**Figure 1. Metagenome sequencing data profile and case filtering criteria.** **(a)** Left panel: fungal (red border) and bacterial (blue border) alignment count number in 9 cohorts, a total of 2,052 cases. Right panel: ratio of fungal and bacterial alignment counts number (purple border) in all samples **(b)** Microbiota rarefaction curve generated based on fungal chao1 diversity. **(c)** Case filtering criteria contained three primary sections, sample sequence quality control (nfiltered = 235), suspected contamination samples filtering (nfiltered = 192), and low- fungal sequence depth samples discarding (nfiltered = 296). Excluding 723 cases, consistent with previous studies, approximately 30% of individuals were fungi free.

**Figure 2. Taxonomic distribution of enteric fungi and alteration of its alpha diversity across cohorts. (a)** Relative abundance of dominant enteric fungal phyla in healthy control, n=525 and CRCs, n=454. Ascomycota, Basidiomycota, Mucoromycota, Microsporidia, and Chytridiomycota were prevalent in both groups. **(b)** Relative abundance of dominant enteric fungal phyla in each cohort. **(c)** Comparison of the fungal difference between healthy control and CRC. **(d)** Comparison of fungal differences in chao1 index diversity indices between CRC (n = 454) and healthy control (n = 525) among the all and each.

**Figure 3. Meta-analysis identified a set of intestinal fungi strongly associated with CRC. (a)** Among 296 non-rare abundance candidates, the meta-analysis significant of fungi (n = 33, FDR < 0.01; n = 74, FDR < 0.1) derived from Mann-Whitney U test and adjusted the p-value with the conservative Bonferroni correction. **(b)** The main set (n = 74) performance across cohorts. The heatmaps revealed the two-sided Wilcoxon test and generalized fold change within individual studies. **(c)** The core set (n = 33) with pair fold change among all cohorts. And highlight the candidates whose fold change is larger than two times or less than a half. **(d)** Violin graph for the two outstanding performance fungi, A. rambellii and A. kawachii, in different studies.

**Figure 4. Fungi-bacteria combined CRC-diagnosis models feature ranking and performance comparison across 8 cohorts. (a)** Top panel: The importance of each species for the cross-validation prediction performance in each cohort estimated using the internal random forest scores. Only species appearing in the three top-ranking features in at least one dataset are reported. Bottom panel: AUC of pure fungal, bacterial, and fungal-bacterial CRC-diagnosis models across 8 cohorts, and the comparison between bacterial and fungal-bacterial CRC-diagnosis models. **(b)** Diagnostic performance of bacterial and fungal-bacterial classification of CRC from control by random forest with LOSO.

**Figure 5. Meta-analysis of correlations among altered fungal and bacterial in CRC compared with the healthy control and adenoma. (a)** Left panel: correlation between the 33 selected fungi and 31 selected bacterial candidates in CRC samples. The pink diamond represented a significantly different paired correlation in CRC compared to healthy control, while the blue circle denoted the enormously different paired correlation in CRC compared to adenoma. Right panel: the top intra-fungal relationship in CRC. **(b)** Left panel: correlation between the 33 selected fungi and 31 selected bacterial candidates in the healthy control group. Right panel: the top intra-fungal relationship in healthy.

**Figure 6. Meta-analysis of comparison relationship between CRC and healthy control. (a)** Density graph with z-score of intra-bacterial, intra-fungal, and fungal-bacterial correlational comparisons. Left panel: the stacked density chart in all correlational comparisons. Right-top panel: the density plot for z-score of intra-bacteria. Right-middle: the density plot for z-score of intra-fungi. Right-bottom: the density plot for z-score of fungi-bacteria. **(b)** Left panel: definition of differential correlation classes. The front and back of the semicolon represent the characteristics of the relationship in CRC and the healthy control, respectively.Right panel: percentage of differential correlational classes. Blue, orange, and yellow bar represented the intra-bacterial, intra-fungal, and fungal-bacterial groups, respectively. **(c)** Network for the differential correlation between CRC and control. Six clusters were automatically separated through the methodology affinity propagation cluster.

**Figure 7. CRC in vitro cell line validation. (TBA)**

**Supplementary figure 1. Taxonomic distribution of enteric bacteria. (a)** Comparison of the bacterial phylum level’s difference between healthy control and CRC in each cohorts. Only the phylum, whose mean relative abundance was higher than 1%, were displayed. **(b)** Comparison of the high bacterial phylum level’s difference between healthy control and CRC in all. Among all the candidates, *Fusobacteria* performed the most significant difference.

**Supplementary figure 2. Meta-analysis identified a set of intestinal fungi strongly associated with CRC compared with adenoma. (a)** Volcano plot of statistical significance against fold-change between CRC and adenoma, demonstrating the most significantly differentially species, *Aspergillus rambellii*, *Aspergillus kawachii*, *Fusarium pseudograminearum*, *Lentinula edodes*, *Cryptococcus neoformans*, *Saitoella complicate*, and *Hanseniaspora gilliermondii*. **(b)** Violin plot of the most significantly differentially seven fungi mentioned above.

**Supplementary figure 3. Meta-analysis of correlations among altered fungal and bacterial in adenoma.** Left panel: correlation between the 33 selected fungi and 31 selected bacterial candidates in adenoma. The blue triangles up and down denoted the enormously different paired correlation in adenoma compared to healthy control. Right panel: the top intra-fungal relationship in adenoma.

**Supplementary figure 4. Intra-fungal relationship in healthy control, adenoma and CRC. (a)** all significant (*p-value* < 0.05) intra-fungalrelationship in healthy control. **(b)** all significant intra-fungal relationship in adenoma. **(c)** all significant intra-fungal relationship in CRC.

**Supplementary figure 5. Fungal-bacterial tran-kingdom relationship in healthy control, adenoma and CRC. (a)** all significant (*p-value* < 0.05) fungal-bacterial tran-kingdomrelationship in healthy control. **(b)** all significant fungal-bacterial tran-kingdom relationship in adenoma. **(c)** all significant fungal-bacterial tran-kingdom relationship in CRC.