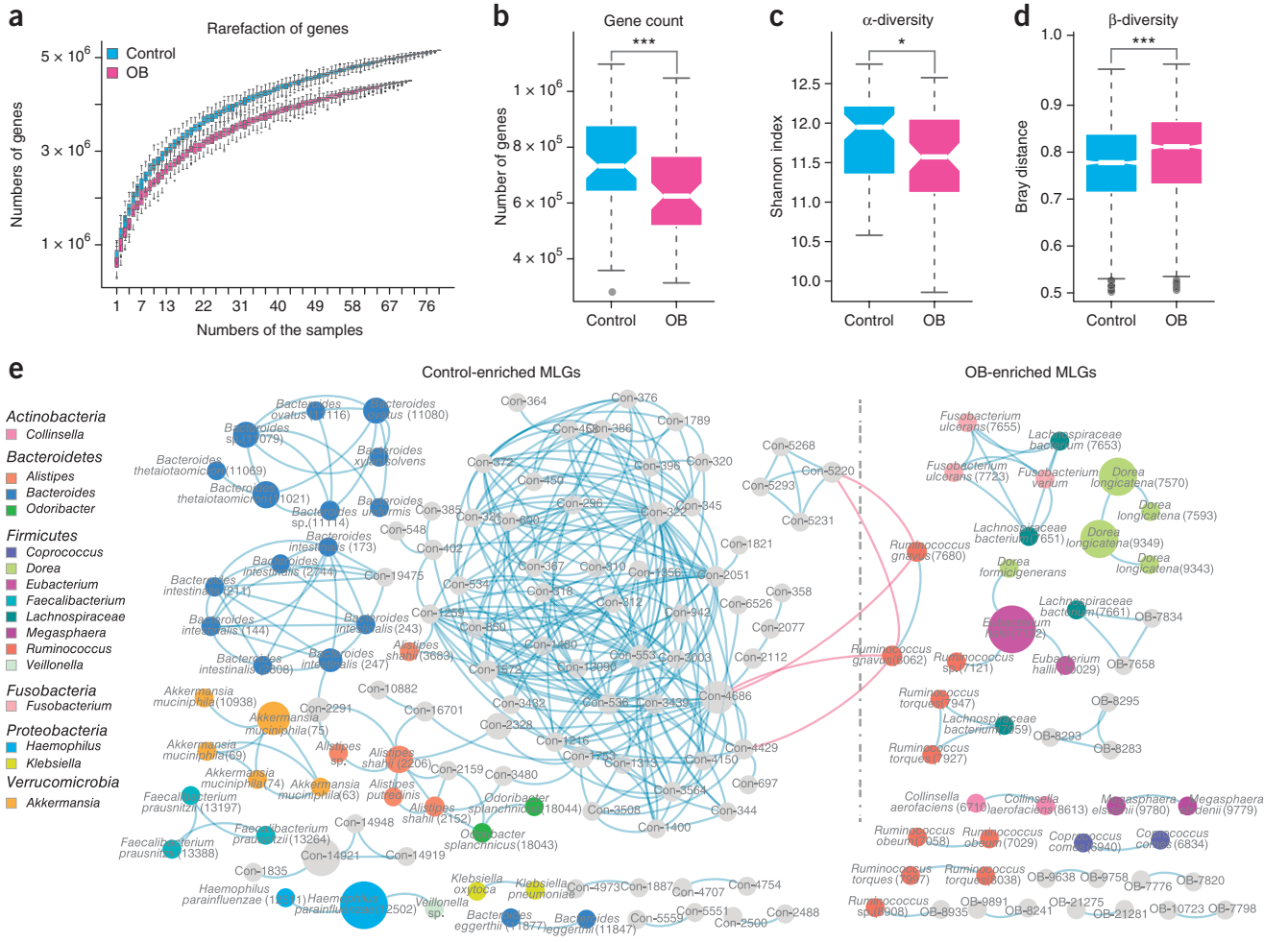

Figure 1 Gut microbial alterations in young, obese individuals. Comparison between shotgun sequencing data of stool samples from lean controls ($n = 79$) and obese individuals ($n = 72$). (**a**) Rarefaction curves based on gene count in lean controls and obese individuals. (**b**) Box plot of the gene count in control and obese subjects. (**c**,**d**) α-diversity (Shannon index; **c**) and β-diversity (Bray-Curtis similarity index; **d**) of the two groups at the gene level. For **a**–**d**, two-tailed Wilcoxon rank-sum test was used to determine significance. In **b**–**d**, boxes represent the interquartile ranges (IQRs) between the first and third quartiles, and the line inside the box represents the median; whiskers represent the lowest or highest values within 1.5 times IQR from the first or third quartiles. Circles represent data point beyond the whiskers. The notches show the 95% confidence interval for the medians. $^{*}P < 0.05$, $^{***}P < 0.001$. (**e**) Co-occurrence network deduced from 217 MLGs (**Supplementary Table 3**) enriched in obese subjects and controls. Sizes of the nodes represent the number of genes in the MLGs (100–4,482). Blue edges, Spearman's rank correlation coefficient > 0.6, adjusted $P < 0.05$; red edges, Spearman's rank correlation coefficient < –0.6, adjusted $P < 0.05$. MLGs with >50% genes annotated to the same species or genus were given the corresponding annotation. Unclassified MLGs could not be annotated to any taxonomic level as a result of the low gene annotation rate (11% on average, see **Supplementary Table 3**). The numbers in parentheses next to each species name represent unique MLG identifiers.

584 KOs differed in abundance between lean and obese subjects ($P < 0.01$; **Supplementary Table 10**). Furthermore, KEGG pathways belonging to the 'phosphotransferase system' involved in importing carbohydrate were highly enriched in the microbiome of obese individuals as compared with lean controls, and the phosphotransferase system modules were positively correlated with species from the *Firmicutes* phylum. Conversely, genes involved in the 'citrate cycle' pathway were depleted in the obese microbiome as compared with lean controls (**Supplementary Fig. 5a**,**b** and **Supplementary Tables 10**–**13**). This was similar to the alterations in the gut microbiomes in obese twins of European and African ancestry[5] and diet-induced obese mice[22]. However, unlike these cases, pathways involved in carbohydrate metabolism, including 'fructose and mannose metabolism', 'galactose metabolism' and 'starch and sucrose metabolism', were all highly enriched in the obese microbiome as compared with lean controls. The 'glycosaminoglycan degradation' pathway harbored by gut commensals, such as *B. thetaiotaomicron*, *B. intestinalis* and other species from the *Bacteroides* genus possessing highly specific sulfatases to metabolize host glycans[23,24], were depleted in the microbiome of obese individuals as compared with lean controls.

Previous studies have suggested a role for *A. muciniphila* and *B. thetaiotaomicron* in maintaining the epithelial barrier[18,25]; thus, depletion of these species may impair gut barrier integrity, increasing transport of lipopolysaccharide (LPS) to circulation and triggering induction of pro-inflammatory factors such as TNFα and IL6 (ref. 26). We found that the abundance of genes related to 'LPS biosynthesis' and 'peptidoglycan biosynthesis' was higher in the microbiome of obese individuals than in that of lean controls, which may be related to the observed higher serum concentration of LBP, TNFα and IL6 in obese individuals (**Supplementary Table 1**). Furthermore, amino-acid-metabolism-related pathways involving 'phenylalanine, tyrosine and tryptophan biosynthesis', and modules of 'glutamine/glutamate