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Title: Normal antioxidative enzyme activities in several genes are associated with less bronchial hyperresponsiveness (BHR) among young Danes

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Body: BACKGROUND AND AIM BHR might be associated to the oxidative defense. We hypothesize that genotypes coding for normal antioxidative enzyme activity (AEA) influence the occurrence of BHR.

METHODS In a cross sectional study 7,271 subjects aged 20-44 year (73% response rate) were recruited using an asthma screening questionnaire. All subjects with asthma (n = 460) and a 20% random sample (n=

728) were clinically investigated, including a bronchial provocation test, skin prick test (SPT) with 13

aeroallergens, and a blood sample. A bronchial provocation test was available for 956 subjects, and BHR

was defined as at least 20% drop in baseline FEV₁. Variants in the following genes were genotyped:

Glutathione peroxidase, GPX1 (Pro198Leu, rs1050450), manganese superoxide dismutase, SOD2

(Ala16Val, rs4880) and 3 glutathione S-transferases; GSTP1 (Ile105Val, rs1695), GSTT1 (gene copy nr)

and GSTM1 (gene copy nr). **RESULTS** The frequency of BHR was 12.8% in the random sample and 42.6%

in the asthma sample. Log. reg. models showed a neg. association between being BHR and having at least

4 genotypes coding for normal AEA compared to no normal genotype, OR 0.24 (0.06-0.94) adj. for smoking,

FEV₁, sex, atopy, height² and SPT-size of HDM. The result were similar after further adjustments for BMI,

county and sample (random/case), OR 0.25 (0.06-1.06). ORs for BHR were decreased for 1 – 3 genotypes

with normal AEA compared to no normal genotype, but not significantly so and no clear dose-response

relations were seen. **CONCLUSION** This study suggests, that a combined effect of several genotypes

coding for normal AEA might be a protective factor for BHR among young adults.