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Title: Meta-analysis of genome-wide association studies of single nucleotide polymorphisms in selected genes of the WNT signaling pathway

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Body: Background: The WNT signaling pathway is involved in a wide range of developmental events and maintenance of homeostasis in adult tissue, including lung development and health. WNT signaling genes have also been suggested to play a role in pathogenesis of lung diseases such as chronic obstructive pulmonary disease (COPD) and asthma. Aims and Objectives: The aim of this meta-analysis was to identify consistent disease markers for COPD, asthma, forced expiratory volume in one second (FEV1), and forced vital capacity (FVC) in nine genes of the WNT signaling cascade pathway (WNT10b, WIF1, WISP1, SFRP2, SFRP5, DKK1, Axin2, TCF7L2, and FZD3) using genome-wide association data from six European cohort

studies. Methods: The six European cohort studies included are: B58C (UK), ECRHS (multicentre), EGEA (France), GINI / LISA (Germany), NFBC1966 (Finland), and SAPALDIA (Switzerland). We identified a total of 105 single nucleotide polymorphisms (SNPs) in the nine genes (including a region 2 kb in size up- and downstream the gene). Effect estimates were analyzed using a fixed or random effect pooled testing (depending on homogeneity) for association in the overall study population. Results and Conclusions: We identified weak genetic associations (p-values between 0.002 and 0.046) in our meta-analysis for COPD (Axin2), asthma (SFRP2, TCF7L2, WIF1, DKK1), FEV1 (SFRP2, TCF7L2, DKK1), and FVC (TCF7L2, WNT10b). Notably in TCF7L2 six different SNPs were identified (p-values between 0.002 and 0.046) in association with asthma, FEV1, and FVC. In literature, WNT signaling genes were linked to COPD (Axin2), asthma (TCF7L2, SFRP2), and decreased FEV1 and FVC (TCF7L2).