**PS 0459** Genetics

**Association of Gene Polymorphism TCF7L2 (rs7903146), KCNJ11 (rs5219), ABCB8 (rs757110) with Type 2 Diabetes in Western Siberia**

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**Background:** The aim of our study was to confirm the associations on the gene polymorphism TCF7L2 (rs7903146), KCNJ11 (rs5219), ABCB8 (rs757110) with type 2 diabetes among residents of Western Siberia.

**Methods:** Russian population surveyed. Polymorphism TCF7L2 (rs7903146) was studied in 550 patients with T2DM and 282 healthy subjects (age 45 to 65 years). Polymorphism of KCNJ11 (rs5219) was studied in 745 patients with T2DM and 483 healthy subjects. Polymorphism ABCB8 (rs757110) was studied in 862 patients with T2DM and 379 healthy people. Determination of alleles and genotypes was performed using the technology TaqMan, allele specific PCR with the detection result in real time. Statistical analysis was performed using software GenAmp, Genetica Software R-project [www.r-project.org]. Compliance with Hardy-Weinberg equilibrium was assessed using Fisher’s exact test.

**Results:** The frequency of the risk allele T polymorphic locus rs7903146 TCF7L2 gene in patients with type 2 diabetes was 0.30 versus 0.21 in the control group OR [CI95%] = 1.64 [1.29-2.08], p = 0.00006. The frequency of the risk allele T polymorphic locus rs5219 KCNJ11 gene in patients with type 2 diabetes was 0.39 versus 0.37 in the control group OR [CI95%] = 1.04 [0.88-1.24], p = 0.64. The frequency of the risk allele G polymorphic locus rs757110 ABCB8 gene in patients with type 2 diabetes was 0.40 versus 0.38 in the control group OR [CI95%] = 1.04 [0.88-1.24], p = 0.64.

**Conclusions:** The study found an association of gene polymorphism TCF7L2 (rs7903146) with the development of DM2 in Western Siberia. Association of gene polymorphisms KCNJ11 (rs5219), ABCB8 (rs757110) with the development of type 2 diabetes among residents of Western Siberia, in contrast to other populations has not been established.

**PS 0460** Genetics

**Problems in Differential Diagnosis of Rare Genetic Disorders**

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**Background:** Prader–Willi syndrome (PWS) is a rare genetic disorder in which seven genes (or some subset thereof) on paternal chromosome 15q (q11–13) are deleted or unexpressed (chromosome 15q partial deletion). The incidence of PWS is between 1 in 550 patients with T2DM and 282 healthy subjects (age 45 to 65 years). Polymorphism ABCC8 (rs757110) was studied in 862 patients with T2DM and 379 healthy people. Determination of alleles and genotypes was performed using the technology TaqMan, allele specific PCR with the detection result in real time. Statistical analysis was performed using software GenAmp, Genetica Software R-project [www.r-project.org]. Compliance with Hardy-Weinberg equilibrium was assessed using Fisher’s exact test.

**Results:** The frequency of the risk allele T polymorphic locus rs7903146 TCF7L2 gene in patients with type 2 diabetes was 0.30 versus 0.21 in the control group OR [CI95%] = 1.64 [1.29-2.08], p = 0.00006. The frequency of the risk allele T polymorphic locus rs5219 KCNJ11 gene in patients with type 2 diabetes was 0.39 versus 0.37 in the control group OR [CI95%] = 1.04 [0.88-1.24], p = 0.64. The frequency of the risk allele G polymorphic locus rs757110 ABCB8 gene in patients with type 2 diabetes was 0.40 versus 0.38 in the control group OR [CI95%] = 1.04 [0.88-1.24], p = 0.64.

**Conclusions:** The study found an association of gene polymorphism TCF7L2 (rs7903146) with the development of DM2 in Western Siberia. Association of gene polymorphisms KCNJ11 (rs5219), ABCB8 (rs757110) with the development of type 2 diabetes among residents of Western Siberia, in contrast to other populations has not been established.

**PS 0461** Genetics

**Free Circulating DNA Levels in Individuals with Lung Cancer Risk and Characterization of Copies Number Alterations**

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**Background:** Lung cancer (LC) is the leading cause of cancer-related mortality worldwide and in Antofagasta region, and the second cause of cancer mortality in Chile. The high incidence and mortality of LC has been associated to diagnosis in advances stages. Free circulating DNA (DNAfc) in serum or plasma has been described as a promising cancer marker. A high concentration as well as genetic and epigenetic alterations of DNAfc has been associated to various types of cancer. This work has studied the levels of DNAfc in a population with high risk of LC and also to characterize its Copy Number Alterations (CNAs).

**Methods:** Volunteers enrolled in an early detection project (CtCancer), were classified as healthy control (C), Pre Neoplastic Lesions (PNL) and Lung Cancer (LC), according to results of Quantitative Automatic Cytology (QAC) in sputum specimen, DR70 tumour marker Autofluorescence Bronchoscopy (AFB) and Histopathology assay. The amplified DNAfc was co-hybridized against genomic DNA from total blood, using microarray-HOC.

**Results:** LC volunteers showed higher DNAfc levels than C and PNL volunteers. Four recurrent and significant deletions were detected in 2p, 7q, 11q and 17p in LC volunteers. Non significant alterations were detected in PNL. Genes located in segments with CNAs were associated to immune response, xenobiotic metabolism, oxidative phosphorylation, cell proliferation and cell cycle regulation, apoptosis, differentiation and cellular adhesion and migration, all functions relevant to neoplastic progression.

**Conclusions:** DNAfc showed higher levels in LC patients than control volunteers and patients with Pre Neoplastic Lesions (PNL). Many genomic loci identified as significantly have been associated with the LC and might be considered candidates as genomic markers. This research was supported by INNOVA CORFO.

**PS 0462** Genetics

**Different Effects of Polymorphisms in HLA-DR Locus are Possible Between Females and Males in the Development of Graves’ Disease**

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**Background:** Graves’ disease is more prevalent in women. HLA-DR locus, an immune response genes, is well-studied in different populations, but the difference in distributions of susceptibility alleles between females and males are required to be clarified.

**Methods:** Totally 140 subjects consisting of 70 patients with Graves’ disease (GD) (44 females, 26 males) and 70 controls (55 females, 15 males) were included to the study. Thirteen polymorphisms for DRB1 with DRB3, DRB4 and DRB5 were analysed by PCR-SSP method. The difference in distributions of DR alleles were compared between females and males. A study model was designed for confirming of Results:

**Results:** None of DR polymorphisms, in existence or absence of alleles, was associated with GD among males. However, in absence of DRB1*07, GD risk was higher than the carriage of at least one allele in females (p=0.012, OR=9.56). In addition, the development of GD among females was higher in the carriage of at least one DRB1*11 allele (p=0.004, OR=4.67). Carriage of DRB5 was also found in association with GD among females with suggestive risk (p=0.003, OR=4.07). However, underlying cause of the risk was unclear due to the haplotype inheritance of DRB1*11*DRB5.

**Conclusions:** We concluded that, gender is an effective factor on the evaluation of the association between DR polymorphisms and GD.