microbial diversity in SLE.

20. (195) **TRANSCRIPTOMIC STUDY REVEALS GENES AND BIOCHEMICAL PATHWAYS ASSOCIATED WITH CLINICAL EVOLUTION OF PATIENTS WITH CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA**

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Acute lymphoblastic leukemia (ALL) is the most incident pediatric cancer. While considerable progress has been made on treatment efficacy and survival rates, about 15-30% of patients relapse and/or die. We aimed to identify gene-expression profiles in childhood ALL that could help better predict disease outcome, response to treatment and therapy-related toxicity. We collected 39 bone marrow samples at time of diagnosis of ALL from 3 hospitals from Argentina. Total RNA was isolated to perform transcriptome analysis (RNAseq). Clinico-pathological characteristics and disease outcome were evaluated and recorded by oncohematologists. We analyzed differential gene expression (DGE) and gene set variation analysis (GSVA) comparing: early response to prednisone, event-free survival, risks group, acute toxicity and minimal residual disease at day 15. We observed that about 30% of dysregulated genes were non-coding RNAs, being long non-coding RNA (lncRNA) the predominant biotype. We identified 6 differentially expressed pathways relevant to ALL biology ($p<0.01$) and 7 lncRNAs (MIR99AHG, LINC02866, ZNF385D-AS2, LINC02848, MYO18B-AS1, Lnc-PPDPFL-1, Lnc-RIT2-2; $padj \leq 0.05$) among ALL risk groups. Because the biological activity of most lncRNAs is still unknown and under the hypothesis that lncRNAs modulate biochemical pathways, we calculated the correlation between significant lncRNA and pathway expressions. We found that MYO18B-AS1 positively correlated with "inactivation of MAPKK activity" ($r=0.4$;$p=0.02$) and LINC02866 negatively correlated with "CXCR3 chemokine receptor binding" ($r=-0.4$;$p=0.02$) and "transmembrane receptor protein tyrosine phosphatase activity" ($r=-0.4$;$p=0.01$). This study identified dysregulated lncRNAs and biochemical pathways that might be relevant in the pathology of childhood ALL. The analysis of these gene-expression profiles at diagnosis might help improving risk stratification, therapy efficacy and reducing the occurrence of relapse and toxicity.

21. (216) ***GENE HUNTER*: A NOVEL WEB-TOOL TO VISUALIZE SIMULTANEOUSLY DIFFERENTIAL GENES EXPRESSION ACROSS MULTIPLE DATASETS**

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Bioinformatics are becoming a prominent component of cancer research, resulting in an increased number of publicly available datasets to study and making it possible to evaluate gene expression across a variety of populations or disease stages. However, having to search for a specific gene in multiple datasets can often be time consuming and unfriendly to novel bioinformaticians. Our aim was to develop a user-friendly search tool to access simultaneously data of differential expression analyses for a particular gene or even gene signatures across multiple datasets.
For this purpose, 7 publicly available transcriptomic prostate cancer (PCa) datasets ($n_{total}= 875$) were selected to either be used by researchers interested in PCa or as an example to understand the tool before adapting it to their specific need, and differential expression analyses were performed in R, using the limma package. A *Shiny*-based tool, that can be accessed through a user interface, was then built to execute the search.
Our *Shiny* app includes a search bar that allows researchers to look for either a specific gene or a family of genes within all the datasets. Search results are presented in tables containing information on the comparison made for the analysed dataset, the gene ID and symbol, t and B statistical parameters, the log Fold Change, the p-value, adjusted p-value and the dataset's GSE identifier. Additionally, users can also plot different variables to visualize gene expression in all selected datasets more easily. Among the options, clinical significance of a gene can be assessed by overall survival and Kaplan-Meier plots.
In summary, *Gene Hunter* is a novel *Shiny*-based tool with the potential to ease high-throughput analyses in basic cancer research. It does so by providing the opportunity to explore differential expression between tumoral conditions, while straddling the limits of individual studies. This platform has the potential to extend to dataset comprehending other pathologies.

22. (234) **META-ANALYSIS OF HVEM EXPRESSION IN BREAST AND BRAIN CANCER**

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HVEM is an immunological checkpoint with dual immunomodulatory function; while its binding to LTα and LIGHT favors T cell activation, its binding to CD160 and BTLA suppresses their function. Thus, HVEM has emerged as an interesting therapeutic target for enhancing antitumor immune responses. Since HVEM expression has been detected in breast cancer (BRCA) and glioma biopsies, we performed a meta-analysis of transcriptomic data from The Cancer Genome Atlas to assess the expression of HVEM in these tumors. In BRCA biopsies, we found that HVEM expression is higher in normal vs. tumoral tissue, being lower in triple negative BRCA (TNBC) biopsies than in other BRCA subtypes. In TNBC, the expression of HVEM correlated with the expression of lymphocytic activation markers such as HLA-DR (r: 0,7109) and CD69 (r: 0,6013), but also with exhaustion markers as CTLA4 (r: 0,6349), PDL1 (r: 0,5331), LAG3 (r: 0,6547) and TIM3 (r: 0,6663). Even though HVEM expression did not show association with TNBC patient survival, its expression was positively correlated with the expression of gene signatures corresponding to helper and cytotoxic T cells, Tregs, macrophages and dendritic cells (DC). As for glioma biopsies, HVEM expression was higher in gliomas carrying wild-type IDH, an enzyme whose mutation has been recently associated with better prognosis. In addition, HVEM expression correlated with the aggressiveness of glioma subtypes, being higher in glioblastoma (GBM). In GBM, HVEM positively correlated with HLA-DR (r: 0,5021), CD69 (r: 0,4460), CTLA4 (r: 0,3721), PDL1 (r: 0,3725) and TIM3 (r: 0,5136). Although HVEM expression was not associated with patient survival, it correlated with the expression of helper and cytotoxic T cells, DC and macrophages. These results suggest that the pathways triggered by HVEM may have different outcomes depending on the tissue and tumor subtype, and that this checkpoint should be studied in depth as a target for cancer treatment.

23. (235) **AUTOMATED INMUNOHISTOCHEMICAL STAINING QUANTIFICATION IN HUMAN BIOPSIES: PRELIMINARY RESULTS USING DEEP LEARNING**

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Among the current challenges in histopathological assessment for diagnosis in clinical contexts is an accurate determination of the actual tissue malignancy. This task is often performed using microscopy over immunohistochemical (IHQ) staining applied on tissue samples, on which several specialists judge the tissue condition following specific criteria. However, this task is proven to be prone to high inter- and intra-subject variance, which raises the need to elaborate more robust tools and frameworks to assist on this task. The recent influx of deep learning technologies, which are proven to be successful in a variety of contexts, appears to be an adequate alternative in this context. In this aim, we present a joint effort between research groups from Cancer Biology Laboratory (INIBIBB-CONICET) and the Imaging Sciences Laboratory (LCI-UNS-CONICET). Starting with IHQ stained images taken with Olympus CX31 microscope from thyroid and breast cancer biopsies, we applied a Mask C-RNN network for cell nuclei detection. For this purpose, we retrained the net with a series of labeled examples provided by the biochemical specialists. After this initial detection, a ROI was determined surrounding the nuclei, within which the proportion of diaminobenzidine stain (brown-colored precipitation) is computed as a proxy indicator of the Immunoreactive Score (IRS). For this, a Random Forest classifier was trained using stain/no stain labeled pixels also provided by the experts. The results appear promising in the sense that the resulting system is able to consistently provide malignancy assessment even in difficult cases or when the quality of the microscopy acquisition is below standard.

24. (237) **ANTIANDROGENS POSE A PROTECTIVE EFFECT AGAINST COVID-19 BY BOOSTING THE HUMAN MYXOVIRUS RESISTANCE GENE 1 (*MX1*)**

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Population-based studies have shown that prostate cancer (PCa) patients undergoing androgen-deprivation therapies (ADT) were partially protected from COVID-19. Men treated with proxalutamide in a recent clinical trial, showed reduced COVID-19 hospitalization rate. In this work we assessed gene expression profiles and androgen regulation of the main host cell receptors described for SARS-CoV-2 and potential antiviral genes involved in response to coronavirus infection.
Multiple bioinformatics analyses were performed to study host cell receptors and antiviral proteins in SARS-CoV-2 infection and the gene expression changes upon ADT was assessed. We used publicly available datasets from: a) SARS-CoV-2 positive and negative patients' nasopharyngeal swabs at time of diagnosis (GSE152075, n=453), b) SARS-CoV-2 infected human cell lines and ferrets (GSE1407507), c) ChIP-seq experiments evaluating androgen receptor binding (GSE66037, GSE28950, GSE108704).
Results showed that SARS-CoV-2 positive cases had higher *MX1* expression, and multivariable regression showed that *MX1* expression significantly increased with viral load. Also, *MX1* was significantly up-regulated in tracheal samples from ferrets intranasally infected with SARS-CoV-2. Similar results were found in A549 and Calu3 lung cell lines. Since ADT might result in a therapeutic advantage against COVID-19, we next evaluated *MX1* regulation by dihydrotestosterone (DHT). First, comparable *MX1* levels in lung, prostate and salivary gland of healthy humans were observed (GTEx). LNCaP cells treated with DHT showed a decrease ($p<0.05$) in *MX1* mRNA levels. ChIP-seq experiments showcased AR binding sites on the *MX1* sequence upon DHT. Further, comparison of paired PCa patient's samples before and after ADT showed *MX1* upregulation ($p<0.05$) after ADT.
In summary, *MX1* raises as a critical responder in SARS-CoV-2 infection and we demonstrate *MX1* modulation by DHT. We propose *MX1* as a key player in the therapeutic advantage posed by ADT.

25. (242) **ELIGLUSTAT INHIBITS GLUCOSYLCERAMIDE SYNTHASE AND GLOBOTRIAOSYLCERAMIDE EXPRESSION WITHOUT INTERACTING WITH SHIGA TOXIN 2**

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Shiga toxin-producing *Escherichia coli* is responsible for Hemolytic Uremic Syndrome (HUS), a cause of renal failure in children. Renal damage has been associated with Shiga toxin (Stx), which binds to the globotriaosylceramide (Gb3) receptor on the plasma membrane of target cells. We have previously shown that Eliglustat (EG), an inhibitor of glucosylceramide synthase (GLS), the first step of glycosphingolipids pathway, also inhibits Gb3 expression and prevents the cytotoxic effects of Shiga toxin type 2 (Stx2) in human cortical renal tubular epithelial cells (HRTEC) primary cultures. The aim of this work was to clarify the mode of interaction of EG in the active site of GLS and its possible interaction with Stx2 and Gb3, and compare to Gb3 expression in HRTEC treated with EG and Stx2. For this, a computational procedure called molecular docking was carried out with Smina software and Gibbs free energy was calculated for determining the stability of the conformation formed between the ligand and the receptor. On the other hand, the expression of Gb3 receptor was analyzed by TLC in samples of HRTEC treated with EG (50 nM, 24 h) in the presence and absence of Stx2 (1 ng/ml). Docking analysis showed that EG presents an *in silico* 9-fold selectivity over GLS in comparison with Stx2, suggesting a stronger affinity between EG and GLS. These results were according to TLC assay, which showed that EG significantly inhibits Gb3 expression at 24 h. Besides, HRTEC cultures co-treated with EG+Stx2, showed a similar significant decrease in Gb3 expression. The incubation of HRTEC with Stx2 alone maintained the same Gb3 expression level as control non-treated cells. These results demonstrate that Stx2 does not interfere with Eliglustat effect on Gb3 inhibition. Study supported by PUE0041, CONICET.

26. (248) **INTERACTION EVALUATION OF A SUNFLOWER MANNOSE-BINDING LECTIN WITH VIRAL SURFACE GLYCOPROTEINS OF INFLUENZA AND SARS-COV-2**

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Each year, influenza virus infections cause more than half a million deaths worldwide. The novel coronavirus (SARS-CoV-2) has caused over 4.6 million deaths as of September 2021. The influenza virus hemagglutinin (HA) and coronavirus spike (S) glycoproteins mediate virus entry. HA and S are heavily glycosylated, making them potential targets for carbohydrate binding agents such as lectins. We have previously isolated a mannose-binding sunflower lectin (Helja) that showed the ability to inhibit hemagglutination mediated