Supplement information

1.0 Materials

TP was prepared following the previously established procedures(Fig. 1A).[1] Briefly, *Tremella fuciformis* polysaccharides (TFPs) was extracted from the crushed fruiting bodies of *T. fuciformis* by boiling water extraction, purification, and freeze-drying. Subsequently, TFPs was degraded by ultrasonic irradiation and H_2O_2 treatments in a stirring condition at room temperature, and the viscosity of the TFPs solution was 119.6 mPa·S at the beginning and 20.3 mPa·S at the end of the degradation. The resulting solution was then dialyzed (cut-off 1,000 Da), concentrated, and lyophilized to obtain TP.

2.0 Structure characterizations of TP

The carbohydrate content was determined by the phenol-sulfuric acid method, with mannose as the standard.[2] In detail, ten mg of TP were dissolved in 100 mL of distilled water, and 1 mL of the solution was diluted to 2 mL in a tube, followed by adding 1 mL of phenol (5%) and 5 mL of sulfuric acid (98%) rapidly, then reacted in a boiling water bath for 30 min. Simultaneously, a tube without standard mannose was served as blank control. The absorbance of the solutions was measured at 490 nm on an ultraviolet-visible spectrophotometer (TU-1901, Beijing Puxi General Instrument Co., Ltd. China). The content of polysaccharide of TP was calculated based on the mannose concentration-absorbance curve. The protein content was detected by the bicinchoninic acid (BCA) method.[3] In detail, 10 $mg \cdot mL^{-1}$ of TP distilled water solution was prepared. Bovine serum protein was used as the standard, and then the protein content of the TP

solution was measured using a BCA protein assay kit (CoWin Biosciences, Jiangsu, China) according to the instructions of the manufacturer. The content of uronic acids was measured by the sulfamate/m-hydroxydiphenyl method using glucuronic acid for standard.[4] In detail, one mL of 0.5 mg·mL^{-1} TP distilled water solution was mixed with 5 mL of sodium tetraborate sulfuric acid solution (0.476 g of sodium tetraborate dissolved in 100 mL of sulfuric acid), followed by reacting in a boiling-water bath for 5 min and subsequently cooling in an ice-water bath. Then, one mL of 0.15% (w/w) m-hydroxybiphenyl solution (15 mg of m-hydroxybiphenyl dissolved in 10 mL of 0.5% NaOH solution) was added to develop color. Distilled water was used as a blank control. The absorbance of the solution was measured at 525 nm, and the content of uronic acid was calculated based on a concentration-absorbance curve established with standard glucuronic acid. The molecular weight distributions of TP were measured by high-performance gel permeation chromatography (HPGPC) using a gel permeation chromatography system (Ultimate 3000, Thermo Fisher Scientific, USA) following the previous method with slight modifications.[2] TP was dissolved in 0.02 mol/L KH_2PO4 (pH 6) to a concentration of 3.0 mg·mL^{-1}. Then, 20 μL of TP solution were injected into the GPC system coupled with a Ulrahydrogel 1000 column (7.8mm× 300 mm, Waters, USA) linked with a Ulrahydrogel 500 column (7.8mm× 300 mm, Waters, USA) after being filtered through 0.45 μm of microporous filter membrane. The signaling was recorded at a flow rate of 0.8 mL/min for 35 min at column temperature 35 °C. A molecular weight-retention time curve was plotted by measuring a series of dextran standards with different molecular weights (1440, 668, 410, 273, 148, 48.6,

28.3, 11.6, and 5.2 kDa, Sigma-Aldrich, USA). The monosaccharide composition of TP was analyzed using the acetylation derivatization method using the GC-MS system (Agilent, Santa Clara, CA, USA).[1, 5] In detail, ten mg of TP was dissolved with 4 mL of 2 M trifluoroacetic acid (TFA) in a glass tube, sealed, and hydrolyzed at 121°C for 4 h. The hydrolysate was evaporated at 60 °C, and the evaporation was repeated three times with methanol to remove TFA completely. The hydrolyzed TP were reacted with 10 mg of hydroxylamine hydrochloride and 0.5 mL of pyridine at 90 °C for 30 min and then the resulting solution was cooled to room temperature. One mL of acetic anhydride was added to the solution and acetylation was conducted at 90 °C for 30 min to obtain the acetylated derivatives. The standards of fucose (Fuc), rhamnose (Rha), arabinose (Ara), galactose (Gal), glucose (Glc), xylose (Xyl), mannose (Man), and glucuronic acid (GlcA) were acetylated as the same protocol. The acetylated derivatives were analyzed using a 6890N Agilent gas chromatography (Agilent, Santa Clara, CA, USA) coupled with a DB-1701 capillary column (30 m×0.25 mm, Agilent). The parameters were set as follows: nitrogen flow rate: 1 mL/min; inlet temperature: 250°C; evaporation chamber temperature: 250 °C; detector temperature: 300 °C; injection volume: 1 μL; split ratio:20:1. Fourier transform infrared (FT-IR) spectroscopy of TP was recorded using an FT-IR spectrometer (Nicolet IS50-Nicolet Continuum, Thermo Fisher Scientific, USA).[1] Around 3 mg of TP were ground with 100 mg KBr powder and pressed into 1 mm pellets. The FT-IR spectrum was recorded in the range of 4000–400 cm^{-1}. Twenty mg of TP were fully dissolved in 2 mL of D_2O and freeze-dried. These processes were repeated twice. Subsequently, the lyophilized TP was dissolved

in 0.7 mL of D_2O and loaded into an NMR tube. Then, the ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra of TP, including ^1H and ^{13}C and two-dimensional ^1H-^1H correlation spectroscopy (COSY) (pulse program: cosygppqf), were generated on a 400 MHz NMR spectrometer (Bruker AVANCE III, MA, USA) at 298K.[1] OMNIC software (Thermo Fisher Scientific) was used for data processing.

3.0 Results of structure characterizations

The carbohydrate, protein, and uronic acid content of TP was 93.2%, 0.7%, and 6.7% (dry weight), respectively. As shown in Fig. S1, the large peak in the HPGPC chromatogram before 20 min of retention time represented TP molecules (Fig. S1A). The weight-average molecular weight of TP was 4.48×10^6 Da, calculated by the curve equation built by the retention time and molecular weights of the standards. Obviously, TP was primarily composed of five types of monosaccharide residues according to the GC-MS chromatogram. They were mannose, fucose, xylose, glucose, and arabinose in a molar ratio of 5.07:1.15:1.00:0.98:0.11 based on the retention time of standards and the peak area integrals, and a small amount of glucuronic acid were also observed. The FT-IR spectrum exhibited typically characteristic peaks of the sugar rings. An absorption peak at 2930 cm^{-1} was due to the stretching vibration of C-H[6]. Multiple peaks at the region of 950-1200 cm^{-1} were ascribed to the vibration of C-O, C-C, and C-O-H groups in the sugar rings.[7] Peaks at 916 and 800 cm^{-1} were attributed to the existence of D-glucopyranosyl and α-D-mannopyranose in the molecules,[8, 9] respectively. The ^1H NMR spectrum of TP contained signals at δ 5.52, 5.36, 5.15, 5.07, 4.49, 4.47, 4.38, and 4.35 ppm corresponding to anomeric protons (Fig. S1D).[10] Based

on the integrals of anomeric proton signals, the TP contained a higher proportion of α-configurations and a lower proportion of β-configurations. The ^{13}C NMR spectrum obviously displayed five anomeric carbon signals at δ 102.99, 102.01, 101.46, 100.67, and 97.15 ppm (Fig. S1E).[10] Summarizing information from the ^{1}H NMR, ^{13}C NMR, and ^{1}H-^{1}H COSY NMR spectra demonstrated that TP was mainly composed of five types of monosaccharide residues (Fig. 1D-F), in accordance with the results of GC-MS analysis. Meanwhile, a signal at δ 1.19 ppm in the ^{1}H NMR spectrum was due to the CH_3 moiety of fucose residue. Taken together, TP was an α-heteromannan. The structure characteristics of TP were highly similar to those of our previously reported *T. fuciformis*-derived polysaccharides,[1] demonstrating the high reproducibility of the established extraction processes.

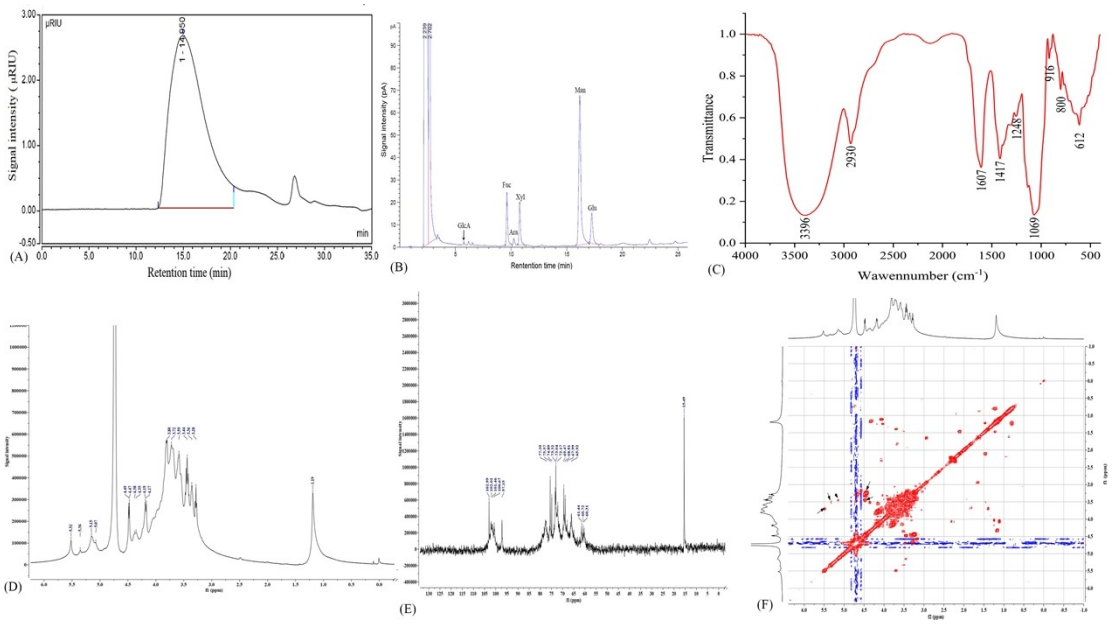

Fig.S1 Structure characterizations of TP regarding molecular weight distributions (A), monosaccharide compositions (B), FT-IR spectrum (C), ^{1}H NMR spectrum (D), ^{13}C NMR spectrum (E), and ^{1}H-^{1}H COSY spectrum (F).

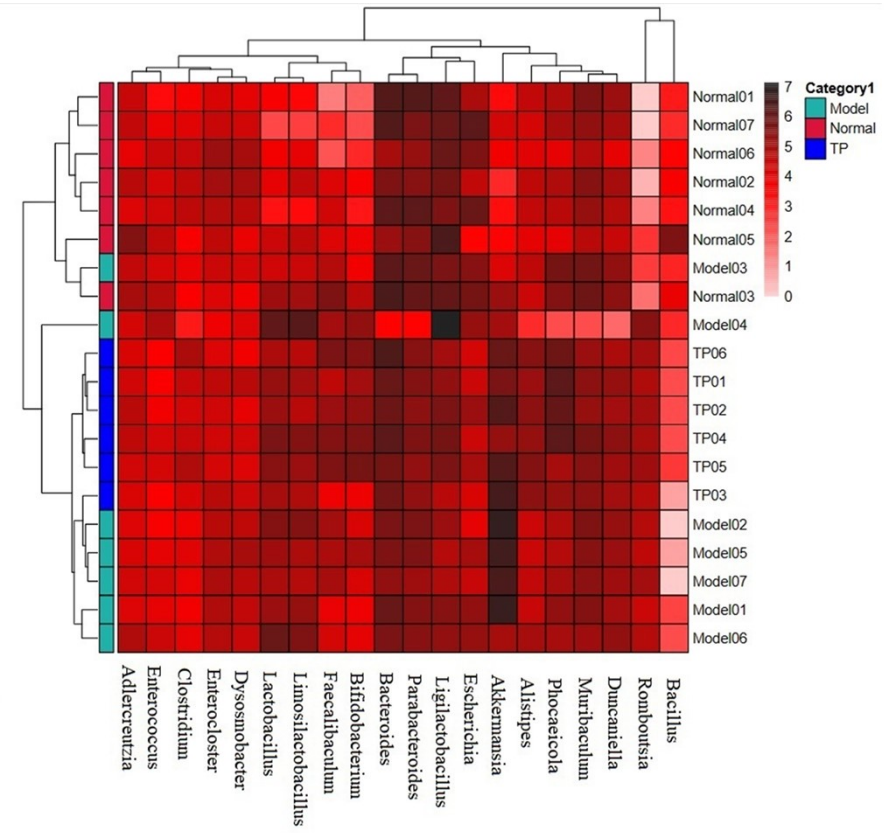

Fig.S2 Clustering analysis of microbial compositions at genus level among the three groups. The darker in red color, the higher in relative abundance.

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