Results and discussions Our in-house pipeline ChimComp allowed the detection of 118 new potentially oncogenic fusions. Following the validation by RT-qPCR, we showed that ChimComp could be reliable at ~90%. A new fusion, LMO3-BORCS5, was found in a patient with EWS and in 12 cell lines from different origins suggesting that it is not an isolated event. Then, we explored the function and oncogenic potential of LMO3-BORCS5. Until now, we show that the stable transfection of this fusion into A673 Ewing’s sarcoma and NIH3T3 murine fibroblasts cell lines, leads to an increase of cell proliferation and an increase or an induction of tumorigenicity after injection in mice, as well as a decrease of sensitivity to antitumor drugs vincristine and camptothecin in A673 cells.

Conclusion Our results support PLCG1 playing a major role in controlling CTCL progression towards advanced stages. Downstream of PLCG1 or due to genetic amplification, PRKCQ can mediate the activation of NFAT and STAT3. Thus, mutations in PLCG1, PRKCQ amplifications and/or nuclear NFAT and STAT3 accumulation can serve as diagnostic markers for CTCL. Moreover, these can also provide rational to develop specific therapies targeting PRKCQ alone or in combination with calcineurin or JAK-STAT inhibitors.

Poster Presentation: Translational Research
Bioinformatics in Therapies and Clinical Trials

PO-508 DETECTION AND ROLE OF NOVEL FUSION ONCOGENES IN PAEDIATRIC CANCERS

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Introduction Paediatric cancers (PC) represent the 1st cause of death by disease in children as 20% of patients still die from a recurrence of the malignancy. PC differ from adult cancers regarding their aetiology, cellular origin or mutational rate. Improving the knowledge on the biology of the relapsed tumours and identifying new targets are needed to provide new treatments. Fusion genes are responsible for ~20% of cancers and are the consequence of the juxtaposition of two previously separate genes which can activate proto-oncogenes or inactivate tumour suppressor genes. They are of great interest in clinics as they can be used as therapeutic targets or biomarkers. Our aim is to explore new fusion genes in relapsing/resistant paediatric patients through bioinformatics analysis of the NGS data from the molecular profiling program MOSCATO-01, and to study their function and oncogenic potential.

Material and methods We developed an approach to optimise the detection of fusion transcripts in RNA-seq data. A biological validation of selected candidates was performed by RT-qPCR in patients’ tumour samples and available cell lines. A fusion never previously described found in a Ewing’s sarcoma (EWS) patient retained our attention; therefore we established 2 cellular models in order to assess the effect of this transcript on proliferation, migration, sensitivity to antitumor agents, gene expression in vitro and tumorigenicity in mice.

Results and discussions Our in-house pipeline ChimComp allowed the detection of 118 new potentially oncogenic fusions. Following the validation by RT-qPCR, we showed that ChimComp could be reliable at ~90%. A new fusion, LMO3-BORCS5, was found in a patient with EWS and in 12 cell lines from different origins suggesting that it is not an isolated event. Then, we explored the function and oncogenic potential of LMO3-BORCS5. Until now, we show that the stable transfection of this fusion into A673 Ewing’s sarcoma and NIH3T3 murine fibroblasts cell lines, leads to an increase of cell proliferation and an increase or an induction of tumorigenicity after injection in mice, as well as a decrease of sensitivity to antitumor drugs vincristine and camptothecin in A673 cells.

Conclusion These results suggest that LMO3-BORCS5 could play a key role in tumorigenesis and in response to treatment and could be used as a therapeutic target for patients where LMO3-BORCS5 is detected. More broadly, this study emphasises the key role of fusion genes in disease progression and their clinical interest in personalised medicine.
proposed a specific treatment for luminal tumours (androgen receptor inhibitors) and for immune high tumours (immunotherapy).

**PO-510 INVESTIGATION OF POTENTIAL THERAPEUTIC TARGETS BY USING IN SILICO METHODS IN GLIOBLASTOMA**

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**Introduction** Glioblastoma is the one of the most common primary malignant tumour of brain. Due to anatomical and physiological characteristics of brain, drug delivery to the tumour site is hampered. In glioblastoma, survival time is short and recurrence is generally inevitable. The metastatic dissemination of glioblastoma is relatively rare but it could be more aggressive. Therefore, in vitro and in silico studies are accelerated in terms of the investigation of molecular characteristics of metastatic glioblastoma. The aim of this study, to investigate the expressed biomarkers of immigrant glioblastoma cells and potential therapeutic targets by using in silico methods.

**Material and methods** GEO (Gene Expression Omnibus) of the National Cancer Institute (NCI) provides an international public repository of research society, which archives and freely distributes microarrays, next generation sequencing and other forms of high-resolution functional genomic data. Data set enumerated as GSE76018, is used for this research from GEO data portal. The data was analysed by using R software for statistical calculations and graphs. The level of the gene expression, and the resulting data were standardised by calculating a z-score, the fold changes (log2FC). As a threshold, |log2FC| ≥2 and adjusted p-value was accepted as ≤0.05. Heat maps were drawn using a hierarchical clustering method in R-Bioconductor’s Heatplus library. Functional annotation tools and to understand biological meaning behind large list of genes analysed by using DAVID bioinformatics resources.

**Results and discussions** JAK-STAT pathway is found by using DAVID bioinformatics database. IFNA8, IL9, SOCS1, JAK3, CSH1, IFNL2 and IL12RB2 genes have played an active role in charge of protein coding Janus kinase (JAK) 2/signal transducer and activator of transcription (STAT) 3 pathway. So these genes affect the migration of glioblastomas and biomarkers is except to be effective at drug target. Sifalinumab and Rontalizumab connected to IFNA8, IL9 related to Enokituzum, also JAK3 linked to Tofacitinib.

**Conclusion** As a result of our investigation, JAK-STAT pathway, which is known to be an important mediator of tumour cell survival, growth and invasion in glioblastomas was, identified the migratory phenotype indicator. In this pathway, seven genes as therapeutic targets and related drugs potentially identified. Further in vitro and in vivo validation studies should be done for the confirmation for the provided biomarkers and therapeutic targets.

**PO-511 SOMATIC AND GERMINE CALLS FROM TUMOUR/ NORMAL WHOLE GENOME DATA: BIOINFORMATICS WORKFLOW FOR REPRODUCIBLE RESEARCH**

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**Introduction** Whole-genome sequencing of cancer tumours is more a research tool nowadays, but going to be used in clinical settings in the near future to facilitate precision medicine. While large institutions have built up in-house bioinformatics solutions for their own data analysis, robust and portable workflows combining multiple software have been lacking, making it difficult for individual research groups to utilise the potential of this research field. Here we present Sarek, a robust, easy-to-instal workflow for identification of both somatic and germline mutations from paired tumour/normal/relapse samples.

**Material and methods** Sarek is open source and implemented in Nextflow; a domain specific programming language to enable portability and reproducibility. With the help of docker containers the versions of the underlying software can be maintained. Furthermore, with Singularity it is possible to run the workflow on protected clusters with no internet connexion.

The workflow starts from raw FASTQ files, and follows the GATK best practices to prepare the recalibrated files with joint realignment around indels for both the tumour and the normal data. Reads are alignment to the GRCh38 human reference in an ALT-aware settings using BWA, however, it is possible to assign other references. HaploTypeCaller and Strelka2 germline calls are collected for both the tumour and the normal sample, and Manta provides germline structural variants. The somatic variations are calculated by running MuTect2, Strelka and FreeBayes (and MuTect1 optionally). Somatic structural variants are delivered by Manta, and ASCAT estimates ploidy, tumour heterogeneity and CNVs.

The resulting variant call files are annotated by SnpEff and Ensembl-VEP. The annotated calls are further filtered and prioritised by our custom methods. During running the workflow quality control metrics are also calculated and aggregated by MultiQC.

**Results and discussions** Sarek was validated on a real dataset with known genetic set of somatic mutations. In a real settings, whole-genome sequencing (WGS, 45–60x coverage) of patient-matched tumour and blood derived-DNA is being performed on a set of 80 paediatric brain tumour samples of the Swedish Childhood Tumour Biobank. The workflow helps to produce, filter, prioritise and characterise both germline and somatic variations.