Table S1: ECLIPSE Sample Demographics. Descriptive values for COPD patients (N = 114) in ECLIPSE with gene expression data by Cachectic (N = 9) and Non-Cachectic (N = 105) co-morbid status. Unless otherwise noted values denote mean (SD).

| Demographic       | Cachectic | Non-Cachectic | P-value |
|-------------------|-----------|---------------|---------|
| N (%)             | 9 (7.9)   | 105 (92.1)    |         |
| Age               | 64.2±5.4  | 64.9±5.4      | 0.69    |
| Sex N (%)         |           |               |         |
| Male              | 5 (55.6)  | 73 (69.5)     |         |
| Female            | 4 (44.4)  | 36 (31.6)     | 0.62    |
| FEV1pp (%)        | 39.9±17.6 | 51.4±14.7     | 0.028   |
| Pack Years Smoking| 44.0±15.4 | 48.0±29.2     | 0.69    |
| BMI (kg/m²)       | 21.1±4.8  | 27.6±5.3      | <0.001  |

FEV1pp – Forced Expiratory Volume in One Second Percent Predicted, BMI - Body Mass Index, SD – Standard Deviation

Table S2: Gene set enrichment analysis of significantly (FDR p-value < 0.05) differentially expressed between cachectic and non-cachectic COPD patients in COPDGene.

| Gene Set Name                        | N Genes in Set | N Genes Overlap | P-value       | FDR P-value |
|--------------------------------------|----------------|-----------------|---------------|-------------|
| GSE34205 RSV vs Flu INF Infant PBMC Up| 200            | 7               | 4.99 x 10^-13 | 7.87 x 10^-9 |
| Hallmark Heme Metabolism             | 200            | 6               | 7.49 x 10^-11 | 5.92 x 10^-7 |
| Nuytten EZH2 Targets Up              | 1037           | 7               | 4.66 x 10^-8  | 2.45 x 10^-4 |
| Valk AML Cluster 7                   | 28             | 3               | 1.37 x 10^-7  | 5.41 x 10^-4 |
| GSE34205 Healthy vs RSV INF Infant PBMC Down | 200 | 4 | 7.92 x 10^-7 | 0.00250 |
| CHYLA CBFA2T3 Targets Down           | 242            | 4               | 1.69 x 10^-6  | 0.00445 |
| McBryan Terminal End Bud Up          | 12             | 2               | 8.48 x 10^-6  | 0.0191 |
| Steiner Erythrocyte Membrane Genes   | 15             | 2               | 1.35 x 10^-5  | 0.0266 |
| REACTOME Immune System               | 933            | 5               | 1.72 x 10^-5  | 0.0302 |
| GO Heme Biosynthetic Process         | 20             | 2               | 2.44 x 10^-5  | 0.0385 |
| Welch GATA1 Targets                  | 22             | 2               | 2.96 x 10^-5  | 0.0417 |
| REACTOME Interaction Between L1 And Ankynirs | 23 | 2 | 3.24 x 10^-5 | 0.0417 |
| Valk AML Cluster 8                   | 26             | 2               | 4.16 x 10^-5  | 0.0417 |
| GO Tetrapyrrole Biosynthetic Process | 27             | 2               | 4.50 x 10^-5  | 0.0417 |
| PRC2 SUZ12 UP V1 Up                  | 191            | 3               | 4.60 x 10^-5  | 0.0417 |
| GO Heme Metabolic Process            | 29             | 2               | 5.20 x 10^-5  | 0.0417 |
| GSE16522 ANTI CD3CD28 Stim vs Unstim Memory CD8 T-cell Up | 199 | 3 | 5.20 x 10^-5 | 0.0417 |
| GSE19401 PAM2CSK4 VS Retinoic Acid Stim Follicular DC Up | 200 | 3 | 5.28 x 10^-5 | 0.0417 |
| GSE2492 WT vs PPARG KO Macrophage Up  | 200            | 3               | 5.28 x 10^-5  | 0.0417 |
| GSE38304 MYC neg vs Pos GC B-cell Up  | 200            | 3               | 5.28 x 10^-5  | 0.0417 |

FDR - False Discovery Rate. Gene set collections from MSigDB include H, C2, C5, C6, and C7.