Introduction Novel marine compounds supposed an unexplored source of new drugs and expand the possibilities of finding active molecules in all the different signatures of cancer, such as proliferation, invasion and metastases. Here we report the capacity of four marine invertebrate extracts that inhibit proliferation, invasion and migration in colon cancer cell model.

Material and methods HCT116 cell line was cultured and exposed to four marine invertebrate extracts (CR from a red coral, PS from an holothurian and NA and NB from nudibranchs) at different concentrations for 24 hour and IC50 was calculated by MTT assay to estimate cytotoxic activity. The rate of cell proliferation and migration was monitored in real-time with the xCELLigence system with E and CIM-16 plates, respectively (Roche Diagnostics GmbH, Germany), which were set in a humidified incubator and maintained in 5% CO2 at 37°C. The impedance value of each well was automatically monitored by the xCELLigence system for 72 hour and expressed as a cell index (CI) value. The anti-invasive rate was determined by Corning BioCoat Matrigel Invasion Chambers with 8.0 μm PET Membrane 24-well Plates (Corning, NY, USA), and crystal violet assay was used to calculate CI.

Results and discussions The four marine invertebrate extracts exhibited pronounced cytotoxic and antiproliferative effect in HCT116 model at different doses. The migration assays revealed that CR and especially NB extracts reduced the migration ability of HCT116 cells.

Conclusion The results support the antiproliferative, anti-migration and anti-invasive activity of CR, PS, NA and NB marine invertebrate extracts in the highly invasive colon cancer model HCT116. Due to its strong activity, further studies will be focused on the potential of NB extract in the inhibition of metastases-related processes.
Material and methods Using DNA microarrays, ChIP-Seq, qRT-PCR, immunohistochemistry (IHC) and RNA interference (RNAi) for *in vitro* and inducible shRNA constructs for *in vivo* experiments, we functionally characterised the role of SOX6 in EwS.

Results and discussions Using microarray analysis of cancer and normal tissue samples as well as IHC, we show that the transcription factor SOX6 is strongly but variably overexpressed in EwS. Analysis of publicly available ChIP-Seq data revealed a prominent EWSR1-FLI1 peak in intron 1 of SOX6 that overlaid with regulatory histone marks and mapped to a GGAA-mSat, which showed EWSR1-FLI1-dependent enhancer activity in reporter assays. Notably, the number of consecutive GGAA-repeats at this microsatellite correlated with the SOX6 expression levels of EwS cell lines. These data prove that SOX6 is a direct EWSR1–FLI1 target gene controlled by an intronic GGAA-mSat.

Functionally, RNAi-mediated SOX6 knockdown significantly reduced proliferation and clonogenic growth of different EwS cell lines through G2-phase arrest and induction of cell death. Inducible shRNA-mediated SOX6 knockdown markedly reduced tumour growth of EwS xenografts *in vivo*. Consistently, gene-set enrichment analysis of primary tumours and cell lines after SOX6 knockdown showed that SOX6 is associated with cell cycle progression. By crossing transcriptome profiles of SOX6-silenced EwS cells and ChIP-Seq data for SOX6, we identified three likely direct SOX6 target genes, which cooperate to promote its pro-proliferative effect. Through analysis of published drug-screen data and functional drug-response assays we found that SOX6 overexpression confers an exquisite sensitivity to Bora-depleted cells shed light on the underlying pathways. In addition, a pre-clinical *ex vivo* model using patient ascitic cells showed that BORA ablation decreased the tumor-sphere forming capacity and spheroid viability, a phenotype reproduced in the *in vivo* model by a reduction in tumour growth.

Conclusion Collectively, our data indicate that SOX6 is a direct EWSR1-FLI1 target gene contributing to proliferation, clonogenicity and tumour growth of EwS cells, and that high SOX6 expression may constitute a druggable vulnerability of EwS.

**PO-048 THERAPEUTIC RELEVANCE OF THE CELL CYCLE PROTEIN BORA IN CANCER**

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Introduction Polo-like kinase 1 (Plk1) is an attractive mitotic target to treat cancer. A variety of anti-Plk1 agents are presently in clinical trials with successful results. Nonetheless, the use of Plk1 ATP-competitive inhibitors have been associated to dose-limiting toxicity and low specificity. Hence, to find alternative strategies to target Plk1 with less adverse effects is paramount. We propose to target the C-terminal part of Plk1 by its main coactivator, BORA (Aurora Borealis) since BORA binds to the Plk1-PDB and changes Plk1’s conformational status to be active. BORA *per se* has been described as a regulator of spindle stability being essential for proper chromosome segregation and disorders in genomic integrity generate vulnerabilities that can be exploited therapeutically. In this regard, we aim to provide new insights into the mechanistic consequences of BORA inhibition in cancer as potential therapeutic tool.

**PO-049 QUANTITATIVE PROTEONICS UNVEILS KEY MITOTIC REGULATORS INVOLVED IN THE TRANSITION TO ANDROGEN INDEPENDENT PROSTATE CANCER**

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Introduction Prostate cancer (PCa) is the most commonly diagnosed invasive malignancy and the second leading cause of cancer-related deaths among men. Androgens are crucial for the initiation and progression of PCa and thus, androgen deprivation therapy (ADT) has been the standard first line therapy for the early metastatic disease for over 40 years. Almost all PCa patients initially respond to different types of androgen ablation, however the majority of them develop resistance and progress to a castration-resistant PCa (CRPC) state, where the disease remains untreatable. The project aims at gaining novel molecular insights into PCa progression, with special emphasis on the involvement of mitotic regulators in androgen dependent and independent tumours.

Material and methods LNCaP androgen dependent (AD) cell line, representing an early stage of the disease, and its androgen independent (LNCaP-PI) counterpart, that represent the transition to a castration-resistant stage, were used. Cells were arrested in mitosis and proteomes were compared using SILAC in combination with LC-MS. Protein candidates were further