COMPARISON OF EXPRESSION OF MIR21

Introduction miR-21 is an oncomir that is overexpressed in many types of solid tumours. According to some studies miR-21 expression is higher in breast tumours than normal breast tissue and it is significantly correlated with shorter survival of patients. Many studies have focused on miR-21–5 p and its correlation with clinic pathological features and survival of breast tumours. In some of the studies miR-21–5 p expression has been shown to be associated with ER status, PR status, HER2 status, clinical stage, lymph node, tumour grade and size. The purpose of this study was to compare the expression of miR-21–3 p and miR-21–5 p in progression of breast tumours and their association with corresponding clinic pathological data from the breast cancer patients.

Material and methods Six non-neoplastic breast tissues and 144 tumours, from breast cancer patients diagnosed 1987–2003, were obtained from the Department of Pathology at Landspitali University Hospital. The expression levels of miR-21–3 p and miR-21–5 p were measured with StepOnePlus Real-Time PCR System by applying EXIQON primer sets and SYBR Green master mix using miR-16–5 p as endogenous control.

Results and discussions In the evaluation cohort (n=24 early breast cancer cases) the TEP RNA-based breast cancer classification had an accuracy of 90% with an AUC of 0.96 (95% confidence interval (CI) 0.92–1.00; p<0.001). In the validation cohort, the TEP RNA-based classification algorithm reached an overall accuracy of 86% and an AUC of 0.93 (95% CI 0.89–0.98, p<0.001). Most important, the accuracy was 91% in stage I/II disease. In a confirmatory rule-out application (positive mammography) sensitivity would be 94% with a specificity of 67%; whereas in a screening setting sensitivity would be 80% with a specificity of 93%. The classifier performance is consistent across subgroups based on patient age, tumour stage, subtype, tissue density, or BRCA1/2 status. The breast cancer TEP profiles were distinct from those of women with other tumour types (n=192, accuracy: 87%, AUC: 0.91, 95% CI 0.87–0.96, p<0.001). Although results look promising, sensitivity and specificity should be improved for clinical implementation. Follow-up studies should, among others, require sample collection in actual screening and confirmatory settings.

Conclusion We show that platelet RNA signatures may enable blood-based screening for early breast cancer, and warrant validation in a confirmatory and screening setting.

A NOVEL ROLE FOR JUNCTIONAL ADHESION MOLECULE-A (JAM-A) IN HER2-POSITIVE GASTRO-OESOPHAGEAL CANCERS

Introduction Junctional Adhesion Molecule-A (JAM-A) is a cell-cell adhesion protein that regulates physiological adhesion in epithelial and endothelial cells. Our previous work has shown that increased JAM-A expression on breast tumour epithelial tissue associates with poor prognosis in patients with invasive breast cancer, and identified a correlation between high JAM-A expression and levels of the important oncoenzyme human epidermal growth factor receptor-2 (HER2). An important role for HER2 in gastro-oesophageal cancer is emerging, however the specific role of JAM-A in this setting is unclear.

Material and methods In a pilot study, gastric cancer patient tissue sections (n=11) were stained for JAM-A expression. A
LOSS OF SOX9 EXPRESSION IS A PREDICTIVE MARKER OF RELAPSE IN GASTRIC CANCER

1P Mesquita*, 1AF Freire, 1N Lopes, 2B Cavadas, 1B Pereira, 1R Barros, 1RJ Coelho, 1DL David, 2L Pereira, 1,3,4RA Almeida. 1i3S/IPATIMUP – Institute for Research and Innovation in Health/Institute of Molecular Pathology and Immunology of the University of Porto, Differentiation and Cancer, Porto, Portugal; 2i3S/IPATIMUP – Institute for Research and Innovation in Health/Institute of Molecular Pathology and Immunology of the University of Porto, Genetic Diversity, Porto, Portugal; 3Faculty of Medicine of the University of Porto, Pathology, Porto, Portugal; 4Faculty of Sciences of the University of Porto, Biology, Porto, Portugal

Introduction Gastric cancer is one of the most frequent tumours and the third leading cause of cancer-related death worldwide. The investigation of new biomarkers that can predict patient outcome more accurately and allow better treatment and follow-up decisions is of crucial importance. The transcription protein SRY-box 9 (SOX9) is a member of the high-mobility-group box class DNA-binding proteins. SOX9 is an important regulator of cell-fate decisions in embryogenesis and adulthood, playing critical roles in differentiation and proliferation, also in the gastrointestinal tract. SOX9 has been correlated to tumour behaviour in different tissues, including in gastric cancer, nevertheless with contradictory results. In this work we sought to ascertain the relevance of SOX9 transcription factor as a prognostic marker in gastric cancer.

Material and methods SOX9 expression was analysed by immunohistochemistry in a series of 333 cases of gastric adenocarcinoma, and its association with clinico-pathological and follow-up data was evaluated. A second gastric cancer validation cohort consisted of 354 cases from the cancer genome atlas (TCGA), showing high versus low SOX9 expression.

Results and discussions SOX9 expression was present in 83% of gastric cancer cases. Loss of SOX9 expression was significantly associated with relapse, however SOX9 expression was more frequent in stage IV cases. SOX9 loss of expression predicted worse disease-free survival but not overall survival, in this series. The prognostic value of SOX9 was independent of Lauren classification but it was more pronounced in tumours with expansive versus infiltrative growth (p=0.008). In patients that presented with disease in stage I to III, loss of SOX9 expression was significantly associated with venous invasion and lymph node metastases. In an independent series of gastric cancer, where SOX9 expression was assessed at the mRNA level (TCGA), low SOX9 expression levels were also associated with poor patient outcome. Functional studies, after down- and up-regulation of SOX9, are now being undertaken in order to better understand the clinico-pathological observations and the relevance of SOX9 as a potential biomarker in gastric cancer.

Conclusion We have identified SOX9 as a marker of relapse in gastric cancer. Further experiments are needed to elucidate its biological relevance at the cellular level and to test its potential role in invasion.

PO-502 A POTENTIAL ROLE FOR HSP90 IN HER2-DRIVEN BREAST CANCER (BC)

1I Falcone*, 2L Carbognin, 1L Ciuffreda, 1F Conciatori, 1C Bazichetto, 1F Cognetti, 1G Tortora, 1M Millesi, 2E Bria. 1Regina Elena National Cancer Institute, Medical Oncology I, Rome, Italy; 2University of Verona- A.O.U., Breast unit, Verona, Italy; 3University of Verona- A.O.U.-, Breast Unit, Verona, Italy

Introduction HER2 (amplified in 30% of BC) is involved in the activation of many pathways and its function is regulated by HSP90. Thus, HSP90 co-targeting is emerging as a potential molecular target for HER2-directed BC therapy.

Material and methods We analysed HER2 and HSP90 expression in a panel of BC cell lines, including MCF7 cells stably transfected with a constitutively active HER2. HER2/HSP90 expression and growth inhibition were monitored over time upon exposure to trastuzumab (T) and docetaxel (D), in the presence or absence of HSP90 silencing. We also retrospectively evaluated a series of 24 locally advanced/operable BC patients (pts) who underwent neoadjuvant T+D for HSP90 expression and correlated it with pathological complete response (pCR).

Results and discussions In the BC cell lines analysed there was no clear-cut correlation between HSP90 and HER2 expression. HER2 transfection into MCF7 cells increased HSP90 mRNA and protein expression; however, treatment with T further increased HSP90 levels. Conversely D increased HER2, but did not affect HSP90, expression. In HER2 +BC cell lines, simultaneous T+D combination resulted in synergistic growth inhibition in vitro, while their staggered combination, particularly T followed by D, did not afford synergistic effects. Effects of simultaneous and staggered treatments on HSP90 and HER2 expression were analysed by WB: HER2 expression decreased in the simultaneous and staggered combination (D followed by T), while HSP90 expression did not change upon combined treatment. The effects of HSP90 silencing and overexpression on functional response to T+D are being analysed in HER2 +BC models: preliminary results indicate that HSP90 silencing in HER2 +BC decreases the therapeutic synergism of the simultaneous T+D combination. Accordingly, in