Their parents/carers completed the Sensory Profile Caregiver's Questionnaire. This is a standardised tool designed to assess children's sensory processing dysfunction in their daily functional performance.

Results There were 13 boys and 2 girls. Nine children were attending mainstream schools and six attended special schools. The assessments completed highlighted that all children experienced some form of sensory processing difficulty (Figure 1).

Abstract 243 Figure 1

Conclusion The findings support the key theme found in literature indicating that individuals with autism commonly experience sensory processing difficulties. There seem to be clear links between sensory processing difficulties and reduced functional performance during school and home activities. Further controlled studies on sensory processing in children with autism are recommended.

244 CHILD GENDER AND BIRTH ORDER INFLUENCE OUTCOMES OF AN EARLY INTERVENTION PROGRAM AT AGE 7 YEARS

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^{1,2}S Tough, ³R Mychasiuk, ^{1,3}KM Benzie. ¹Department of Paediatrics; ²Department of Community Health Sciences; ³Faculty of Nursing, University of Calgary, Calgary, AB, Canada

Background and aim Early intervention programs are critical to optimize development for children in low-income families. Principles of social justice and inclusion increase the tendency to employ similar early intervention approaches for all program children. This approach fails to maximize intervention outcomes, and may benefit certain sub-groups of children more than others. The purpose of this study was to explore differences in receptive language scores in children who participated in a two-generation preschool program while controlling for child characteristics.

Method The program included centre-based care, parenting education, and family support. We assessed 62 children using the Peabody Picture Vocabulary Test III (PPVT-III) at program entry and exit, and age 7 years.

Results Repeated measures ANOVA's using child characteristics as covariates, revealed gender differences in receptive language scores at age 7 years favoring males, $F(1, 61) = 3.71, p=0.06$. Children with an older sibling exhibited significantly better receptive language scores, $F(1, 61) = 4.38, p=0.04$. Ethnicity, English as a first language, time in program, and family income were unrelated to receptive language scores, $p's > 0.10$.

Conclusions The finding that males outperformed females is surprising because females tend to have stronger language skills than age-matched males. Younger siblings may have benefited from increased exposure to older siblings who had participated previously in the program. Results suggest that early intervention programs for children living in low-income families may benefit from alterations to program curricula that promote sex-differentiated learning strategies and focus on family dynamics.

245 SPECTRUMS AND FREQUENCIES OF SLC26A4 AND SLC26A5 GENES MUTATION AMONG PATIENTS WITH INHERITED HEARING LOSS FROM DIFFERENT REGIONS OF RUSSIA

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L Dzhemileva, S Lobov, E Khusnutdinova. Human Molecular Genetics, Institute of Biochemistry and Genetics, Ufa Research Center, Russian Academy of Sciences, Ufa, Russia

Background The molecular etiology of hearing impairment in Russia has not been fully investigated. Study of *GJB2*, *GJB3*, *12S rRNA*, *tRNA^{Ser}(UCN)* and *MYO7A* genes revealed that 55% of the patients with hearing loss carried *GJB2* mutations in different regions of Russia. The *SLC26A4* and *SLC26A5* genes mutations are analyzed in this study.

Methods Two hundred and fifty unrelated deaf patients were included. The all coding exons of *SLC26A4* and first ten exons of *SLC26A5* genes were sequenced in all 250 patients, including 130 patients carrying bi- and mono-allelic recessive *GJB2* mutations, two patients carrying a known *GJB2* dominant mutation c.224G>A (p.Arg75Gln), as well as six patients with *mtDNA* (m.1555A>G, m.961insC_(n), m.961delTinsC_(n) and m.7444G>A) mutations.

Results Eight patients (3.2%, 8/250) with non-syndromic hearing loss were found carrying *SLC26A4* and *SLC26A5* mutation and polymorphic variants. Among them, one patient with bi-allelic *SLC26A4* mutations (c.85G>C (p.Glu29Gln) and c.149T>G (p.Leu50Arg)) had EVA by CT scan. One patient with non-syndromic hearing loss was heterozygous for mutations c.919-2A>G in *SLC26A4* gene. The most common *SLC26A5* gene mutation, g.-53-2A>G, accounted for 0.4% (1/250) of all *SLC26A4* mutant alleles. Two patients with non-syndromic hearing loss were heterozygous for polymorphic variant c.49548A>G (p.Gly740Ser) in *SLC26A4*, and one was heterozygous for polymorphic variant g.38190T>C in *SLC26A5*. The novel *SLC26A4* gene mutation g.29607delA was identified in one patient with EVA.

Conclusion Our results suggest that *GJB2*, *SLC26A4* and *SLC26A5* mutations together make up a major cause of congenital hearing loss in the different populations from Russia.

246 MATERNAL UPD2: A NEW GENETIC LOCUS FOR RUSSELL-SILVER SYNDROME

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¹MJ Dasouki, ²X Tan, ³A Patel, ²MG Butler. ¹Departments of Pediatrics & Medicine; ²Department of Psychiatry, University of Kansas Medical Center, Kansas City, KS; ³Department of Molecular and Human Genetics, Baylor College of Medicine, Baylor University, Houston, TX, USA

Background and aims Russell-Silver syndrome (RSS) is a genetically heterogeneous and phenotypically recognizable disorder characterized by IUGR followed by postnatal growth deficiency with head sparing, trigonocephaly, limb-length asymmetry, variable hypoglycemia, and learning disabilities. Hypomethylation of the paternal imprinting center 1 (IC1) of chromosome 11p15.5 and maternal UPD7 are identified in 35%–50% and 10% of affected individuals respectively.

Methods We studied the gDNA of a 16 month old Caucasian girl with growth failure and facial features consistent with RSS using Chromosomal Microarray Analysis (CMA) and DNA microsatellite genotyping.

Results Oligonucleotide-based CMA showed no copy number abnormality while SNP-array based CMA showed segmental Long Continuous Stretches of Homozygosity (LCSH) of 64 Mb in size involving chromosome 2 [2q11.1q13 (17.66 Mb), 2q22.1q31.1 (28.67 Mb) and 2q36.2q37.3 (17.69 Mb)]. DNA microsatellite analysis showed maternal isodisomy 2q of these regions. TIGD1 and MYEOV2 map to 2q37.1 and 2q37.3 and are predicted to be paternally expressed. However, causative imprinting of either gene was excluded since both genes map outside the smallest region of overlap between our patient and two unrelated patients with features of RSS reported by Bruno et al (J Med Genet, 2011) showing LCSH at 2q.

Conclusions Taken together, these results exclude possible imprinting in 2q as a cause of RSS in this child and suggest an autosomal recessive mutation which was unmasked by the segmental maternal isodisomic abnormality. Next Generation Sequence analysis of chromosome 2q regions of homozygosity identified in this child is underway and will most likely identify another novel RSS locus.

247 SERIAL CYTOKINE EXPRESSIONS IN INFANTS WITH INCONTINENTIA PIGMENTI

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¹SL Liao, ²SH Lai, ³WI Lee. ¹Pediatrics, Chang Gung Memorial Hospital, Keelung, Keelung City; ²Pediatrics, Chang Gung Memorial Hospital, Taoyuan, Taiwan R.O.C.

Background NF- κ B dysfunction resulting from NEMO (NF-kappaB essential modulator) mutation can lead to significant alterations in cytokine production. However, little is known about changes in the expression of downstream molecules in patients with incontinentia pigmenti (IP).

Objective This study aims to investigate serial cytokine expressions during the first 2 years of life in young infants with IP, the period in which skin inflammation and morphological changes are most significant.

Methods Gene analysis was performed for the two neonates with IP. Peripheral mononuclear cells were obtained shortly after birth and successively at a 6-month interval up to the age of two years. Levels of TNF- α and IL-6 were analyzed with ELISA before and after stimulating with TLR ligands.

Results The male patient had normal NEMO allele. His cytokine level, although initially lower, had returned to a level comparable with those of controls at 12 months of age. The female infant had a mutated NEMO gene. Her baseline TNF- α level was significantly higher than those of the control subjects at birth and remained high by 6 months of age. All cytokine responses had decreased significantly by 2 years of age, the time in which all vesicular skin lesions had resolved.

Conclusion This is the first report that demonstrates serial changes of cytokine profiles in humans with IP. This study showed that in the presence of NEMO mutation, alteration of cytokine production was remarkable during the first year of life, which may account for the prominent inflammatory changes in skin morphology.

248 NOVEL MUTATION CAUSING GLUCOSE 1 TRANSPORTER DEFICIENCY SYNDROME

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DK Gandhi, R Gupta. Paediatric Neurology, Birmingham Children's Hospital, Birmingham, UK

Introduction Glucose transporter-1 (GLUT1) deficiency syndrome (OMIM #606777) is an autosomal dominant condition resulting in reduced glucose transport into the brain. GLUT1 deficiency syndrome was first described in 1991 by De Vivo et al. The diagnostic finding is a low glucose concentration in the cerebrospinal fluid (CSF; mean 1.7 [SD 0.3mmol/L]) in the presence of normoglycaemia. GLUT1 deficiency syndrome can be confirmed by mutation analysis of the SLC2A1 gene. The spectrum is ever expanding with new mutations as also varying presentations. We present one such novel mutation.

Case report A Caucasian male was referred to the neurology department with global developmental delay, head nods, seizures and excessive daytime sleepiness. Over the years he had many investigations including repeated MRIs and EEGs and investigations for conditions with progressive myoclonic epilepsy. At the age of 14 years the parents gave a history of food intake reducing his head

nods and other seizure types. He was then investigated for possible GLUT1 deficiency.

Results The initial investigations revealed a CSF sugar of 2.4 when the blood sugar was 5.9 (ratio of 0.4) which was low but not low enough for GLUT1 deficiency. Genetic testing revealed a mutation in the Exon 5 of the SLC2A gene c.647T>C (p.Ile216Thr) not previously reported.

Conclusion GLUT1 deficiency should be suspected in a child with developmental delay, epilepsy and movement disorder. Novel mutations can result in the condition. Our case is one such example for novel mutation as well as refusal of ketogenic diet from late diagnosis.

249 CEREBRAL PALSY AND CHEMOKINE CCL18 POLYMORPHISM IN VERY PRETERM INFANTS

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¹H Kallankari, ¹J Huusko, ¹T Kaukola, ¹M Ojaniemi, ²SF Kingsmore, ¹M Hallman. ¹Department of Paediatrics, Institute of Clinical Medicine, University of Oulu, Oulu, Finland; ²National Center for Genome Resources, Santa Fe, NM, USA

Background Cerebral palsy (CP) is a nonprogressive motor impairment syndrome caused by damage in the developing brain and it reveals clustering to preterm infants. Recently, genetic factors have been suggested as risk modifiers for CP. However, the individual genes causing predisposition to CP are still poorly understood. Low cord blood levels of CCL18 have been found to associate with CP in preterm infants. Since CCL18 gene is restricted to primates, it may be considered as a candidate for functionality in human brain.

Aims To investigate the association between the CCL18 gene single nucleotide polymorphisms (SNPs) and the cord blood levels of CCL18. Further to study the association between the CCL18 SNPs and the susceptibility to CP.

Methods A prospective cohort consisted of 161 children born very preterm (gestation < 32 weeks) in Oulu University Hospital during 1997–2006. Concentration of the cord blood CCL18 was analysed (n=99). Five CCL18 SNPs (rs1102934, rs2015086, rs2015070, rs2735835, rs712044) were genotyped. Cerebral palsy was confirmed at 5 years of age.

Results Two CCL18 SNPs associated with CCL18 (P=0.011; P=0.039). Additionally, CCL18 (SNP rs2735835) associated with CP. Thus, CP occurred in 11 (18%) of 61 children with GG genotype compared with 6 (6%) of 100 children with AA/GA genotype (OR 4.1; 95% CI 1.3–12.5, P=0.013).

Conclusions Variation of the CCL18 gene associates with CCL18 concentration and with predisposition to CP in very preterm infants. This is consistent with the hypothesis that CCL18 has a role in the complex sequence leading to brain damage.

250 SEASONALITY OF CONGENITAL ANOMALIES IN EUROPE

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JM Luteijn, H Dolk, EUROCAT Working Group. EUROCAT Central Registry, Institute of Nursing Research, School of Nursing, University of Ulster, Jordanstown, UK

Investigation of seasonal patterns of congenital anomalies (CAs) can help identify environmental risk factors. Smaller datasets and spatiotemporal variation in previous studies have led to conflicting evidence. The aim of our study was to investigate previously described associations and to generate new hypotheses on the role of seasonal factors in the etiology of CAs using a large high quality European dataset.

The European Surveillance for Congenital Anomalies (EUROCAT) is a European network of standardized population-based registries for the surveillance of CAs. A 2000–2009 dataset involving 19 EUROCAT registries and over 63,000 CAs was utilized to investigate seasonal patterns. Analysis of EUROCAT defined CAs was