a superior anti-tumour activity *in vivo*, in both cell line derived and patient-derived xenograft models.

Conclusion The AP-1 transcriptional complex plays an important role in the resistance mechanism of HNSCC and ESCC cancer to inhibition of the PI3k pathway. These results support the rational for combined inhibition of JNK\c-JUN\AXL axis and PI3K in HNSCC and ESCC patients.

PO-449 **3D GLIOMA-ON-A-CHIP MODELS FOR PERSONALISED MEDICINE IN ORGANOPLATES®**

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Introduction Treatment of gliomas is complicated by variable response rates of individual patients' tumours to therapies. The Department of Neurosurgery of the Erasmus MC has developed a 2D culture platform (GLIOscreen) for screening patient-derived glioma tissues with potential therapeutic compounds. Unfortunately, not all patient-derived glioma tissues are amenable to 2D culture, probably caused by tumour heterogeneity, raising the necessity for additional, complementing culture models.

Material and methods Here we show the development of an organotypic glioma model in the OrganoPlate to establish screenable cellular models for all glioma patients. The OrganoPlate is an easy to use, high throughput microfluidic platform enabling 3D cell culture and co-culture options, creating physiologically relevant models with a minimal requirement of cell material.

Results and discussions The 3D glioma model will be used to culture individual patient's cancer cells for the screening of potential effective (combinatorial) treatments, such as Temozolomide, a first line therapy in glioma treatment. GLIOscreen-derived glioma cell line GS261 was seeded in BME2 (reduced growth factor ECM), in the OrganoPlate and cultured for 8 days. On day 8 cells were analysed by phase contrast imaging and the live/dead cell viability assay (Life Technologies). The cell viability can also be studied in time with RealTime-Glo (Promega), a non-toxic cell viability assay.

Conclusion Glioma cells can be cultured in the OrganoPlate for up to 2 months and are suitable for high-throughput chemotherapeutic drug screening.

Molecular pathology

PO-450 **INTERPLAY BETWEEN CODING AND NON-CODING GENOME IN HUMAN PARATHYROID TUMOURS**

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Introduction Parathyroid tumours are the second most common endocrine neoplasia in women, after thyroid cancer. Mutations in the oncosuppressor CDC73 are the key event in most carcinomas whereas alterations in the tumour suppressor MEN1 (located at 11q13.1) occur in up to a third of sporadic adenomas. Although lncRNAs play a regulatory role in endocrine cancer pathogenesis, a lncRNAs profiling in human parathyroid tumours is still missing. Here, we identified a 'molecular signature' able to distinguish among parathyroid histotypes and a new potential epigenetic role of MEN1 in lncRNAs regulation.

Material and methods Ninety lncRNAs were investigated in 4 parathyroid carcinomas (PCas), 12 adenomas (PAds) and 2 normal glands (PaNs). Hierarchical clustering (HCL) and Significance Analysis of Microarray (SAM) were performed to identify differences in lncRNAs expression. Significant lncRNAs were validated in additional 7 PCas, 26 PAds, 6 atypical PAds (aPAds) and 4 PaNs. CDC73 and MEN1 genes mutations were detected by Sanger sequencing. PAds genomic characterisation was obtained by array Comparative Genomic Hybridization (aCGH). HEK293 cells were transiently silenced for MEN1 expression to analyse MEN1-lncRNAs correlation.

Results and discussions Nine lncRNAs were identified as differentially expressed in parathyroid tissues. Specifically, KCNQ1OT1 and SNHG6 were enriched in PaNs, reduced HAR1B, MEG3, HOXA3as and NEAT1 expression characterised PAds, whereas BC200, HOXA6as and WT1-AS were upregulated in PCas. HCL identified 3 clusters in which PaNs and PCas were distinctly separated, while aPAds were closer to PCas. Moreover, PAds clustered in a highly heterogeneous way. Notably, PCas and aPAds harbouring CDC73-mutations overexpressed the majority of the lncRNAs, compared to CDC73 wild-type samples. Interestingly, BACE1-AS, KCNQ1OT1, NEAT1 and SNHG6 levels in PAds were positively correlated with MEN1 levels. aCGH analysis revealed that Chr11 loss of heterozygosity (LOH) was the main chromosomal aberration in PAds. Of note, Chr11 LOH was associated with significant HAR1B upregulation and these data were confirmed in HEK293 cells knocked-down for MEN1.

Conclusion Parathyroid histotypes are characterised by different lncRNAs signatures, suggesting a correlation with tumour aggressiveness and pathogenetic mechanisms. Further, our data highlight that lncRNAs profiles are related to CDC73 gene mutation status, chromosome 11 derangements and MEN1 inactivation.

PO-451 **TARGETED PROTEOMICS TO IMPROVE THERAPY STRATIFICATION OF CANCER PATIENTS**

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Introduction The heterogeneity of tumours calls for patient stratification to select the most effective, personalised therapies. The NCT MASTER (Molecularly Aided Stratification for Tumour Eradication Research) program aims at comprehensive characterisation of cancer patients seen at NCT Heidelberg and Heidelberg University Hospital. SNVs, small InDels, CNVs, and gene expression data obtained by whole-genome/