Supplementary Figure Legends

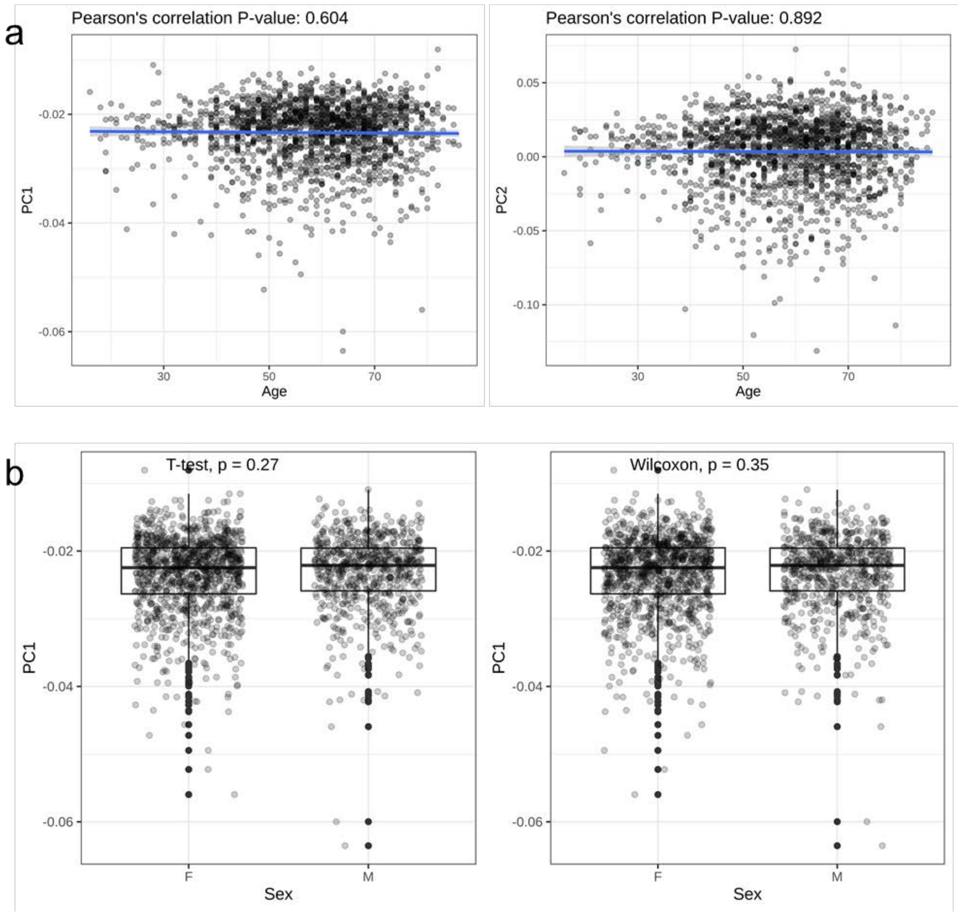
Supplementary Fig. 1. Correlation between age, sex, and serum microbiome

Pearson's correlation was evaluated at principal components 1 and 2 (PC1 and PC2) to determine if there was significant correlation between the **a)** age or **b)** sex of clinical subjects and their serum microbiome profiles. Significance was established at $p \leq 0.05$.

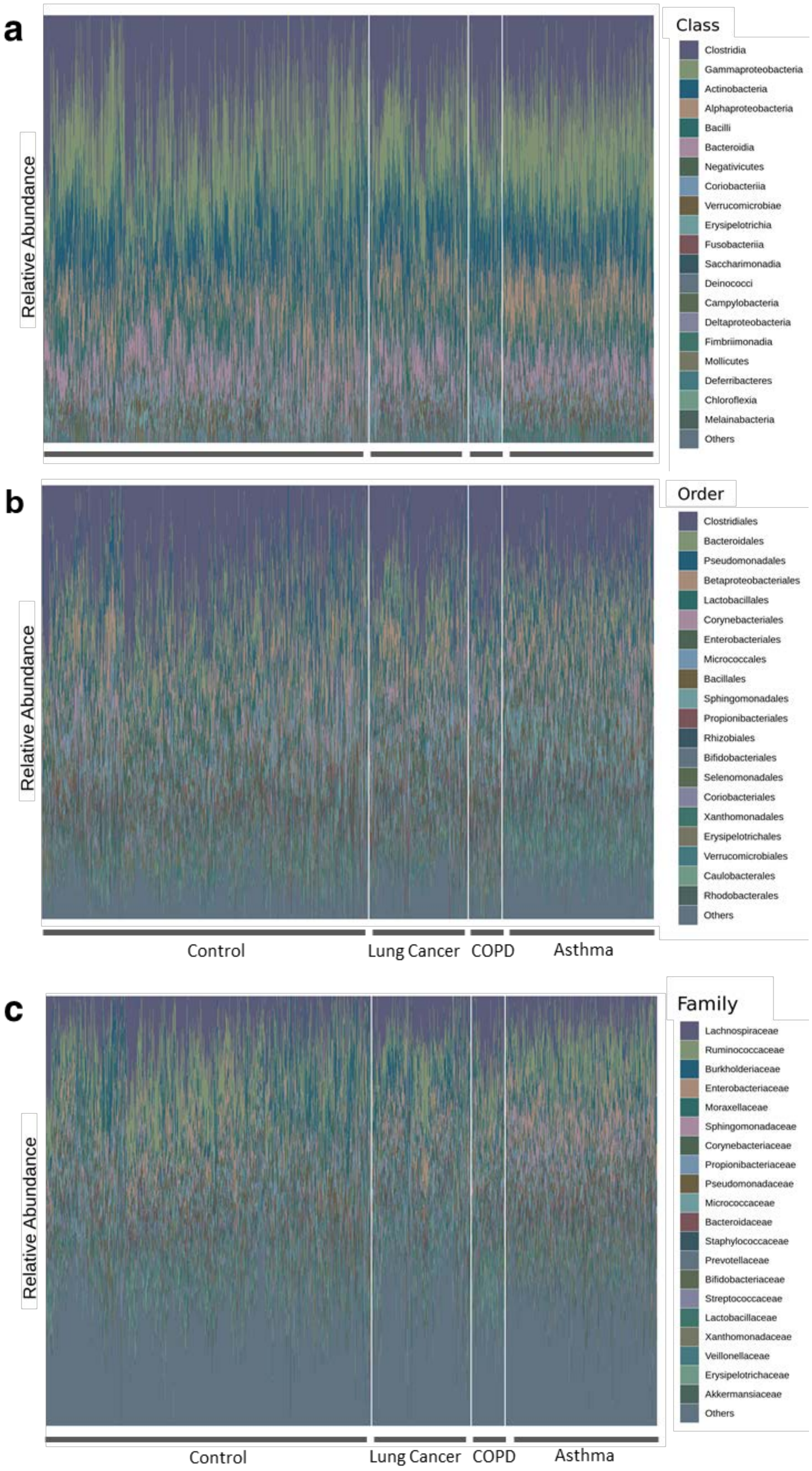
Supplementary Fig. 2. Serum microbiome compositional profiles between clinical groups (class, order, and family levels)

Composition of the most abundant taxa of the serum EV microbiome in healthy control, COPD, and lung cancer clinical groups at the **a)** class, **b)** order, and **c)** family levels was expressed as bar plots based on the relative abundance of taxa within each sample.

Supplementary Fig. 1



Supplementary Fig. 2



Supplementary Tables

Supplementary Table 1. Basic subject clinical characteristics

Group	Institution	No.	Sex (M/F)	Age (mean [SD])
Control	Inje University Haeundae Hospital	928	0.35	58.78 [10.68]
COPD	Konkuk University Medical Center	92	22.00	69.68 [7.33]
Asthma	Asan Medical Center	428	0.69	51.53 [15.59]
Lung cancer	Samsung Medical Center	251	1.68	62.72 [10.67]
	Dankook University Hospital	28		

COPD: Chronic Obstructive Pulmonary Disease; SD: Standard Deviation.

Supplementary Table 2. Summary of raw serum microbial EV sample read counts and profiled OTU counts

	Read Count			OTU		
Group	Mean	Median	SD	Mean	Median	SD
Control	57,252	42,485	40,749	9,589	8,457	6,929
COPD	29,441	25,908	13,283	13,039	12,012	5,354
Asthma	71,328	64,823	33,806	9,736	7,704	7,750
Lung cancer	35,409	28,359	20,597	13,345	11,022	8,249
Total	55,993	44,444	37,745	10,384	9,145	7,433

OTU: Operational Taxonomic Unit; COPD: Chronic Obstructive Pulmonary Disease; SD: Standard Deviation.

Supplementary Table 3. Assessment of important serum microbial EV features in respiratory disease models

Model	**Phylum**	**Weight**	**No. of Features**	**Feature Weight Range**
COPD	Firmicutes	0.092	326	-2.15E-04 ~ 1.82E-02
	Actinobacteria	0.037	250	-1.64E-04 ~ 2.72E-03
	Verrucomicrobia	0.015	17	5.82E-04 ~ 2.16E-03
	Proteobacteria	0.015	469	-2.05E-04 ~ 4.07E-03
	Bacteroidetes	0.006	125	-1.44E-04 ~ 1.09E-03
	Epsilonbacteraeota	0.002	6	1.05E-05 ~ 1.61E-03
	Acidobacteria	0.001	28	-3.06E-05 ~ 4.66E-04
Asthma	Proteobacteria	0.123	469	-1.62E-04 ~ 9.60E-03
	Armatimonadetes	0.034	3	9.64E-04 ~ 2.09E-02
	Bacteroidetes	0.022	125	-4.78E-05 ~ 3.33E-03
	Actinobacteria	0.016	250	-1.25E-04 ~ 3.31E-03
	Firmicutes	0.012	326	-1.49E-04 ~ 2.22E-03
	Verrucomicrobia	0.009	17	6.73E-05 ~ 1.71E-03
	Cyanobacteria	0.002	31	-3.84E-06 ~ 5.71E-04
Lung cancer	Proteobacteria	0.090	469	-1.28E-04 ~ 1.59E-02
	Firmicutes	0.062	326	-1.01E-04 ~ 5.58E-03
	Epsilonbacteraeota	0.031	6	7.70E-04 ~ 1.13E-02
	Actinobacteria	0.020	250	-1.61E-04 ~ 1.91E-03
	Bacteroidetes	0.009	125	-7.15E-05 ~ 3.19E-03
	Deinococcus-Thermus	0.008	4	1.70E-04 ~ 4.87E-03
	Verrucomicrobia	0.006	17	9.70E-06 ~ 1.90E-03
	Tenericutes	0.003	12	-3.36E-05 ~ 1.99E-03
	Fusobacteria	0.002	7	1.12E-04 ~ 5.19E-04