## **Supplementary Information**

Figure S1 – Principal Coordinates Analysis (PCoA) plot of unweighted UniFrac distance of the nasal vs. bronchial microbiome in children with severe persistent asthma (② in Figure 1).

Figure S2 – Bacterial diversity of the nasal microbiome of healthy children vs. children with severe persistent asthma. (⑥ in Figure 1).

Figure S3 – Principal Coordinates Analysis (PCoA) plot of the nasal microbiome of children with severe persistent asthma vs. healthy children. (⑥ in Figure 1).

Table S1: Baseline characteristics of the study population

Table S2A: Genes upregulated in bronchial vs. nasal brushings from children with severe persistent asthma

Table S2B: Genes upregulated in nasal vs. bronchial brushings from children with severe persistent asthma

Table S3A: Gene Ontology terms for genes upregulated in bronchial vs. nasal brushings from children with severe persistent asthma

Table S3B: Gene ontology terms for genes upregulated in nasal vs. bronchial brushings from children with severe persistent asthma

Table S4A: Differential gene expression (DE) analyses for ACT and asthma medication use in children with severe persistent asthma

Table S4B: Alpha diversity analyses for ACT and asthma medication use in children with severe persistent asthma

Table S5: Summary of microbiome networks

Table S6: Network of associations among nasal microbiota in children with severe persistent asthma

Table S7: Network of associations among bronchial microbiota in children with severe persistent asthma

Table S8: Network of associations between nasal and bronchial microbiota in children with severe persistent asthma

Table S9: Summary of microbiome-transcriptome networks

Table S10: Network of associations between the nasal transcriptome and nasal microbiome in children with severe persistent asthma

Table S11: Network of associations between the bronchial transcriptome and bronchial microbiome in children with severe persistent asthma

Table S12A: Nasal genes underexpressed in children with severe persistent asthma vs. healthy controls

Table S12B: Nasal genes underexpressed in children with severe persistent asthma vs. healthy controls

Table S13: Network of associations among nasal microbiota in healthy controls

Table S14: Network of associations between the nasal transcriptome and nasal microbiome in healthy children

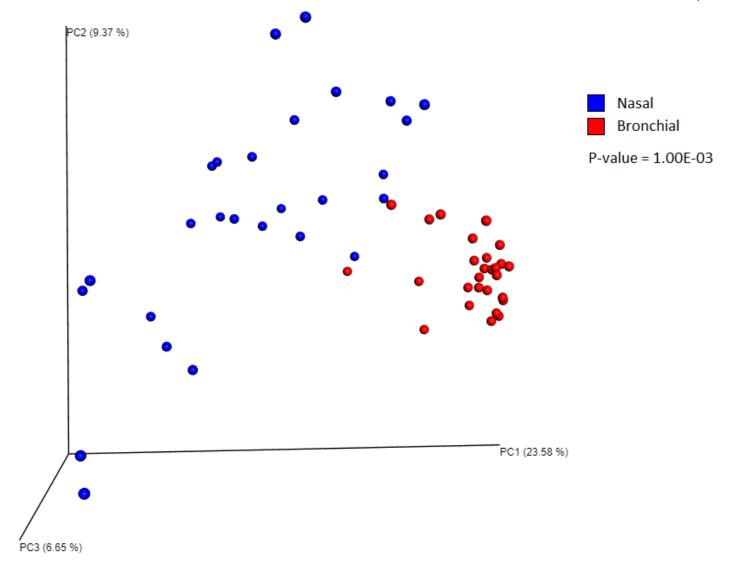


Figure S1 – Principal Coordinates Analysis (PCoA) plot of unweighted UniFrac distance of the nasal vs. bronchial microbiome in children with severe persistent asthma (② in Figure 1).

PCoA plot of unweighted UniFrac distance shows clear separation of bacterial composition between the nasal and bronchial microbiome of children with severe persistent asthma (n=27). Each point corresponds to a sample colored by airway site. P-value was calculated using PERMANOVA with 1,000 permutations.

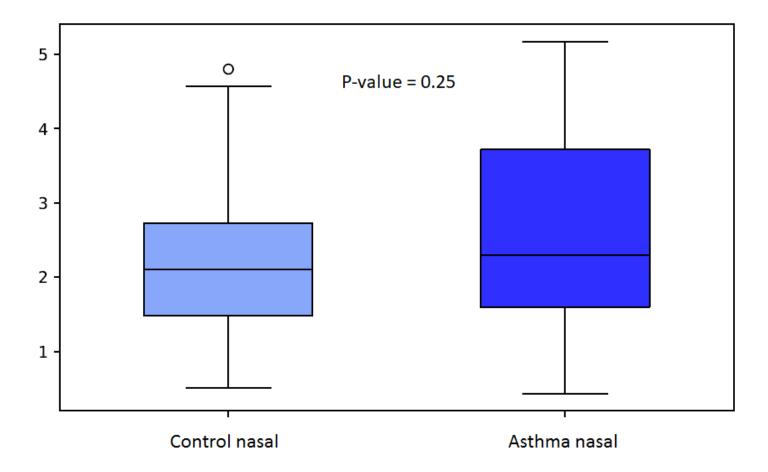


Figure S2 – Bacterial diversity of the nasal microbiome of healthy children vs. children with severe persistent asthma. (⑥ in Figure 1).

Alpha diversity was estimated by Shannon Index at rarefaction depth of 1,950 using 27 control nasal samples and 27 asthmatic nasal samples. Mean and standard deviation of alpha diversity were estimated by subsampling 10 times for each sample at this rarefaction depth. The Monte Carlo method was used with 1,000 permutations and correction for multiple comparisons by FDR.

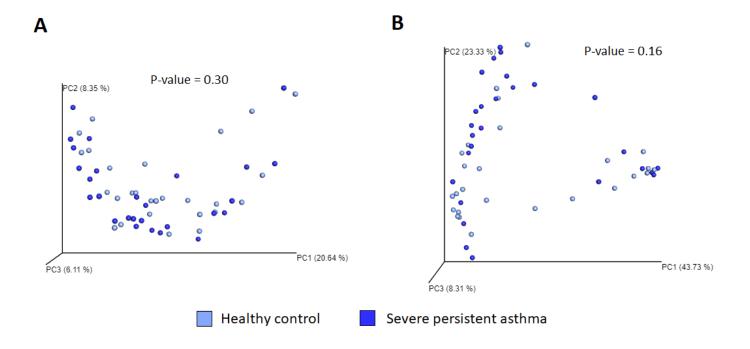


Figure S3 – Principal Coordinates Analysis (PCoA) plot of the nasal microbiome of children with severe persistent asthma vs. healthy children. (⑥ in Figure 1).

PCoA plots of unweighted **(A)** and weighted **(B)** UniFrac distances of children with severe persistent asthma (n=27) vs. healthy children (n=27). Each point represents a sample and is colored by airway site. P-values were calculated using PERMANOVA with 1,000 permutations.