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LINKAGE ANALYSIS OF X CHROMOSOME IN SPONTANEOUS PRETERM BIRTH

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Background: Preterm birth accounts for 2-3 million annual deaths worldwide and is the major cause of acute and chronic morbidity in children. More than 50% of preterm births have a spontaneous onset. Family studies suggest that genetic factors affect the risk of spontaneous preterm birth (SPTB). However, the genetic background is poorly known.

Aim: To search for X chromosomal regions associating with SPTB using linkage analysis.

Methods: Seven large northern Finnish families with recurrent SPTBs and maternal transmission were selected for the study. DNA samples from family members were genotyped using Affymetrix 500Kb Array, consisting of 500,568 single-nucleotide polymorphism markers. Results of linkage analysis using autosomal markers in this array were previously reported; here the results of X chromosomal markers are presented. Analyze, v. 1.9.3 BETA, was used in parametric two-point linkage analysis of SPTB.

Results: Linkage analysis revealed three markers with significant signals (heterogeneity LOD score, HLOD >3) when the infant was studied as affected: rs6525299 (HLOD=3.72), rs11266593 (HLOD=3.05), and rs7056400 (HLOD=3.05). The first marker is located on chromosome locus Xq13.1 and the latter two on Xq21.1. Three interesting genes located near these loci were identified: those encoding androgen receptor (AR), interleukin 2 receptor, gamma (IL2RG), and chemokine (C-X-C motif) receptor 3 (CXCR3). These genes will be considered as candidates for SPTB in an upcoming case-control study of SPTB.

Conclusions: This is the first linkage study of X chromosomal markers in SPTB. We identified three potential candidate genes that may play a role in the pathology of SPTB.