microenvironment. Neutralising VEGF by avastin effectively abrogates metastasis induced by the ISX-BRD4 complex. In NSCLC carcinoma samples, significantly increased ISX expression was noted, correlating with distinct clinical metastatic features and poor prognosis.
Conclusion These results suggest that the ISX-BRD4 axis mediates EMT signalling and exerts significant regulatory effects on tumour initiation and metastasis.

PO-355 ENHANCERS MAPPING UNCOVERS PHENOTYPIC HETEROGENEITY AND EVOLUTION IN PATIENTS WITH LUMINAL BREAST CANCER

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Introduction Breast cancer (BC) is the most common cancer type and the second most frequent cause of cancer related death in women. 70% of all BC cases contain variable amounts of oestrogen receptor-alpha (ERα) positive cells. ERα is central to BC pathogenesis and serves as the target of endocrine therapies (ET). ERα-positive BC is typically subdivided in two 'intrinsic' molecular subtypes (luminal A and luminal B) characterised by distinct prognosis, highlighting functional inter-patient heterogeneity. Recent analyses demonstrate that patient-to-patient heterogeneity is more pervasive (reflected by histological, genetic architecture and transcriptional differences) ultimately influencing long-term response to endocrine treatment. Additionally, the presence of genetic intra-tumour heterogeneity has also now been extensively documented in several cancer types, demonstrating the role of clonal evolution in cancer. Parallel to genetic evolution, phenotypic/functional changes driven by epigenetic mechanisms can also contribute to breast cancer progression and ET resistance in cell lines. Nevertheless, little is known about the epigenome of BC patients, its influence on intra-tumour phenotypic heterogeneity and its role in breast cancer progression.
Material and methods Here we show the results of a systematic investigation of the epigenetic landscape of ERα positive primary and metastatic breast cancer from 47 individuals. Our results represent the first large scale topographic mapping of the active regulatory landscape of longitudinal ERα-positive BC. Using H3K27ac we mapped active promoters and enhancers across treatment naïve primary and endocrine treated metastatic patients. We used bioinformatic approaches to deconvolute the complex regulatory landscape and identified inter- and intra-patient epigenetic heterogeneity.
Results and discussions We mined promoters and enhancers from clinically relevant breast cancer samples for potential regulatory drivers identifying YY1 as a novel key player in ERα-positive BC. Finally, we demonstrate that epigenetic mapping can efficiently estimate phenotypic heterogeneity changes throughout BC progression.
Conclusion Collectively, our data show that epigenetic mechanisms significantly contribute to phenotypic heterogeneity and evolution in systemically treated breast cancer patients.

PO-356 WHITE BLOOD CELLS FROM PROSTATE CANCER PATIENTS CARRY DISTINCT CHROMOSOME CONFORMATIONS

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Introduction Current diagnostic blood tests for prostate cancer are unreliable for the early stage disease, resulting in numerous unnecessary prostate biopsies in men with benign disease and false reassurance of negative biopsies in men with prostate cancer. Three-dimensional genome architecture and chromosome structures undergo early changes during tumourigenesis both in tumour and in circulating cells and can be potentially used for cancer diagnosis.
Material and methods In this report, we have performed chromosome conformation screening for 14 240 chromosomal loops in the loci of 425 cancer related genes in peripheral blood mononuclear cells (PBMCs) of prostate cancer patients (n=107) and non-cancer controls (n=105).
Results and discussions Our data show that PBMCs from prostate cancer patients acquire specific chromosome conformation changes in the loci of cancer-related genes. New chromosomal loops in the loci of CASP2, ETS1, SLC22A3, MAP3K14 genes were unique to the prostate cancer cohort. In prostate cancer patients, chromosome conformations identified in PBMCs had high similarity to those in primary prostate tumours. Blind testing on an independent validation cohort of prostate cancer patients yielded prostate cancer detection with 80% sensitivity and 80% specificity.
Conclusion Our results indicate that there are specific chromosome conformations in the blood of prostate cancer patients that are not present in control group. These conformations are shared between PBMCs and primary tumours, but exact mechanism of their appearance is not yet identified. It is possible that these epigenetic signatures may potentially lead to development of a blood-based prostate cancer diagnostic tests. Similar approaches could be used to investigate the prognostic significance of these signatures to determine the risk of tumour progression.

PO-357 SREBP1 DRIVES CELL-AUTONOMOUS CYTOSKELETAL CHANGES BY KRT80 REMODELLING DURING ERα BREAST CANCER PROGRESSION

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Introduction Approximately 30% of oestrogen receptor α positive (ERα) breast cancer patients progress to invasive metastatic disease despite adjuvant treatment with targeted endocrine