OT with worst prognosis presented increased levels of Phosphocholine, Choline, Fatty acids and Alanine. In the same way OT harboring 1p/19q ROH present higher glutathione levels.
Conclusions: Each tumour is singular but alterations detected in this study depict the genetic landscape for oligodendroglial tumours and could reveal the divergent response showed by these molecular subgroups in survival and chemotherapy treatment.

808 Comparative proteomic study of multidrug resistance in chronic myeloid leukemia

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Background: Chronic myeloid leukaemia (CML)'s treatment has improved with the advance of Imatinib mesylate (Glivec®, IM, Norvatis). IM is a tyrosine's kinase inhibitor for CML biomarker, the BCR-ABL oncoprotein. Despite this improvement, BCR-ABL dependent and independent mechanisms of IM therapy's resistance are known to occur. The latter has been associated to multidrug resistance (MDR) phenotype emergence. MDR is known as the major cause of failure in cancer treatment, and it is most related with the expression of ABC transporters, such as P-glycoprotein (Pgp – *ABCB1*). Although the identification and the knowledge of ABC transporters, the resulting pathways in drug resistance in leukemic cells remain uncharacterized. In the present work, we investigated the possible relationship between MDR and resistance to IM therapy in CML.
Material and Methods: We screened drug transporters and *BCR-ABL* RNA transcripts levels, by real time Q-PCR, in the multidrug resistant cell line Lucena (K562/VCR) and verified its cellular viability, apoptosis and cell cycle after IM treatment. Then, we compared its proteomic profile to the parental cell line K562. Proteomics results were validated *in vivo* by real time Q-PCR and multivariate statistical analysis were applied.
Results: Our results demonstrate that MDR cell line Lucena has a resistant pattern to IM treatment. The proteomic approach resulted in identification of forty-six differentially expressed proteins. Among them, *LRPPRC, MCM7* and *RBM17*, jointly with *ABCB1* gene, were validated in fourteen CML patients and six donors. We found, through multivariate statistical analysis that, altogether, they were able to categorize patients' status as responsive or resistant to IM therapy.
Conclusions: By the data presented in this work, we showed that MDR can be closely attached to IM's failure, demonstrating its importance as a CML's prognostic factor. Moreover, the proteomic approach pointed out some new possibly markers associated in MDR phenotype, which could lead to additional information of this phenomenon and clinical improvement for MDR detection in patients.
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809 Prediction of lymph node metastases in small T1 breast cancers by expression profiling

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Background: The principal cause of mortality in breast cancer is distant metastases. Tumour size and lymph node positivity were classically used as prognostic factors for relapse risks. However, up to 30% of lymph node negative patients eventually develop metastases. We aimed to study breast cancers less than or equal to 2 cm where metastases to regional lymph nodes is generally uncommon, and hypothesised that these small tumours have acquired the ability to metastasise as an early event in oncogenesis.
Methods: Fresh frozen tissues from breast tumours that were $\leqslant$2 cm, positive (n = 23) and negative (n = 42) for lymph node metastases were expression profiled using the Illumina HumanWG-6 v3.0 Expression BeadChips.
Results: Distinct differences in the expression profiles between oestrogen receptor positive (ER+) tumours as compared to the oestrogen receptor negative (ER−) tumours were obtained by unsupervised clustering. As such, we subsequently performed supervised clustering on ER+ tumours (n = 47) and ER− tumours (n = 16) as separate subgroups using genes that were differentially expressed and with *P* values of <0.05. Our analysis showed segregation of breast cancers that were lymph node positive from those that were lymph node negative in ER− tumours. There were four HER2 positive tumours (defined as having immunohistochemical staining of 3+ or positivity with fluorescence *in situ* hybridisation) in this ER− subgroup. By selecting only genes that had at least 2-fold differences between the node negative and positive tumours, we identified 53 differentially expressed genes which were mostly involved in signal transduction, cell communication, metabolic processes and response to stimuli. Of these 53 genes, 13 were downregulated and 40 were upregulated in those with lymph node metastases.
Conclusion: Our results suggest that in ER− breast cancer, it may be possible to discriminate patients with or without lymph node metastases using gene expression profiling. The details of the differentially expressed genes will be presented at the meeting. We will perform further validation on an independent set of breast tumours.

810 Differential enrichment of pathways in association with TP53 mutation status of breast cancers

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Background: Various studies have so far tried to explain the biology of breast cancer associated with TP53 mutation status in terms of differential expression of genes. Keeping in view that altered functions of many genes belonging to specific biological pathways might result in a particular tumour phenotype, we attempt to infer the association of key pathways related gene sets that might play important role in development of breast cancers with wild type or mutant TP53 status.
Material and Methods: A single expression dataset based on Agilent whole genome microarrays platform, consisting of total 111 samples with 73 wild-type TP53 and 38 mutant TP53 status, was analysed by fitting a regression model as proposed by (Goeman *et al*., 2004, 2009) with gene expressions being the covariates and phenotypic data (TP53 mutation status of breast cancer) as the response variable. We also applied iterative signature algorithm (Bergmann *et al*., 2003, Csárdi 2009) in order to identify modules with enrichment of specific key pathways in our dataset.
Results: Using multiple test-corrected p-values based ranking, we identified top 20 important biological pathways (KEGG) and their associated genes. We also studied the extent of inter-sample similarity in pathway representation. Apart from p53 signaling pathway, we found differentially expression of purine metabolism; glycine, Serine and threonine metabolism; prostate cancer and vitamin B6 metabolism pathways. The biclustering analysis identified a module showing differential enrichment of key pathways − p53 signaling pathway, cell cycle and DNA replication and differential co-expression of corresponding genesets. Another module identified differential enrichment of immune response related pathways – such as cytokine-cytokine receptor interaction, T cell receptor signaling pathway, natural killer cell mediated cytotoxicity pathway.
Conclusions: Our findings from biclustering algorithm add valuable information to the findings from regression model-based pathways analysis and provide new insights about the potential pathway alterations that might be responsible for breast cancer development in association with TP53 mutation status. However, it remains to be established, which alterations are responsible for the cancer development and which alterations are consequences or mere associations to the TP53 mutation status. Therefore, we propose more detailed studies aiming at investigation of the association and possible role of certain pathways, such as purine metabolism and vitamin B6 metabolism pathway, immune response related pathways including natural killer cell mediated cytotoxicity pathway – in breast cancer development.

811 8q24 amplification in metastatic endometrial cancer

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Amplification of 8q24 is a hallmark of metastatic cancer. The target genes of 8q24 somatic amplification have not been precisely established. So far, investigations on different (but also on the same) cancer types have produced varying results. The *EIF3S3* and *ASAP1* have been proposed as targets in prostate cancer, the *PTK2* and *EIF3S3* – in hepatocellular carcinoma, the *BOP1* – in colorectal cancer, etc. The *MYC* and *PRL3* are two of genes in this region, known to be overexpressed in many cancer types, however this has not always been associated to gene amplification.
Endometrial tumours are particular for their paucity of genomic amplification, however overrepresentation of the 8q24 region has been described in metastatic endometrial cancer (EC). We compared the amplification profiles of 5 metastatic (MEC) and 20 metastasis-free EC samples (NMEC) by using Illumina 660K SNP-array. Tissue samples were obtained at the University Hospital of Obstetrics and Gynaecology "Maichin Dom", Bulgaria. All patients gave informed consent.