Research Abstracts for 2018 CLIC-I4C Joint Meeting

Abstract Number, Presenting Author (Last, First) – Title

Legend

* = Presenting author
† = Presenting author is a young investigator
§ = Authors contributed equally

01

MOLECULAR EPIDEMIOLOGY OF PEDIATRIC ACUTE PROMYELOCYTIC LEUKEMIA IN BRAZIL.

Francianne G Andrade†, Suellen V. Moura Feliciano, Ingrid Sardou-Cezar, Daniela Palheiro Mendes-de-Almeida, Paulo Chagas Neto, Marceli S. Santos, Maria S. Pombo-de-Oliveira *(Pediatric-Hematology-Oncology Program (PHOP) Research Center, National Cancer Institute (INCA), Brazil)*

Background: Acute promyelocytic leukemia (APL) presents well-characterized mechanisms of pathogenesis with distinctive acquired fusion gene. The incidence rate of APL seems to vary among geographic regions, being higher in the Latino population, underlying genetic background that plays a role along with environmental factors. Our aim was to establish the incidence rate of APL among children and adolescents according to hospital-based and population-based cancer registries (PBCR) in Brazil. We also aim to describe the molecular features of APL to provide insight into molecular epidemiology potentially associated with APL development. **Methods**: APL cases (<19 years old) were assessed from a dataset of hospital-based registry from a central laboratory (PHOP, INCA) that is a reference for leukemia diagnostic assistance (2002-2017) and from 18 PBCR in Brazil. Diagnostic algorithm included morphology, immunophenotype, and PML-RARa identified by FISH/RT-PCR. Additionally, FLT3, KRAS, NRAS, and PTPN11 mutations were analyzed. **Results**: In the PHOP-based registries, 149 patients out of 734 myeloid malignancies (MM, 20.3%) were diagnosed with APL, while in the PBCR 45 out of 1.421 (3.2%) MMs were APL. The incidence rate based on PBCR showed that APL was highest in Southeast/South (1.60 per million) compared with other Brazilian regions (0.9 per million). MM rate of unspecified cell-type in PBCRs was about 50% and the coverage of PHOP was estimated in 95% of PBCRs. Patients were similarly distributed among age ranges >2-10 and >10-21 years old (47.3% and 50%, respectively); no sex differences were observed, but a remarkable decrease in Blacks (10.5%) vs. Non-Black (90.5%) was found. PML-RARA was identified in the great majority of cases; RAS mutations were observed in 55% of APLs, including FLT3 (45.2%), NRAS (7.3%), KRAS (2.5%) and PTPN11 (rs61736914, a silent aminoacid substitutions=4.9%). **Conclusions**: APL is the most frequent MM subtype highly associated with FLT3 mutations, reflecting the profile of the disease in Brazil. Future studies should explore these association with environmental exposures.

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INCREASED PENETRANCE OF ACUTE LYMPHOBLASTIC LEUKEMIA SUSCEPTIBILITY LOCI IN CHILDREN WITH DOWN SYNDROME.

Adam J. de Smith†§, Austin L. Brown§, Vincent U. Gant§, ME Scheurer, KM Walsh, N Winick, NA Heerema, AJ Carroll, MJ Borowitz, BL Wood, WL Carroll, EA Raetz, E Feingold, W Yang, M Devidas, CG Mullighan, SP Hunger, C Pui, M Loh, LM Morimoto, T Whitehead, HM Hansen, AY Kang, D Sinnett, P Thompson, JM Birch, JW Taub, ME Zwick, MS Pombo-de-Oliveira, C Metayer, X Ma, BA Mueller, SL Sherman, JL Wiemels, MV Relling, JJ Yang, Philip J. Lupo§, Karen R. Rabin§ *(Department of Preventative Medicine, Keck School of Medicine, University of Southern California, California, USA)*

Down syndrome (DS) is one of the strongest risk factors for acute lymphoblastic leukemia (ALL), the most common pediatric malignancy, as children born with trisomy 21 have an approximately 20-fold increased risk of disease. ALL in children with DS (DS-ALL) is associated with inferior outcomes and unique somatic characteristics, including a high frequency of CRLF2 overexpression. However, the role of inherited genetic variation in DS-ALL is unknown. To this end, we performed the first genome-wide association study (GWAS) of DS-ALL, including four independent case-control studies comprising 542 DS-ALL cases and 1192 DS controls. We carried out genome-wide imputation of autosomal and disomic single nucleotide polymorphisms (SNPs), and combined results from all studies using fixed effects meta-analysis. Genome-wide significant SNPs were identified at four loci previously associated with non-DS ALL, including: rs58923657 near IKZF1 (odds ratio [OR] = 2.02, Pmeta=5.32x10-15), missense SNP rs3731249 in CDKN2A (OR=3.63, Pmeta=3.91x10-10), rs7090445 in ARID5B (OR=1.60, Pmeta=8.44x10-9), and rs3781093 in GATA3 (OR=1.73, Pmeta=2.89x10-8). Case-case analyses comparing the frequency of ALL risk alleles (at IKZF1, CDKN2A, ARID5B, GATA3, CEBPE, BMI1, and PIP4K2A) in DS-ALL versus non-DS ALL (n = 3082 cases) revealed significantly higher risk allele frequencies in DS-ALL cases for SNPs in CDKN2A (OR=1.58, Pmeta=4.08x10-4), GATA3 (OR=1.34, Pmeta=4.38x10-5), and IKZF1 (OR=1.18, Pmeta=0.015). Genetic risk scores (GRS) calculated from the seven susceptibility loci were also significantly higher in DS-ALL cases than in non-DS ALL cases (weighted GRS, P=3.33x10-6), indicating that DS-ALL cases harbor significantly more risk alleles than non-DS cases. Furthermore, among controls without ALL, neither the GRS nor any individual ALL risk alleles were associated with DS status, suggesting that the higher risk allele frequencies in DS-ALL cases represents a larger magnitude of effect for known ALL risk loci in the genetic background of trisomy 21. Finally, shRNA knockdown of IKZF1 in lymphoblastoid cell lines (LCLs) revealed significantly higher proliferation rates in DS LCLs versus non-DS LCLs, as measured by serial counts (P<0.05) and proportion of cells in S-phase (P<0.05). Our results support a higher penetrance of ALL susceptibility loci in the DS population, and may inform surveillance strategies for children with DS who are at the greatest risk of developing ALL.

INCIDENCE OF CHILDHOOD CANCER IN COSTA RICA, 2001 – 2013, IN AN INTERNATIONAL PERSPECTIVE.

Friederike Erdmann[†], Tengfei Li, George Luta, Joachim Schüz, Ana Maria Mora (Section of Environment and Radiation, International Agency for Research on Cancer (IARC), Lyon, France)

Background: Higher childhood cancer incidence rates, particularly for leukaemia, are reported from high-income countries (HICs) versus lower income countries. However, estimating childhood cancer incidence globally is hampered by lack of reliable data from developing countries, including for Latin America. Costa Rica is one of the few middle-income countries (MICs) with a longer-term nationwide population-based cancer registry, enabling to study high quality incidence data on childhood leukaemia. **Methods**: Data on incident leukaemia in children aged under 15 reported to the National Cancer Registry of Costa Rica between 1999 and 2013 were analysed by leukaemia type, age, gender, and geographical region at diagnosis. **Results**: For the 13-year period a total of 832 children with leukaemia was reported, resulting in an overall age-standardised incidence rate (ASR) of 58.08/million. The male-to-female ratio was 1.2. The highest age-specific rate was observed in children aged 1-4 years (97.7/million). Most frequent leukaemia type was lymphoid leukaemia. With an ASR of 49.1/million the observed rate was among the highest in the world. A very low rate in international comparison was observed for leukaemia in infants, which was largely driven by the low lymphoid leukaemia rate. With respect to geographical differences, substantially higher leukaemia rates were observed in the regions Huetar Atlatica (69.2/million) and Huetar Norte (68.1/million). **Conclusion**: Childhood leukaemia incidence patterns in Costa Rica were closer to those observed in HICs than found in many low and middle-income countries. Further research is recommended to explore which factors may drive the high overall leukaemia rate as well as the low rates observed in infants. Our data suggests applying caution when interpreting geographical variation, as this example of a MIC with established paediatric oncology and a well-functioning cancer registry showed less differences to childhood leukaemia incidence patterns in HICs.

DIAGNOSTIC MEDICAL RADIATION EXPOSURE AND RISK OF CHILDHOOD LEUKEMIA: RESULTS FROM AN ITALIAN POPULATION-BASED CASE-CONTROL STUDY.

Tommaso Filippini[†], Elisa Arcolin, Carlotta Malagoli, Silvia Cilloni, Federica Violi, Lucia Borsari, Marco Vinceti (Environmental, Genetic and Nutritional Epidemiology Research Center (CREAGEN), University of Modena and Reggio Emilia, Modena, Italy)

Introduction: In utero exposure to low-dose radiation delivered from medical procedures is a risk factor for childhood leukemia (CL), while findings for postnatal exposure are scarce and still inconsistent. In a population-based case-control study carried out in a Northern Italian province we explored the relationship between post-natal exposures to medical radiation and CL risk. **Methods**: We identified CL cases diagnosed in the Modena province in the period 2004-2013 through the Italian National Childhood Cancer Register and we randomly selected four population controls matched by age, sex and calendar year. For each subject we retrieved detailed information about any medical procedure involving ionizing radiations from birth up to six months prior to the onset of the disease by accessing to databases of the Radiology services of Modena province. We collected information about child age, type, total number, body region and reason of the radiological examination. Finally, we estimated for each study participant the total effective dose (mSv) and the red bone marrow-specific dose (mGy) experienced from birth. **Results**: Using a conditional logistic regression model we found an increased risk of developing CL, especially in children aged 5 or more, in association with experiencing one or more diagnostic tests with ionizing radiation (odds ratio 1.68, 95% confidence interval 0.66–4.29). The risk of CL and particularly of acute lymphoblastic leukemia increased in children who received one or more x-ray test in the first 5 years of life. Risk of CL by increasing total effective dose and red bone marrow-specific dose increased in the highest (>0.035 mSv and >0.0125 mGy) compared to null exposure. **Conclusions**: Our study suggests an increased risk of CL related to early exposure to post-natal medical radiation.

MATERNAL INFECTION DURING PREGNANCY AND CHILDHOOD LEUKAEMIA IN THE OFFSPRING: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Jian-Rong He[†], Rema Ramakrishnan, Jane E. Hirst, Audrey Bonaventure, Stephen S. Francis, Ora Paltiel, Siri E. Håberg, Stanley Lemeshow, Sjurdur Olsen, Gabriella Tikellis, Per Magnus, Michael F G Murphy, Joseph L. Wiemels, Martha S. Linet, Terence Dwyer (Nuffield Department of Women's and Reproductive Health, University of Oxford, UK; Division of Birth Cohort Study, Guangzhou Women and Children's Medical Center, Guangzhou Medical University, Guangzhou, China; The George Institute for Global Health, University of Oxford, Oxford, UK)

Background: Strong evidence suggests that a substantial fraction of childhood leukaemias originate in utero, and maternal infection is potentially a contributor to this risk. While many individual epidemiologic studies have previously examined the association of maternal infection during pregnancy and childhood leukaemia risk in the offspring, no systematic review has been conducted. **Methods**: In this systematic review and meta-analysis (PROSPERO number, CRD42018087289), we searched PubMed and Embase from inception up until 16 January, 2018. We included human studies that reported associations of at least one measure of maternal infection during pregnancy with acute lymphoblastic leukaemia (ALL) or all childhood leukaemias (CL) in the offspring. We conducted random-effects meta-analyses to pool odds ratios (OR) of any infection and specific type of infection on ALL and CL. **Findings**: We identified 2,072 records; 20 studies (ALL, n=15; CL, n=14) reported in 32 articles were included. Any infection during pregnancy was associated with higher risk of ALL (OR [95% confidence interval], 1.63 [1.14, 2.33]) and CL (1.36 [1.01, 1.84]) in offspring. Influenza during pregnancy was associated with higher risk of ALL (3.64 [1.34, 9.90]) and CL (1.77 [1.01, 3.11]). Varicella (10.19 [1.98, 52.39]) and rubella (2.79 [1.16, 6.71]) infections were also associated with higher risk of CL. **Interpretation**: Maternal infection during pregnancy may be associated with higher risk of childhood leukaemia. Future studies with larger sample sizes, including a greater collection of prospective evidence, and more accurate methods for infection measurements (e.g. biospecimens or medical records) are needed to confirm these findings.

GESTATIONAL RISK FACTORS IN PEDIATRIC CANCER. A COHORT STUDY IN TAIWAN.

Julia E Heck*, Hsin-Yun Tsai, Chung-Yi Li, Beate Ritz, Onyebuchi A. Arah, Pei-Chen Lee (Department of Epidemiology, Fielding School of Public Health, University of California, Los Angeles, California, USA)

Background: The incidence of childhood hepatic and germ cell tumors is higher in Taiwan, while the incidence of lymphomas, renal tumors, and central nervous system cancers is lower than in other developed nations. Taiwan has unique cancer risk factors such as much higher adult male than female smoking, betel quid use (particularly in aboriginal communities), endemic hepatitis B, low maternal overweight, and low rates of high birthweight. Still, there are few epidemiologic studies from Asian countries. Our study aimed to examine demographic and gestational risk factors for pediatric cancers in a Taiwanese cohort. **Methods**: We included all children born in Taiwan 2004-2014 for whom there were birth records and included 1900 cancer cases and 2,077,137 controls. We used multivariable adjusted logistic regressions to estimate associations between gestational factors and childhood cancer. **Results**: Greater parity of □2 older children was related to AML [odds ratio (OR)=2.01, 95% confidence interval (CI): 1.05, 3.84), central nervous system tumors (OR=1.69, CI: 1.04, 2.75) and neuroblastoma (OR=1.97, CI: 1.16, 3.35). Hepatoblastoma was more likely in very low birthweight (<1500g; OR=21.99, CI: 10.8, 44.78), very preterm birth (<33 weeks gestation; OR=20.29, CI: 10.5, 39.23), plural pregnancies (OR=3.73, CI: 1.69, 8.23), and both small- (OR=2.05, CI: 1.06, 3.98) and large- (OR=2.15, CI: 1.04, 4.41) for-gestational-age children. Acute lymphoblastic leukemia (ALL; OR=0.56, CI: 0.35, 0.90) and non-Hodgkin lymphoma (NHL; OR=0.56, CI: 0.32 -0.98) cases were less likely among small-for-gestational-age children. Germ cell tumors were more common among children born in rural areas (OR=1.62, CI: 1.01, 2.58). **Conclusions**: We observed point estimates for the associations between high birthweight and childhood cancer similar to those reported in meta-analyses of ALL, AML, NHL, and central nervous system tumors, despite the lower rates of high birthweight in Taiwan. Hepatoblastoma risk from fetal growth and plural pregnancies, and findings for varying risk with parity, were similar to that reported elsewhere.

SETIL STUDY: EXPERT ASSESSMENT OF PARENTAL OCCUPATIONAL EXPOSURE TO LOW-FREQUENCY MAGNETIC FIELDS AND THE RISK OF CHILDHOOD LEUKAEMIA, NON HODGKIN'S LYMPHOMA AND NEUROBLASTOMA IN THE OFFSPRING.

Lucia Miligi, Alessandra Ranucci, Patrizia Legittimo, Sara Piro, SETIL WG, Corrado Magnani* *(Unit of Medical Statistics and Epidemiology, Department of Translational Medicine, University of Eastern Piedmont, Novara, and CPO-Piemonte, Novara, Italy)*

Objective: We investigated parental occupational exposure to ELF magnetic fields and risk of Acute Lymphoblastic Leukaemia (ALL), Acute non Lymphoblastic Leukaemia (AnLL), non Hodgkin's lymphoma (NHL) and neuroblastoma (NB). **Methods**: We included cases incident in 0-10 year children in 1998-2001 in 14 Italian regions. Two population controls per leukaemia case were randomly sampled, matched by gender, age and region. The controls were used in NHL and NB studies. Parents were interviewed on: physical agents, chemicals, occupation, and other factors. Job specific modules were used, with questions on machineries. ELF occupational exposure was blindly assessed by an expert, from jobs, machineries, distance from sources, and indirect exposure. Exposure was rated as probability, intensity (not evaluable; not exposed; from 0.01 to 0.1 µT; from 0.11 to 1 µT; from 1.1 to 10 µT; from 10.1 to 100 µT), and frequency of exposure during 8 hours shift. We estimated ORs for maternal exposure during pregnancy and 1 year before conception, and paternal at conception. **Results**: 683 leukaemia cases (87% ALL), 97 NHL, 155 NB, and 1044 controls were included. Analyses included 1373 mothers and 1854 fathers with information. ORs (exposure $> = 0.01$ µT vs. no exposure) for mothers and fathers were: ALL 1.10 (95%CI:0.83-1.46) and 0.83 (95%CI:0.66-1.04); AnLL 0.96 (95%CI:0.51-1.80) and 0.68 (95%CI:0.40-1.14); NB 1.3 and 0.83; NHL: 0.86 and 1.1. Intensity of exposure and adjustment did not change results. **Conclusion**: We did not show an association between occupational ELF and ALL, AnLL, NB or NHL in offspring.

NO ASSOCIATION BETWEEN INDOOR RADON AND CHILDHOOD LEUKEMIA IN FRECCLE (FINNISH REGISTER-BASED CASE-CONTROL STUDY OF CHILDHOOD LEUKEMIA).

Atte Nikkilä[†], Hannu Arvela, Juha Mehtonen, Jani Raitanen, Olli Lohi, Anssi Auvinen *(Tampere University, Tampere, Finland)*

Background: Leukemia is the most common malignancy of childhood. Its etiology remains largely unknown apart from few well-established risk factors. The association between indoor radon and childhood leukemia has been studied before but the results have been conflicting1-6. Further research with high-quality data is needed to characterize the association more accurately. **Materials and methods**: We created two log-linear models for prediction of residential radon levels based on measurements inside 71 788 small houses and 3476 apartments. Missing data of predictive variables was dealt with multiple imputation. We experimented with numerous categorical models with polynomial and multinomial logistic regression and tried modern machine learning methods to improve the models. The robustness of the models was evaluated with multiple sensitivity analyses. Our childhood leukemia dataset consists of all childhood leukemia cases diagnosed in Finland between 1990 and 2011 (N=1093) and thrice as many controls matched by gender and year of birth7. We estimated the cumulative indoor radon exposure throughout the study subjects' complete residential histories. **Results**: The log-linear models predicted observed radon levels adequately (small houses: $r2 = 0.19$, apartments: $r2 = 0.17$). They showed robust behavior with no signs of overfitting in sensitivity analyses and k-fold cross-validation. Spearman correlation between measured and predicted values were respectively 0.48 and 0.41. Cohen's kappas for the categorical models were 0.34 and 0.32. When the predicted average indoor radon concentration was divided into quartiles and the group with lowest exposure (9.0 Bq/m3) was used as the reference group, the OR for the 2nd quartile (29 Bq/m3) was 0.89 (95% CI 0.72, 1.10); third (45 Bq/m3) OR=0.82 (95% CI 0.66, 1.01); and highest (68 Bq/m3) OR=0.95 (95% CI 0.77, 1.17) relative to the lowest quartile. **Conclusions**: The prediction models developed for residential radon performed reasonably well. However, it was unable to identify the dwellings with the highest radon concentrations. No increase in leukemia risk with predicted indoor radon was found. The results should be interpreted cautiously as the exposure modelling has significant uncertainties.

EARLY-AGE LEUKEMIA WITH KMT2A-r AND ITS MANY ASSOCIATIONS WITH MATERNAL EXPOSURE AND GENE VARIANTS.

Maria S. Pombo-de-Oliveira*, Orlando S.Louzada Neto, Gisele Delapicola Brisson, Francianne G. Andrade, Bruno Lopes, Pedro H. Cardoso, Paulo Chagas Neto, Ana Rossini *(Programa de Hematologia-Oncologia Pediatrico Instituto Nacioinal de Cancer (INCA), Rio de Janeiro, Brazil)*

The KMT2A breakpoint region differs in age groups and leukemia subtypes. Few investigations were carried out exploring the intra-uterus of leukemia origin taking into consideration KMT2A partner-gene, maternal exposures, gene variant in double-strand break. Previous case-control study showed that maternal exposure to hormones was associated with leukaemia risk in offspring.The study aimed to test if gene variants on estrogen metabolism and DNBS would be associated with KMT2A-r risk. Data of 608 leukemia and 880 healthy-controls were tested (345 i-ALL and 163 i-AML). The GSTT1*0,CYP1B1, CYP3A4, CYP3A5, GSTM1/GSTT1del, and SULT1A1, ERCC1, OGG1, XRCC1, XRCC6, XRCC4 were genotyped. Methods used were PCR-RFLP, qPCR, HRM and Sanger sequencing. Demography (age ≤24months, sex, ethnicity, leukemia subtype, KMT2A-r) and genotypes were compared among cases and controls. HWE was calculated for all gene variants. Odds ratios (OR) and ethnicity-adjusted OR (aOR) and their 95% confidence intervals were assessed using unconditional logistic regression. Genotyping were analyzed with dominant (DM), recessive (RD) and co-dominant models (cDM). The most frequent leukemia was i-ALL (70.1%); the KMT2A-r rate was 57.9% in the whole cases. GSTT1*0, (OR 1.91), CYP3A4*1B (OR 2.44), and CYP3A5*1 (OR 1.98) were associated with an increased risk of EAL. CYP1B1*3/SULT1A1*3 (OR 0.24) decreased whereas CYP3A4*1B/SULT1A1*2 (OR 2.06) increased EAL risk. CYP3A4*1B increased risk when combined with either GSTM1 (OR 1.73), GSTT1 (OR 2.10), or SULT1A1*2 (OR 2.06) variants. CYP3A5*3/SULT1A1*2 conferred an increased risk (OR 1.93) and GSTM1 (OR 1.84). The analysis of selected NHEJ gene variants have found that ERCC1rs3212986 (RD: aOR, 0.15;p<0.010) has a protective effect for ALL while XRCC1rs25487 an increased risk for AML (RD: aOR 6.30; p <0,001). The XCC4rs28360071 variant increases the risk to i-ALLKMT2A-r (cDM: aOR,2.27; p = 0.031). OGG1 rs1052133 was associated with i-ALLKMT2A-r (cDM: OR: 7.0; p<0.05). In conclusion, gene variants are associated with KMT2A-r. Further studies should test the mechanism to which DNA-damage substances are modulated by maternal-foetal genetic system.

PRENATAL AND POSTNATAL CHARACTERISTICS AND ACUTE LYMPHOCYTIC LEUKEMIA IN CHILDHOOD: A CASE-CONTROL STUDY IN THE STATE OF SÃO PAULO, BRAZIL.

Maria Elizangela Ramos Junqueira[†], Eliana de Aquino Bonilha, Maria de Freitas, Mirna Namie Okamura, Eneida Ramos Vico, Anthony Peter Stevens, Dacio de Lyra Rabello Neto, Claudia T. de Oliveira, Luiz G. Tone, Maria Lucia de M. Lee, Maria Lydia M. de Andréa, Paula Bruniera, Sidnei Epelman, Vicente Odone Filho, Victor Wünsch Filho* *(University of São Paulo, São Paulo, Brazil; University of the State of Bahia, Bahia, Brazil)*

Objective: To examine the association between pre and postnatal characteristics and the development of ALL in children in the state of São Paulo, Brazil. **Materials and methods**: A population-based case-control study, including 121 cases and 440 controls of children between 0 and 8 years of age. The cases were identified in eight hospitals. Four controls were selected for each case. Information on the prenatal and postnatal characteristics were obtained from the Live Birth Information System dataset of the Municipal Health Secretariat of São Paulo and the Ministry of Health. Conditional logistic regression was used to analyze the association between pre and postnatal characteristics and ALL. The crude odds ratios (ORs) were calculated with 95% confidence intervals. **Results**: Characteristics that showed protection for ALL: black race (OR = 0.28; 95% CI 0.07 to 1.23); gestation of period between 37 at 41 weeks (OR = 0.55; CI 95% 0.10-3.08), mother's schooling 12 or more years of study (OR = 0.14; 95% CI 0.00-2.40). Birth weight between 3,500 and 3,999 g increased the risk of ALL (OR = 2.05; 95% CI 0.78-5.44). No association was observed between cesarean delivery and ALL (OR = 0.91; CI 95% 0.614-1.358). **Conclusion**: Considering the study sample size the results observed were not precise. However, same characteristics seems to have protection against ALL. Birth weight alone 3,500 seems to be a risk factor for ALL. According to our results no association was detected between cesarean delivery and ALL.

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ADMIXTURE AND THE RISK OF ACUTE LEUKEMIA: THE ADMIRAL STUDY.

Logan G. Spector*, Michael E. Scheurer* *(Division of Epidemiology/Clinical Research, Department of Pediatrics, University of Minnesota, Minneapolis, Minnesota, USA; Baylor College of Medicine, Texas Children's Cancer Center, Texas, USA)*

There is a strong case, based on multiple lines of evidence, that the lower incidence of acute lymphoblastic leukemia (ALL) in children with substantial African ancestry compared to those with other continental ancestries is largely or primarily genetic. This evidence includes the comparatively low risk both in African and in African diaspora populations; our report of intermediate risk in children with mixed ancestry; SEER analyses which indicate lower incidence compared to white children in all socioeconomic strata; and the persistence of lower risk despite greater exposure to putative environmental risk factors for ALL among African-American children. Common variation described to date incompletely accounts for the difference in incidence compared to white children, suggesting a substantial, undiscovered genetic contribution. Lastly, African and European populations have many divergent hematopoietic and immune traits which are due to genetic differences. Admixture mapping is useful for discovery of loci underlying ancestry-related differences in risk, with power proportional to the magnitude of the difference. Pediatric ALL, particularly B-cell ALL, displays greater than a two-fold difference in risk, making admixture mapping particularly attractive even with modest sample sizes. The collective preliminary data suggest we are similarly likely to find loci and genes that explain the lower risk of ALL in AA children. We have therefore assembled 1,120 African-American children with ALL and existing data or DNA samples, with another 309 samples anticipated over the life of the study, to form the Admixture and Risk of Acute Leukemia (ADMIRAL) study. This research holds the potential to answer a long-standing mystery by revealing critical genes or loci that explain the comparative deficit of ALL in African-American children. In addition, we may uncover genes or variants associated with the worse characteristics at presentation in African-American patients as well as with worse survival, which will indicate avenues for improving outcome in this population.

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NON-CHROMOSOMAL CONGENITAL ANOMALIES AND RISK OF CHILDHOOD LEUKAEMIA: AN ITALIAN POPULATION-BASED CASE-CONTROL STUDY.

Carlotta Malagoli, Tommaso Filippini, Marcella Malavolti, Stefano Volpato, Gianni Astolfi, Giovanni Palazzi, Marco Vinceti* *(Environmental, Genetic and Nutritional Epidemiology Research Center (CREAGEN), University of Modena and Reggio Emilia, Modena, Italy; Department of Epidemiology, Boston University School of Public Health, Boston, USA)*

Introduction: The association between chromosomal conditions such as Down syndrome and increased CL risk of childhood leukemia (CL) is well established, while the association between non-chromosomal birth defects is far less clear. We conducted a population-based case-control study in two provinces of Northern Italy to evaluate CL risk in children born with non-chromosomal anomalies. **Methods**: We identified all leukemia cases diagnosed in children (<15 years) in the Modena and Reggio Emilia provinces through the Italian National Childhood Cancer Register in the period 1998-2013. For each case, we randomly selected four population controls matched by age, sex, province of residence and calendar year. Through the Emilia-Romagna Region population-based Birth Defects Registry, we retrieved information about occurrence and type of congenital malformations for each study subject. We computed the odds ratio (OR) of CL for children affected by non-chromosomal birth defects using a multivariable conditional logistic regression model. **Results**: We eventually included 132 cases and 528 controls, 5 of which (2 cases and 3 controls) were affected by a non-chromosomal congenital malformation. We found an increased risk of CL in children born with non-chromosomal anomalies, with an OR of 2.7 (95% confidence interval 0.4-16.0). **Conclusions**: Despite the limited stability of the risk estimates and the risk of unmeasured and residual confounding, our study appears to suggest an association between non-chromosomal birth defects and risk of childhood leukemia.

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EARLY INFECTION WITH CYTOMEGALOVIRUS AND RISK OF CHILDHOOD HEMATOLOGICAL MALIGNANCIES.

Joseph Wiemels*, Mats Talbäck, Stephen Francis, Maria Feychting *(Center for Genetic Epidemiology, Department of Preventive Medicine, USC Keck School of Medicine, Los Angeles, California, USA)*

A primary etiologic factor for childhood acute lymphoblastic leukemia (ALL) involves patterns of infection during childhood. Until recently, no specific infection was implicated. Prenatal cytomegalovirus (CMV) infection was recently identified as a risk factor for childhood ALL by its presence in in ALL blast cells; CMV sequences were also detected in neonatal blood spots of children who later contracted leukemia. In the current study, we asked whether clinically identified CMV infection prior to hematological malignancies (including ALL) and central nervous system tumors may be an etiologic factor, using high quality Swedish population-based registries. CMV infection was identified with appropriate ICD9 or ICD10 codes in the Patient and Medical Birth Registries, and childhood malignancies below the age of 15 were identified in the Cancer Registry, among 2,782,507 children born in Sweden 1982 to 2015. While active screening for vertical CMV infection indicates incidence at birth at around 0.15-2% around the world (including Sweden), clinical identification of CMV is far rarer. The frequency was 0.0066% for CMV detection at birth among normal children but 0.088% for those contracting hematologic malignancy. Observing all CMV infections registered earlier than 6 months prior to malignancy diagnosis including the pregnancy period, an increased hazard ratio (HR) of CMV-related infections, adjusting for congenital malformations, deformations, and chromosome abnormalities, was detected for hematological malignancies (HR=12.1, 95%CI: 5.8-21.5). Cox proportional hazard ratio for having congenital viral infections, excluding CMV is 0.91(95% CI: 0.59 - 1.42), therefore indicating that CMV is the culprit infection. Central nervous system tumors exhibited no relationship with prior CMV infection. The data are compatible with an in utero infection of CMV leading to increased risk of childhood hematological malignancies. Further conformation and elucidation of the role of CMV in the etiology of childhood hematologic malignancies is warranted.

Abstracts not Available for the Following Posters:

Altaf, Sadaf[†] – *Cytogenic Etiology in Acute Myeloid Leukemia and its Association with Outcomes in Pediatric Patients in Pakistan*

Heck, Julia E. – *Parental Occupation and the Risk of Childhood Retinoblastoma: A Danish Population-Based Registry Study*

Investigators, International Childhood Cancer Cohort Consortium – *International Childhood Cancer Cohort Consortium (I4C: Rationale, Cohorts, Ascertainment of Childhood Cancer, Available Data, and Harmonization)*

Núñez Enríquez, Juan Carlos[†] -- *Electromagnetic Fields and Risk of Childhood B-lineage Acute Lymphoblastic Leukemia in a City with High Incidence of Leukemia and an Elevated Exposure to Electromagnetic Fields: A Population-Based Study from the Mexican Inter-Institutional Group for the Identification of the Causes of Childhood Leukemia (MIGICCL)*

Patel, Deven[†] – *Parental Occupational Exposure to Pesticides, Farm Animals, and Organic Dust and Childhood Cancer Risk: Findings from the International Childhood Cancer Cohort Consortium (I4C)*

Petridou, Eleni – *Quality of Childhood Cancer Registration to Facilitate CLIC+ Research: Preliminary Results from Two NARECHEM-ST Projects*

Ramakrishnan, Rema[†] – *Placental Weight, Birth Weight: Placental Weight Ratio and Childhood Cancer in the International Childhood Cancer Cohort Consortium (I4C)*

Rashed, Wafaa M.[†] – *Risk Factors for Childhood Acute Lymphoblastic Leukemia (ALL)*

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