inversion probe sequencing (MIPS) to identify novel variants and candidate genes in sporadic trios and familial cases of CPHD and IGHD. We captured 693 coding exons of 30 known genes and 37 candidate genes. We captured genomic DNA from 176 pediatric patients from Argentina with CPHD or IGHD and 133 relatives and conducted next generation sequencing. We obtained a 600X average coverage per sample over targeted regions. We discovered 10 likely pathogenic variants; 8 of them are novel. We classified each variant following the ACMG-AMP guidelines, which is so far the most detailed and quantitative system for variant interpretation in genetic testing. We identified heterozygous variants in 6 genes: GH1 (p.Arg209His), GLI2 (p.Leu761Phe, p.Ser1048fs and p.Lys-1162Arg), LHX3 (p.Pro187Ser, p.Leu220Met), LHX4 (p.Gln100His, p.Trp204Leu), PNPLA6 (p.Thr1115Pro) and HESX1 (p.Ile26Thr and p.Gln117*). Mutations in PROP1 are the most common known cause of CPHD, accounting for 11% of total cases worldwide. The frequency of PROP1 mutations varies widely by population group, and the rate was previously unknown for Argentina. We found no cases of PROP1 mutations. We are testing the effects of these variants on the activity of the transcription factors in cell culture. Identification of disease causing mutations in CPHD is complicated by phenotypic variation and incomplete penetrance. Identifying potential pathogenic variants will make it feasible to predict clinical outcomes from genetic data, which is necessary for patient diagnosis and prognosis, and for assessing the risk of future affected individuals.

606. (738) **ANALYSIS OF DIFFERENTIALLY EXPRESSED GENES AFTER EX VIVO X-RAYS IRRADIATION OF HUMAN PERIPHERAL WHITE BLOOD CELLS**

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The understanding and characterization of the radio-induced response at molecular level is pivotal for developing new approaches on practices that employ Ionizing Radiation (IR). Currently, gene expression signatures are being developed for radiation biodosimetry and as predictive biomarkers for personalizing radiotherapy. In order to detect potential radiation-exposure biomarkers, we performed a bioinformatic meta-analysis of public microarrays of ex vivo X-rays-irradiated human peripheral white blood cells and a validation of the resulting differentially expressed genes (DEGs) by qPCR. Gene expression of five datasets from Gene Expression Omnibus were analyzed with R software and Bioconductor packages. DEGs functional enrichment was performed with Over Representation and Gene Set Enrichment Analysis while iRegulon was used to detect master regulators transcription factors (TF) from DEGs. Human peripheral blood samples from six healthy human donors were X-rays-irradiated at 1-4Gy or left unirradiated. Dicentric Chromosome Assay was performed as biodosimetry control while mRNA from samples was obtained 24 h after exposure for qPCR validations with GAPDH as a reference gene (p-values<0.05 were considered significant). Bioinformatic analysis identified a total of 452 DEGs after X-rays exposure (parameters: lfc=0.7, p-value<0.05). While some of them are well known to be involved in radiation response, others resulted as novel. The DGEs showed enrichment in biological processes such as regulation after IR-exposure, DNA damage checkpoint, signal transduction by p53 and mitotic cell cycle checkpoint. PCNA, TIGAR, DRAM, PLK2 and NUDT15 expressions levels significantly increased at 1-4 Gy vs controls, demonstrated by qPCR. Meanwhile, TCF4 exhibited a significant decrease post-irradiation. This gene was previously detected as a master regulator TF by the bioinformatic analysis. Therefore, the detection and validation of this six DEGs can provide potential candidates as radiation-exposure biomarkers. These findings could also reveal novel insights about molecular networks involved in radio-induce response.

607. (789) **IMPLEMENTATION OF ARRAY-CGH IN PATIENTS WITH INTELLECTUAL DISABILITY , MULTIPLE CONGENITAL ANOMALIES AND SELECTED CHROMOSOMAL ABNORMALITIES.**

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Introduction: arrayCGH is a significantly high resolution method to scan the genome for gains and losses of chromosomal material. Although in several countries it is a first-tier test for patients with intellectual disability (ID) or with multiple congenital anomalies (MCA), in our country it represents an expensive technique and a very few laboratories have begun to implement it. Karyotyping remains to be the routine study in public health.
Aim: To report our experience in the use of ArrayCGH for patients with ID, MCA and selected chromosomal abnormalities.
Materials and methods: we studied 176 patients with two arrayCGH platforms (Agilent ISCA-v2-60K and KaryoArray®v3.0-8x60K): 128 had ID, 40 had MCA and 7 presented a cytogenetic abnormality detected by karyotype. Patients with ID and MCA did not show a cytogenetic anomaly or had a failed karyotype test.
Results: We found that 14/128 (11%) ID patients had causal or potentially causal CNVs: 12 were recognizable syndromes. One patient had an imbalance associated with a microdeletion syndrome accompanied with other pathogenic imbalance. Besides, 10/40 (25%) MCA patients presented causal or potentially causal CNVs: 2 were chromosomal abnormalities, 3 were recognizable syndromes and 1 had a microdeletion syndrome accompanied with other pathogenic imbalance. Moreover, we fully characterized all the cytogenetic abnormalities analyzed.
Conclusion: ArrayCGH was useful to perform an accurate analysis of microdeletions or duplications that could not be detected by standard karyotyping. The percentage of pathogenic imbalances was higher in patients with MCA than in those with ID in accordance with the data reported in the literature.

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608. (142) **STAPHYLOCOCCUS AUREUS PROTEINS SPA AND SBI SIGNIFICANTLY CONTRIBUTE TO THE EARLY RECRUITMENT OF NEUTROPHILS TO THE SITE OF INFECTION DURING SKIN ABSCESS FORMATION.**

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Neutrophils play a prominent role in the formation and resolution of skin abscesses. This study was aimed at determining the contribution of *S. aureus* proteins SpA and Sbi to the early recruitment of neutrophils during skin infection. Three hour after Intradermal inoculation of 1x108 CFU of S. aureus increased neutrophils in circulation were found. Interestingly, the percentage of neutrophils found in blood of mice inoculated with the SpA- mutant were significantly higher than that found in the wild type inoculated group (40 % vs 65 %, $p<0.05$). Circulating neutrophils are elicited from the vasculature to the site of infection in response to pro-inflammatory factors. At three hours post-inoculation the expression of SpA and Sbi significantly contributed to TNF-α production, a critical cytokine for the activation of the endothelium. To characterize the early influx of neutrophils to the site of infection in real time we used intra-vital microscopy. A significant increase in the number of neutrophils attracted to the area was observed at two hours post inoculation with wild type S. aureus compared with the control group ($p<0.05$). On the contrary, neutrophil recruitment was not observed in mice challenged