Supplementary Table 1:
Top gene-sets associated with COPD in COPDGene and GenKOLS.

Full list of all 42 gene-sets that reached nominal significance in COPDGene and GenKOLS. Gene-sets are given together with their p-values for the two studies. METAINFO: GENE-SET – name of the gene-set, for a detailed description please see MsigDB, N_all – number of genes in this gene list (MsigDB). COPDGene / GenKOLS / ECLIPSE: N_in – number of successfully incorporated genes per gene-set, P – p-value for gene-set, Pcorr – results of analysis without known COPD genes in the gene-sets. Combined: P – p-value for gene-set after meta-analysis of COPDGene and GenKOLS study results, Pcorr – results of meta-analysis without known COPD genes in the gene-sets. Gene-sets highlighted in bold demonstrated a nominally significant p-value across all studied samples.

Supplementary Table 2:
REACTOME PRESYNAPTIC NICOTINIC ACETYLCHOLINE RECEPTORS pathway gene list and corresponding FORGE gene-based results in COPDGene and GENKOLS.

This pathway was the top pathway associated with COPD case-control status in both COPDGene and in GenKOLs. The FORGE gene-based results are displayed for both studies. METAINFO: GENE – HUGO gene name, CHR – chromosome, START – start position in base pairs from the start of the chromosome, STOP – stop position in base pairs from the start of the chromosome; COPDGene / GenKOLS / ECLIPSE: N – number of SNPs annotated to this gene for the respective study, Min P – p-value for the SNP with the lowest p-value (of all SNPs annotated to the gene), Gene P – gene-based p-value for this gene from FORGE analyses. Combined: Gene P – gene-based p-value for this gene from meta-analysis of COPDGene and GenKOLS single study p-values. Genes are highlighted in bold if they surpass the experiment-wide significance level (1E-06) for the gene-based analyses or a SNP annotated to the gene (5E-08) in the discovery population (COPDGene). Genes are highlighted in italics if they reached nominal significance for the gene-based discovery (COPDGene) and replication (GenKOLS) results. All p-values achieving nominal significance are shaded in grey.

Supplementary Figure 1: **a.** dmGWAS consensus module generated using the COPDGene results that replicated in GenKOLS. Node color is proportional to p-value significance where the lighter the node shading the smaller the p-value from the gene-based analysis in FORGE. **b.** dmGWAS analysis repeated excluding *UBC* using COPDGene results that replicated in GenKOLS.

Supplementary Figure 2: dmGWAS consensus networks that were generated when the FORGE p-values in COPDGene and GenKOLS were shuffled and run in dmGWAS 10 times.