

Supplementary Table 2. Complete list of enriched gene sets associated with lung function using staged pathway analysis of two independent GWAS cohorts (CHARGE, SpiroMeta). The gene sets were clustered using gene membership profiles to identify functional modules (see Figures 2 and 3 in main article). All enriched pathways were required to be significantly associated with at least one lung function measure in both CHARGE and SpiroMeta (highlighted in red if FDR < 0.05).

Pathway/Gene set	Functional Module	FEV ₁ , CHARGE	FEV ₁ /FVC CHARGE	FEV ₁ , SpiroMeta	FEV ₁ /FVC SpiroMeta
HSA00534 HEPARAN SULFATE BIOSYNTHESIS	Glycoprotein				
CHONDROITIN	Glycoprotein				
HEPARAN SULFATE BIOSYNTHESIS	Glycoprotein				
PROTEOGLYCAN BIOSYNTHETIC PROCESS	Glycoprotein				
SULFOTRANSFERASE ACTIVITY	Metabolism				
CARBOHYDRATE KINASE ACTIVITY	Metabolism				
OXIDOREDUCTASE ACTIVITY ACTING ON SULFUR GROUP OF DONORS	Metabolism				
ETCPATHWAY	Metabolism				
ANTIporter ACTIVITY	Channel/Transporter				
REGULATION OF HEART CONTRACTION	Channel/Transporter				
AUXILIARY TRANSPORT PROTEIN ACTIVITY	Channel/Transporter				
CHANNEL REGULATOR ACTIVITY	Channel/Transporter				
POTASSIUM ION TRANSPORT	Channel/Transporter				
POTASSIUM CHANNEL ACTIVITY	Channel/Transporter				
CATION TRANSMEMBRANE TRANSPORTER ACTIVITY	Channel/Transporter				
SUBSTRATE SPECIFIC TRANSPORTER ACTIVITY	Channel/Transporter				
VOLTAGE GATED CALCIUM CHANNEL ACTIVITY	Channel/Transporter				
CATION TRANSPORTING ATPASE ACTIVITY	Channel/Transporter				
HSA04020 CALCIUM SIGNALING PATHWAY	Cell Signaling				
G PROTEIN SIGNALING COUPLED TO CAMP NUCLEOTIDE SECOND MESSENGER	Cell Signaling				
SECOND MESSENGER MEDIATED SIGNALING	Cell Signaling				
G PROTEIN SIGNALING COUPLED TO CYCLIC NUCLEOTIDE SECOND MESSENGER	Cell Signaling				
GPCRDB CLASS A RHODOPSIN LIKE	Cell Signaling				
HSA04080 NEUROACTIVE LIGAND RECEPTOR INTERACTION	Cell Signaling				
PHOSPHOINOSITIDE MEDIATED SIGNALING	Cell Signaling				
ST WNT CA2 CYCLIC GMP PATHWAY	Cell Signaling				
CACAMPATHWAY	Cell Signaling				
GCRPATHWAY	Cell Signaling				
PKCPATHWAY	Cell Signaling				
TCRPATHWAY	Cell Signaling				
TRKAPATHWAY	Cell Signaling				
PLCPATHWAY	Cell Signaling				
ACTIVATION OF NF KAPPAB TRANSCRIPTION FACTOR	Cell Signaling				
POSITIVE REGULATION OF TRANSCRIPTION FACTOR ACTIVITY	Cell Signaling				
POSITIVE REGULATION OF DNA BINDING	Cell Signaling				
FREEPATHWAY	Cell Signaling				
RELAPATHWAY	Cell Signaling				
NTHIPATHWAY	Cell Signaling				
NUCLEAR REPLICATION FORK	Transcription				
CIRCADIANPATHWAY	Transcription				
HSA04710 CIRCADIAN RHYTHM	Transcription				
LIGAND DEPENDENT NUCLEAR RECEPTOR ACTIVITY	Transcription				
STEROID HORMONE RECEPTOR ACTIVITY	Transcription				
HISTONE MODIFICATION	Transcription				
ESTABLISHMENT AND OR MAINTENANCE OF CHROMATIN ARCHITECTURE	Transcription				
CHROMATIN MODIFICATION	Transcription				
THYROID HORMONE RECEPTOR BINDING	Transcription				
RNA POLYMERASE II TRANSCRIPTION FACTOR ACTIVITY	Transcription				
REGULATION OF TRANSCRIPTION DNA DEPENDENT	Transcription				
COPPER ION BINDING	Other				
CARBOXY LYASE ACTIVITY	Metabolism				
HISTIDINE METABOLISM	Metabolism				
RIBONUCLEOPROTEIN COMPLEX	Transcription				
SMALL NUCLEAR RIBONUCLEOPROTEIN COMPLEX	Transcription				
RNA SPLICING FACTOR ACTIVITY TRANSESTERIFICATION MECHANISM	Transcription				
NUCLEAR SPECK	Transcription				
CELLULAR RESPONSE TO STRESS	Transcription				
RABPATHWAY	Development				
G PROTEIN SIGNALING ADENYLATE CYCLASE INHIBITING PATHWAY	GABA & Glutamate				
METABOTROPIC GLUTAMATE GABA B LIKE RECEPTOR ACTIVITY	GABA & Glutamate				
GLUTAMATE RECEPTOR ACTIVITY	GABA & Glutamate				
GLUTAMATE SIGNALING PATHWAY	GABA & Glutamate				
NEUROTRANSMITTER SECRETION	GABA & Glutamate				

REGULATED SECRETORY PATHWAY	GABA & Glutamate				
HSA00062 FATTY ACID ELONGATION IN MITOCHONDRIA	Metabolism				
SYNAPTIC VESICLE	GABA & Glutamate				
VACUOLE ORGANIZATION AND BIOGENESIS	Other				
LYSOSOME ORGANIZATION AND BIOGENESIS	Other				
PHOSPHOLIPID TRANSPORTER ACTIVITY	Channel/Transporter				
LIPID TRANSPORTER ACTIVITY	Channel/Transporter				
IMMUNOLOGICAL SYNAPSE	Immunity				
INTERLEUKIN 8 BIOSYNTHETIC PROCESS	Immunity				
INTERLEUKIN 8 PRODUCTION	Immunity				
DEFENSE RESPONSE	Immunity				
INFLAMMATORY RESPONSE	Immunity				
RESPONSE TO STRESS	Immunity				
IMMUNE SYSTEM PROCESS	Immunity				
IMMUNE RESPONSE	Immunity				
ACTIVATION OF IMMUNE RESPONSE	Immunity				
REGULATION OF RESPONSE TO STIMULUS	Immunity				
DEFENSE RESPONSE TO VIRUS	Immunity				
TRANSMEMBRANE RECEPTOR PROTEIN PHOSPHATASE ACTIVITY	Immunity				
EPHA4PATHWAY	Immunity				
TCRAPATHWAY	Immunity				
HSA04940 TYPE I DIABETES MELLITUS	Immunity				
HSA04612 ANTIGEN PROCESSING AND PRESENTATION	Immunity				
HSA04514 CELL ADHESION MOLECULES	Adhesion				
PROTEIN TYROSINE KINASE ACTIVITY	Adhesion				
TRANSMEMBRANE RECEPTOR PROTEIN TYROSINE KINASE ACTIVITY	Adhesion				
TRANSMEMBRANE RECEPTOR PROTEIN KINASE ACTIVITY	Adhesion				
HSA04510 FOCAL ADHESION	Adhesion				
HSA05218 MELANOMA	Adhesion				
HSA05216 THYROID CANCER	Adhesion				
HSA04530 TIGHT JUNCTION	Adhesion				
ACTIN CYTOSKELETON	Adhesion				
CYTOSKELETON	Adhesion				
CELL DIVISION	Adhesion				
CYTOKINESIS	Adhesion				
NUCLEOTIDE KINASE ACTIVITY	Adhesion				
ANCHORED TO PLASMA MEMBRANE	Adhesion				
ANCHORED TO MEMBRANE	Adhesion				
HSA05217 BASAL CELL CARCINOMA	Development				
HSA04340 HEDGEHOG SIGNALING PATHWAY	Development				
GLAND DEVELOPMENT	Development				
NEGATIVE REGULATION OF CELL DIFFERENTIATION	Development				
NEGATIVE REGULATION OF DEVELOPMENTAL PROCESS	Development				
ANATOMICAL STRUCTURE MORPHOGENESIS	Development				
ANATOMICAL STRUCTURE FORMATION	Development				
REGULATION OF ANGIOGENESIS	Development				
NEUROGENESIS	Development				
GENERATION OF NEURONS	Development				
NEURON DIFFERENTIATION	Development				
AXON GUIDANCE	Development				
CENTRAL NERVOUS SYSTEM DEVELOPMENT	Development				
NERVOUS SYSTEM DEVELOPMENT	Development				
TISSUE MORPHOGENESIS	Development				
ECTODERM DEVELOPMENT	Development				
EPIDERMIS DEVELOPMENT	Development				
CELL RECOGNITION	Other				
LIPOPROTEIN BINDING	Other				
NEGATIVE REGULATION OF CELL CYCLE	Proliferation				
CELL PROLIFERATION GO 0008283	Proliferation				
REGULATION OF CELL PROLIFERATION	Proliferation				
REGULATION OF CELL ADHESION	Proliferation				
NEGATIVE REGULATION OF CELL ADHESION	Proliferation				
CELL CELL ADHESION	Proliferation				
EPIDERMAL GROWTH FACTOR RECEPTOR SIGNALING PATHWAY	Proliferation				
POSITIVE REGULATION OF CELL MIGRATION	Proliferation				
REGULATION OF CELL MIGRATION	Proliferation				
PROSTAGLANDIN AND LEUKOTRIENE METABOLISM	Arachidonic acid				
HSA00590 ARACHIDONIC ACID METABOLISM	Arachidonic acid				