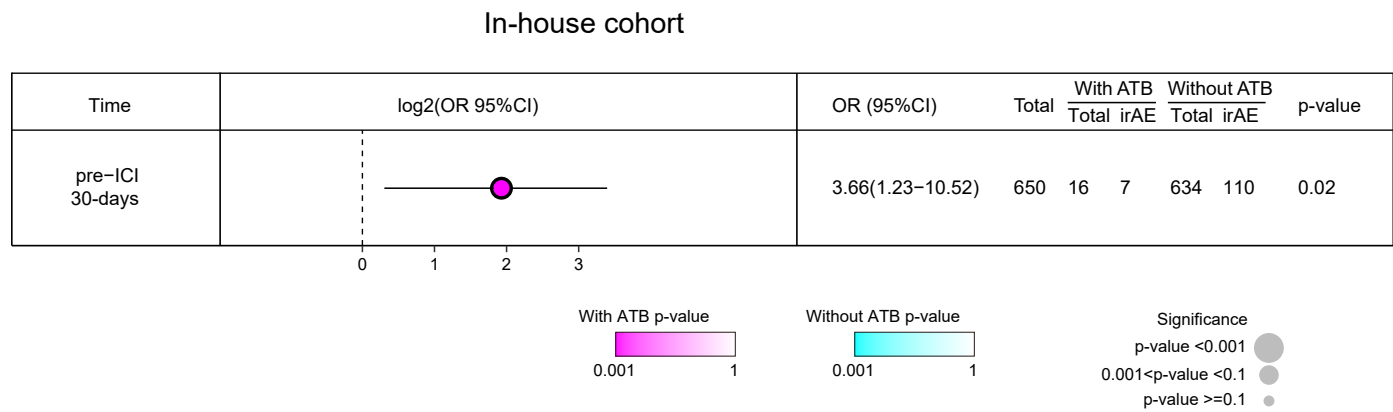


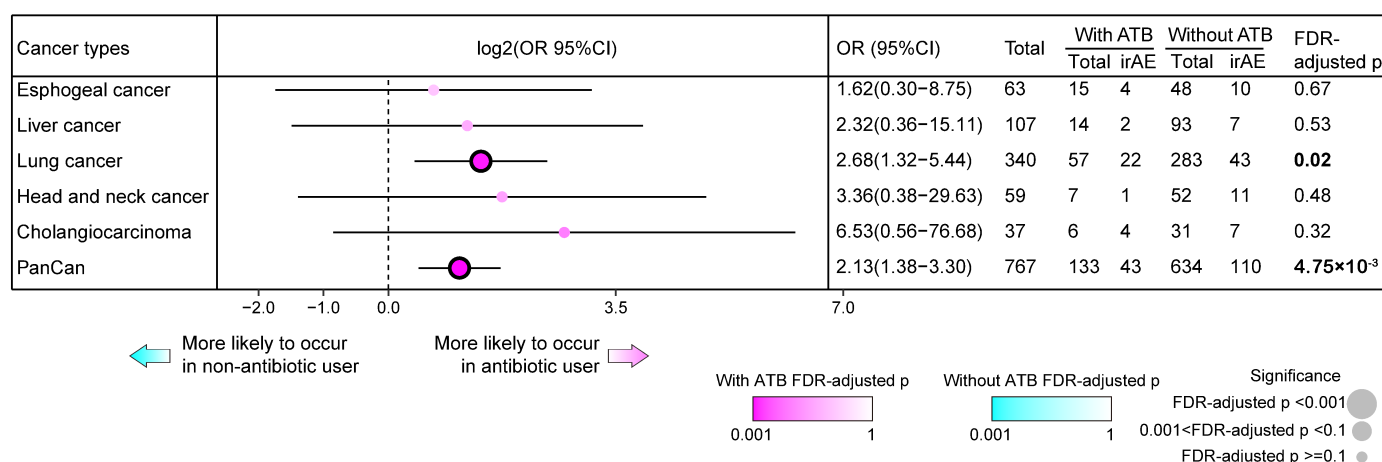
Fig. S1



**Fig S1. Association between antibiotics administered 30 days before (pre-ICI 30-days) first dose of ICI therapies and irAE risks in all cancer patients.**

Magenta indicates that irAEs are more likely to occur in antibiotic users; cyan indicates that irAEs are more likely to occur in non-antibiotic users; shade of the dot indicates FDR-adjusted p value. Dot size from large to small respectively indicates FDR-adjusted p < 0.001, 0.001 < FDR-adjusted p < 0.1, and FDR-adjusted p ≥ 0.1. ATB: antibiotics.

Fig. S2

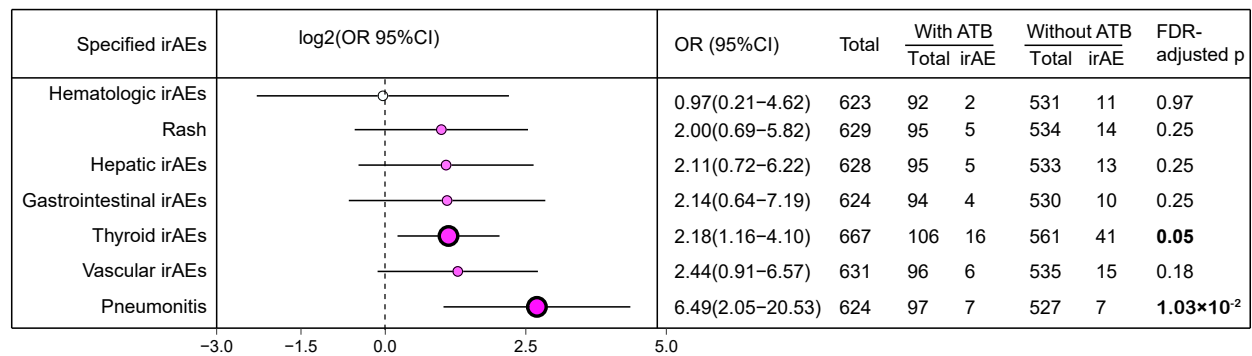


**Fig. 2. Analysis of irAEs in antibiotic and non-antibiotic users among patients with different cancer types receiving anti-PD-1/PD-L1 by adding duration of treatment as covariates.**

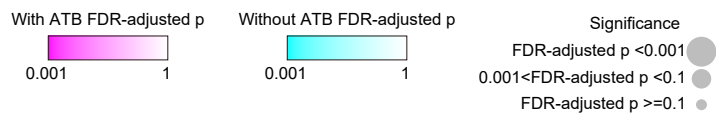
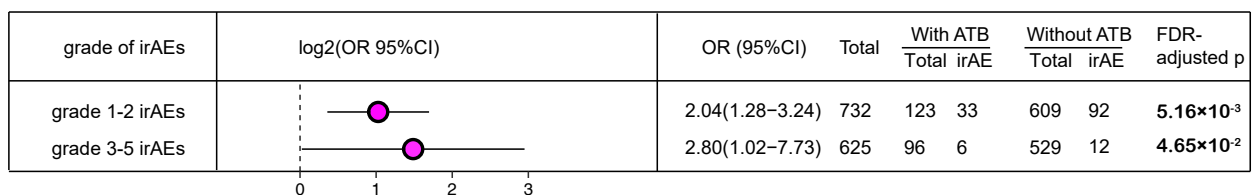
Magenta indicates that irAEs are more likely to occur in antibiotic users; cyan indicates that irAEs are more likely to occur in non-antibiotic users; shade of the dot indicates FDR-adjusted p value. Dot size from large to small respectively indicates FDR-adjusted p < 0.001, 0.001 < FDR-adjusted p < 0.1, and FDR-adjusted p ≥ 0.1, as shown. ATB: antibiotics.

## Fig. S3

A



B

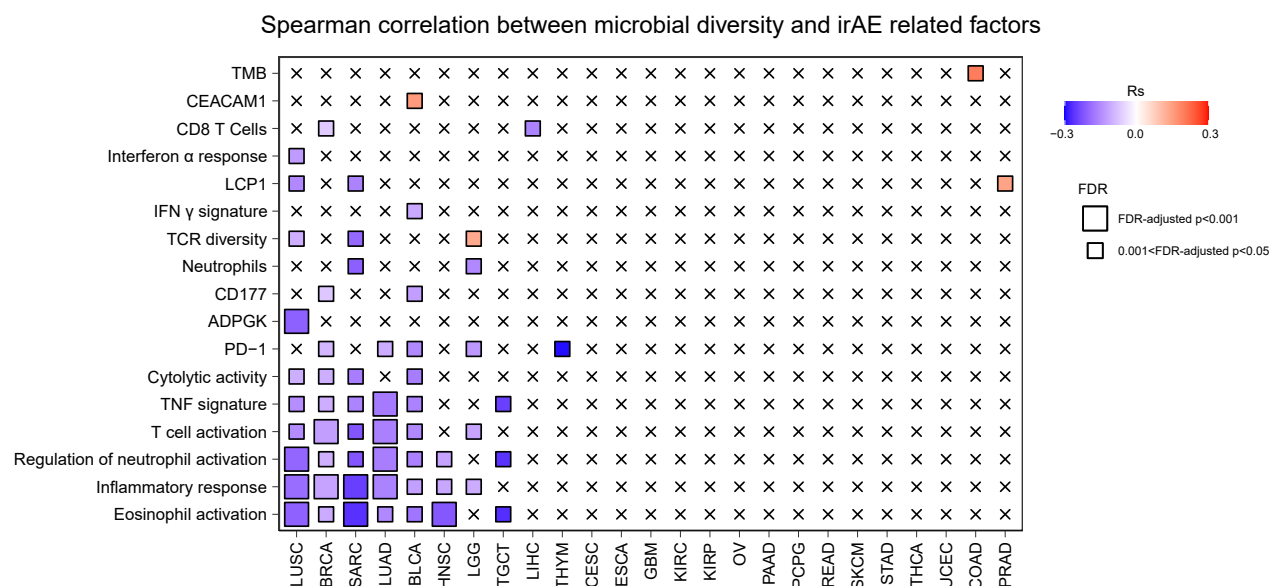


**Fig S3. Multivariable logistic regression analysis on in-house cohort for association between antibiotic use and different irAE subgroups.**

(A) Analysis of individual irAE in antibiotic and non-antibiotic users among cancer patients receiving anti-PD-1/PD-L1. (B) Analysis of different irAE grade in antibiotic and non-antibiotic users among cancer patients receiving anti-PD-1/PD-L1.

Magenta indicates that irAEs are more likely to occur in antibiotic users; cyan indicates that irAEs are more likely to occur in non-antibiotic users; shade of the dot indicates FDR-adjusted p value. Dot size from large to small respectively indicates FDR-adjusted p < 0.001, 0.001 < FDR-adjusted p < 0.1, and FDR-adjusted p >= 0.1. ATB: antibiotics.

Fig. S4



**Fig S4. Spearman correlation between irAE related factors/signatures and microbial diversity across 25 cancer types.** Inverse Simpson index was used to evaluate microbial diversity.

Red indicates positive correlation; blue indicates negative correlation; shade of the square indicates spearman R ( $R_s$ ); size of the dots indicate significance; Dot size from large to small respectively indicates FDR-adjusted  $p < 0.001$ , and  $0.001 < \text{FDR-adjusted } p < 0.05$ .

LUSC, lung squamous cell carcinoma; BRCA, breast invasive carcinoma; SARC, sarcoma; BLCA, bladder urothelial carcinoma; LUAD, lung adenocarcinoma; HNSC, head and neck squamous cell carcinoma; LGG, brain lower grade glioma; TGCT, testicular germ cell tumors; LIHC, liver hepatocellular carcinoma; THYM, Thymoma; CESC, cervical squamous cell carcinoma and endocervical adenocarcinoma; ESCA, esophageal carcinoma; GBM, glioblastoma multiforme; KIRC, kidney renal clear cell carcinoma; KIRP, kidney renal papillary cell carcinoma; OV, ovarian serous cystadenocarcinoma; PAAD, pancreatic adenocarcinoma; PCPG, pheochromocytoma and paraganglioma; READ, rectum adenocarcinoma; SKCM, skin cutaneous melanoma; STAD, stomach adenocarcinoma; THCA, thyroid carcinoma; UCEC, uterine corpus endometrial carcinoma; PRAD, prostate adenocarcinoma; COAD, colon adenocarcinoma.