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**Supplementary Fig. 1.** Representative image of the patient’s thoracic CT showing lower lobes of the lung involved with extensive emphysema, with loss of normal lung tissue density (arrowhead) and large bulla formation (arrow).

**Supplementary Table S1**. SNPs within *IGSF3* associated with COPD phenotypes.****

**Supplementary Table ST2.** Gene enrichment linked to subcellular localization in subject differentially expressed in patient versus control lymphoblastoids

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| *GO cellular component complete* | *N (patient)* | *N (control)* | *Expected* | *Fold Enrichment* | *+/-* | *raw P value* | *FDR* |
| *endoplasmic reticulum chaperone complex* | 11 | 5 | 0.39 | 12.86 | + | 1.46E-04 | 6.75E-03 |
| *ubiquitin conjugating enzyme complex* | 9 | 4 | 0.32 | 12.58 | + | 7.52E-04 | 2.79E-02 |
| *endoplasmic reticulum exit site* | 27 | 7 | 0.95 | 7.34 | + | 1.26E-04 | 6.42E-03 |
| *rough endoplasmic reticulum membrane* | 29 | 6 | 1.02 | 5.85 | + | 1.08E-03 | 3.66E-02 |
| *U2-type precatalytic spliceosome* | 43 | 7 | 1.52 | 4.61 | + | 1.46E-03 | 4.65E-02 |
| *melanosome* | 106 | 15 | 3.75 | 4 | + | 1.62E-05 | 9.73E-04 |
| *proteasome complex* | 67 | 9 | 2.37 | 3.8 | + | 1.11E-03 | 3.70E-02 |
| *large ribosomal subunit* | 125 | 13 | 4.42 | 2.94 | + | 9.04E-04 | 3.12E-02 |
| *mitochondrial protein complex* | 272 | 22 | 9.61 | 2.29 | + | 5.52E-04 | 2.12E-02 |
| *focal adhesion* | 404 | 31 | 14.28 | 2.17 | + | 1.34E-04 | 6.51E-03 |
| *extracellular exosome* | 2097 | 133 | 74.11 | 1.79 | + | 1.03E-10 | 1.10E-08 |
| *membrane protein complex* | 1203 | 66 | 42.51 | 1.55 | + | 7.63E-04 | 2.78E-02 |