors in mechanically stimulated bone media that may be responsible for this. Using our second approach we have been able to identify a set of genes that we believe to be involved in breast cancer metastasis to the bone. We further selected a subset of genes and validated protein and gene expression in cell models. We are planning to investigate the expression of these genes in our patient cohort.

Conclusion Our work suggests that bone cells are releasing specific key factors which are regulating the activity of breast cancer cells and allowing them to metastasize to the bone. We have identified genes that are highly dysregulated in tumours with a higher chance of metastasizing to the bone and have verified the expression of these genes in cancer cell lines. This work will help to identify novel therapeutic targets that can prevent bone metastasis in breast cancer patients.

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PO-240 TARGETING CANCER STEM CELLS IN MAMMARY TRIPLE NEGATIVE CELL LINE BY RETINOIDS AND LAPATINIB TREATMENTS

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Introduction Cancer stem cells (CSC) are resistant to chemotherapy and radiation and they are also considered as ‘metastasis seed’.

In order to suggest CSCs as a new therapeutic-intervention target, in this work we propose to study the effect of retinoid ATRA (differentiation therapy) and HER2 inhibitor Lapatinib treatment on:

A. Expression profile of pluripotent genes, retinoid receptors system and E-Cadherin levels.

B. In vitro growth, invasive capacity and in vivo metastatic potential.

For this purpose, we use the triple negative murine cell line 4 T1 (tumorigenic and metastatic in BALB/c mice). Previously we corroborate that CSC from 4 T1, MCF7 and T47D (both these last, HER2 negative human breast cell lines), express HER2 only in that cell component.

Material and methods

- Experimental Model: triple negative murine cell line 4 T1 (tumorigenic and metastatic in BALB/c mice).
- Treatments: ATRA (1 μM) and Lapatinib (1 μM)
- RT-qPCR were used to evaluate retinoic acid receptors and pluripotent genes expression- Mammmospheres culture was used to enrich in CSC component.
- Clonogenic assay was performed by seeding CSC in low density