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# Genetics and Pharmacogenomics

### 4.2 Chromosome 2q12: the Adrenergic Receptor 2b (ADRA2b) Gene and Metabolic Syndrome in Swedish – is there a Link?

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**Introduction.** Several linkage studies identified chromosome 2q12 as a hot spot for hypertension and other individual components of the metabolic syndrome (MetS). The common I/D polymorphism of the adrenergic receptor 2B (ADRA2B) gene, mapping in the same chromosomal region, was associated with hypertension and metabolic phenotypes.

**Aim.** To test if a 2 3 cM long region on chromosome 2 could be linked to metabolic syndrome (MetS) or its individual components and if a common I/D polymorphism of the ADRA2B gene mapping in that region is associated with the same traits.

**Methods.** 260 healthy, normotensive siblings belonging to 118 nuclear families from Malmö were included in the linkage analysis. We conducted a fine mapping of the region on chromosome 2 spanning between 107 to 130 cM using 11 informative polymorphic markers. Variance-component linkage analysis was performed for each MetS individual components and a composite sum of MetS phenotypes (MetS score) as quantitative trait after adjustment for significant covariates using 'Solar software package'. Successively, the I/D polymorphism of the ADRA2B gene was genotyped in 5283 subjects recruited in the Malmö Diet and Cancer-cardiovascular arm (MDC-CVA) seeking for association with the MetS defined according to the NCEP/ATP III, the IDF and the European Group for the Study of Insulin Resistance (EGIR) criteria and, separately, with its individual components.

**Results.** For 24-hour pulse pressure and for the waist/hip ratio LOD score >2 has been found all over the region between 107 to 122 cM. For the MetS score, LOD score >1 has been found between 116 and 120 cM. Of the 5283 subjects included in the association analysis 21.8%, 29.3% and 20.5% resulted affected by MetS (according to the NCEP/ATP III, IDF and EGIR definition, respectively). There was no difference between carriers and non-carriers of the D-allele of the ADRA2B gene in MetS prevalence but D-carriers were associated with higher levels of diastolic BP (87.24+ /-9.43 vs 86.50+ / -9.35 mmHg; p=0.006).

**Conclusions.** Our results suggest that chromosome 2 could harbour one or more genes implied in BP homeostasis and MetS development. The ADRA2B I/D polymorphism is not associated with MetS and metabolic/anthropometric parameters whereas is associated with diastolic BP.