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SEX AND GENDER IN SPORT: FALLACY OF THE "LEVEL PLAYING FIELD"

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There is controversy regarding participation in high profile competitive events by female athletes perceived as inappropriately "masculine" by competitors and others. Over 50 years, international sports bodies such as the International Olympic Committee (IOC) and the International Association of Athletics Federations (IAAF) employed - and ultimately discarded - various procedures to ensure feminiity. Though ostensibly to detect male imposters, in practice these identified women with genetic Disorders of Sex Development (DSD), such as androgen insensitivity syndrome, complete or partial; 5 alpha-reductase deficiency; mixed gonadal dysgenesis. Further, increased participation in women´s sport has vastly enlarged the competitive field and the probability of athletes with a DSD competing.

Do female athletes with a DSD have any "unfair" competitive advantage, especially since specific genetic endowment provides advantage to excel in specific events? This "endowment" can include recognized medical disorders such as height in Marfan Syndrome and delayed maturation and short stature in gonadal dysgenesis, even simple genetic variation such as more fast or slow twitch muscle fibers. A Finnish athlete with exceptional success in endurance Nordic skiing was found to have high hemoglobin and increased oxygen carrying capacity due to an inherited mutation in the erythropoietin receptor; similar mutations occur world wide. Even longer toes are associated with greater "lift-off" and success in sprint events.

Thus the ideal of a "level playing field" is illusory and fundamentally women with some DSDs have no more competitive advantage than other elite athletes with favorable genetic characteristics.

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ANALYSIS OF GENETIC PREDISPOSITION IN LARGE THREE-GENERATION FAMILY WITH MANIFESTATION OF MULTIPLE AUTOIMMUNE DISEASES

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The aim of study was genetic analysis in 24 members of three-generation family strongly affected by coeliac disease (CD). Excepting this one, other autoimmune diseases (AD) such as type 1 diabetes (T1D) and systemic lupus erythematodes (SLE) were diagnosed within the family. The key role of genetic predisposition play alleles encoding the HLA-molecules (HLA-DQA1*0501 and HLA-DQB1*02 encoding HLA-DQ2 molecule, HLA-DQA1*0301 and HLA-DQB1*0302 encoding HLA-DQ8 molecule, both associated with CD and T1D, HLA-DRB1*0301 and HLA-DRB1*1501 associated with SLE). We studied a correlation between presence of HLA-alleles and manifestation of these AD.

Methods: Peripheral blood DNA was used for detection of HLA alleles by the PCR-SSP technique. For statistical verification was used Fisher´s exact test with 95% confidence interval.

Results: We confirmed a linkage between HLA-DQ2 molecule and manifestation of CD and T1D (P=0.0003, RR=0.1765, CI=0.06318-0.4929) with the strongest effect of HLA-DQB1*0201 allele (P=0.0119, RR=0.2059, CI=0.05966-0.7105). We have not confirmed HLA-DRB1*0301 and HLA-DRB1*1501 alleles in member with SLE.

Conclusion: The prevalence of CD in family is strongly associated with carriage of HLA-DQ2 molecule. Only one member of the family carrying this molecule has manifested T1D. With regard to preponderant manifestation of CD in family we suppose in this person influence of some other genes shifting manifestation of autoimmunity towards T1D. The unknown genetic factors are probably responsible for case of SLE, thus proving existence of complex genetic predisposition to

various autoimmune diseases in family. Testing of other genes is in progress now.

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ASSOCIATION OF ADAM33 GENE POLYMORPHISM WITH BRONCHIAL ASTHMA

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Background: Genetic association studies have linked occurrence of asthma with ADAM33 gene polymorphisms in different populations, but none from India. Such studies will improve individualized case management strategies over time.

Objectives:

Primary: To assess association of ADAM33 gene polymorphisms (F+1 G/A, S2 G/C, ST+4 A/C, ST+5 C/T, V4 C/G) with asthma.

Secondary: Among asthmatics, to assess association of hospitalization, family history and severity of asthma and environmental exposure with ADAM33 gene polymorphisms.

Study design: Case-control.

Methods: Diagnosis of asthma was done according to GINA guidelines 2007. Controls were age and sex matched non-relatives of cases without any respiratory disease. Genotyping was done with PCR-RFLP method.

Results: From August 2007 to November 2009, 211 cases (aged 74.4 months ±4.6, with 32.2% females) and 137 controls (aged 73.6 months±42.6, with 29.9% females) were recruited. Distributions of S2, ST+5 and F+1 genotypes were statistically significantly different, while allele frequencies were statistically significantly different for all 5 markers between cases and controls ($p< 0.05$). In ST+5 total hospitalization rate was high among cases with wild & hetero genotype [OR =3.75(95% CI: 1.33-1.63), $p < 0.05$]. Significant association of ST+4 wild and hetero [OR=4.147(95% CI: 1.52-11.33), $p < 0.05$] and ST+5 hetero [OR=2.77(.99-7.95), $p < 0.05$] genotypes was observed with positive family history patients. No association was found of ADAM33 gene polymorphisms genotypes in cases with severity of asthma or environmental exposure to pollutants.

Conclusion: The SNPs (F+1 G/A, S2 G/C, ST+4 A/C, ST+5 C/T, V4 C/G) of the ADAM33 gene are associated with asthma.

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A GENOME-WIDE ASSOCIATION STUDY OF SPONTANEOUS PRETERM DELIVERY

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Background and aims: Up to 40% of preterm deliveries (PTDs) may have a genetic component. PTD inheritance patterns are consistent with maternal genotype effects, fetal genotype effects via maternally-derived alleles, or both. However, while many candidate genes have been proposed, no common genetic variant has yet been confirmed as contributing to PTD. A genome-wide association study (GWAS) of PTD has never before been undertaken. Consequently, our objective was to examine maternal and fetal genetic contributions to spontaneous PTD in a GWAS.

Methods: We selected 1,000 preterm (gestation < 37 weeks) mother-child pairs and 1,000 term (40-week gestation) pairs, all with spontaneous onset of delivery, from the Danish National Birth Cohort, and genotyped them using the Illumina Human660W-Quad BeadChip. We analyzed the effect of genotype (maternal and fetal separately) on PTD using case-control methods and also by treating gestational length as a quantitative trait. We further examined spontaneous PTD subtypes separately.

Results: While no SNP in either maternal or fetal genotype reached formal GWAS significance ($p < 10^{-7}$) for PTD overall, 7 SNPs had p-values $\leq 10^{-6}$. SNPs mostly strongly associated with PTD were not in or near known candidate genes.

Conclusions: The GWAS approach allowed us to identify new chromosomal regions of potential importance to PTD etiology. Replication of promising SNPs in independent populations is underway to determine if any of our findings represent true positives and thereby potential new insights into the causes of PTD.