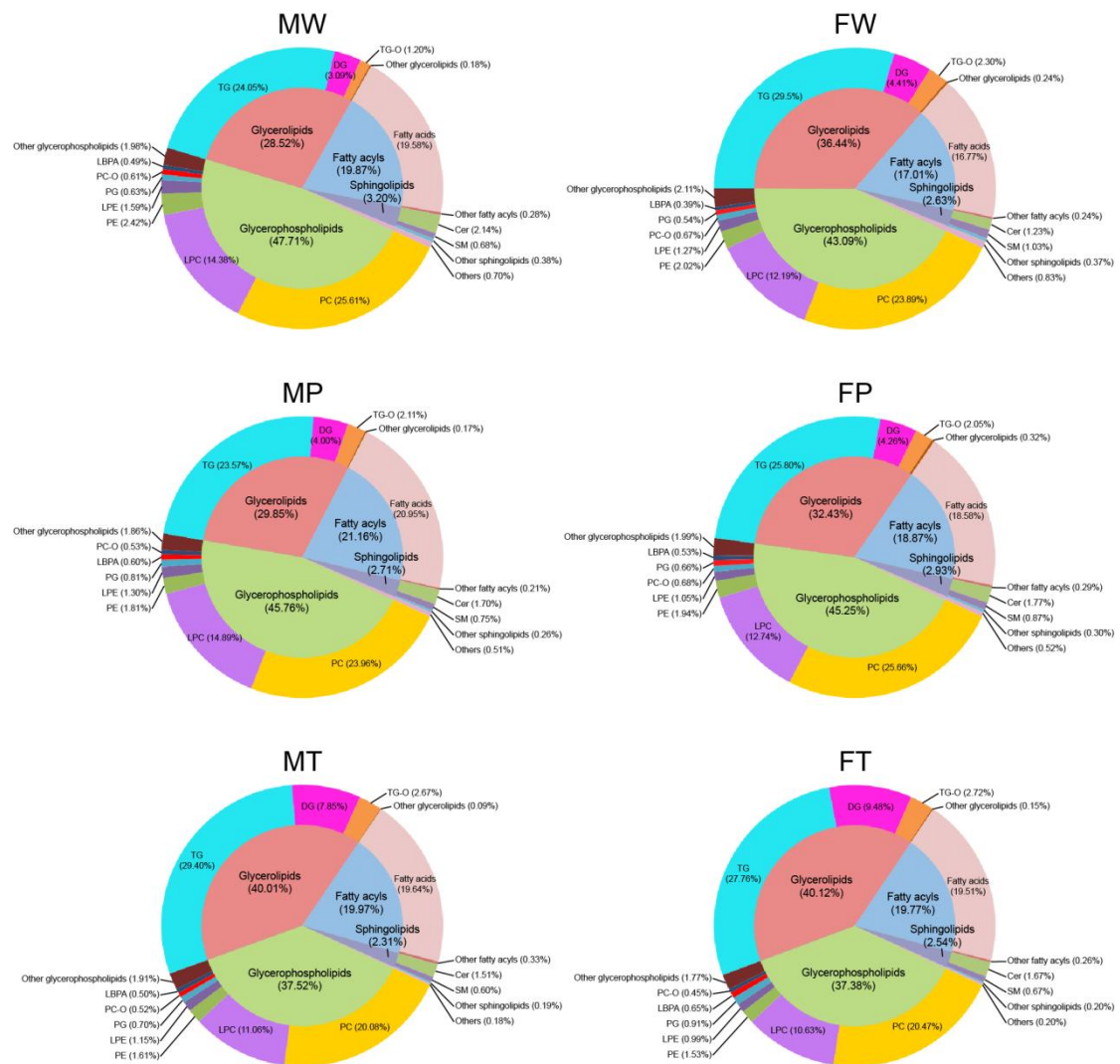
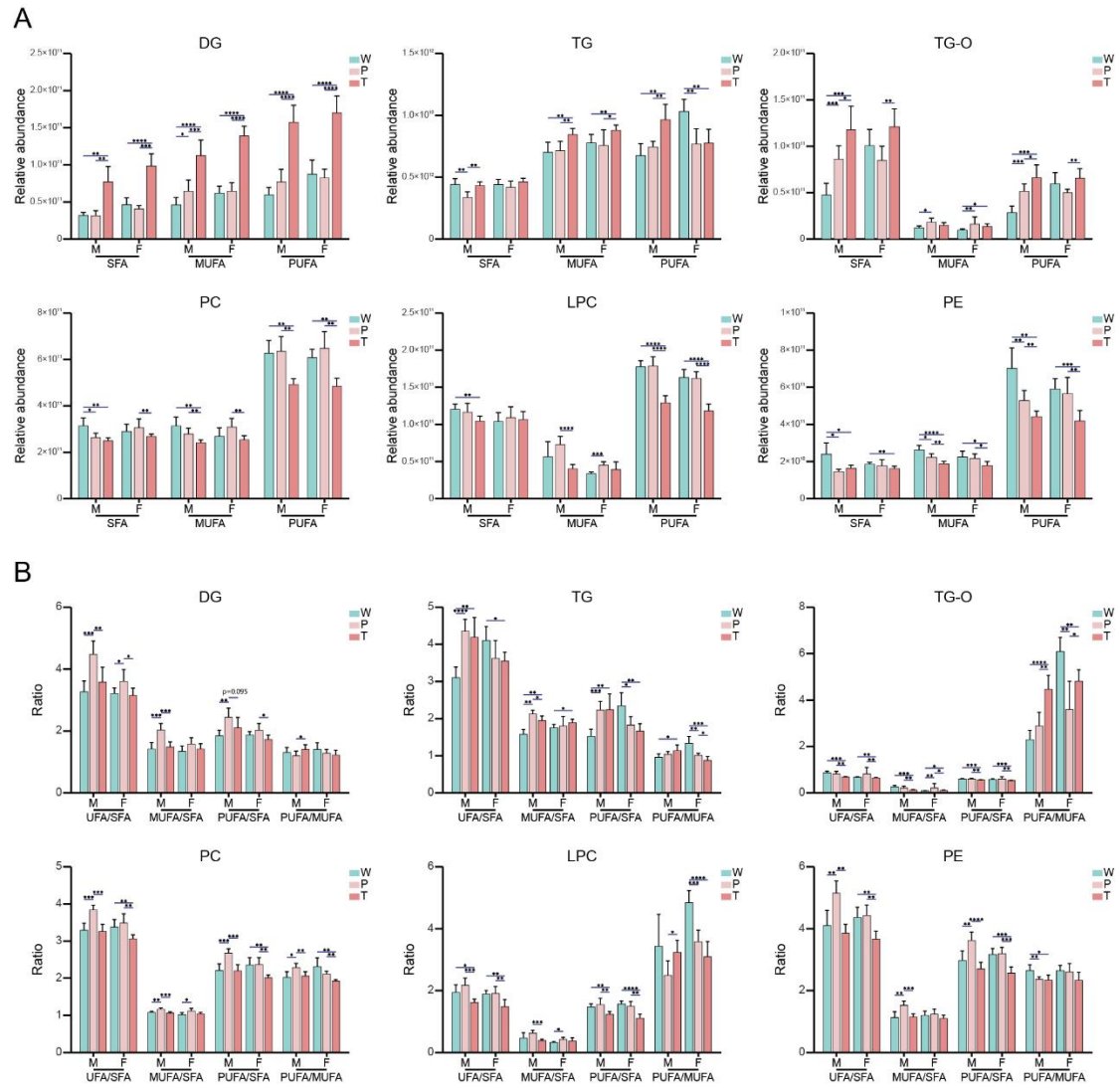


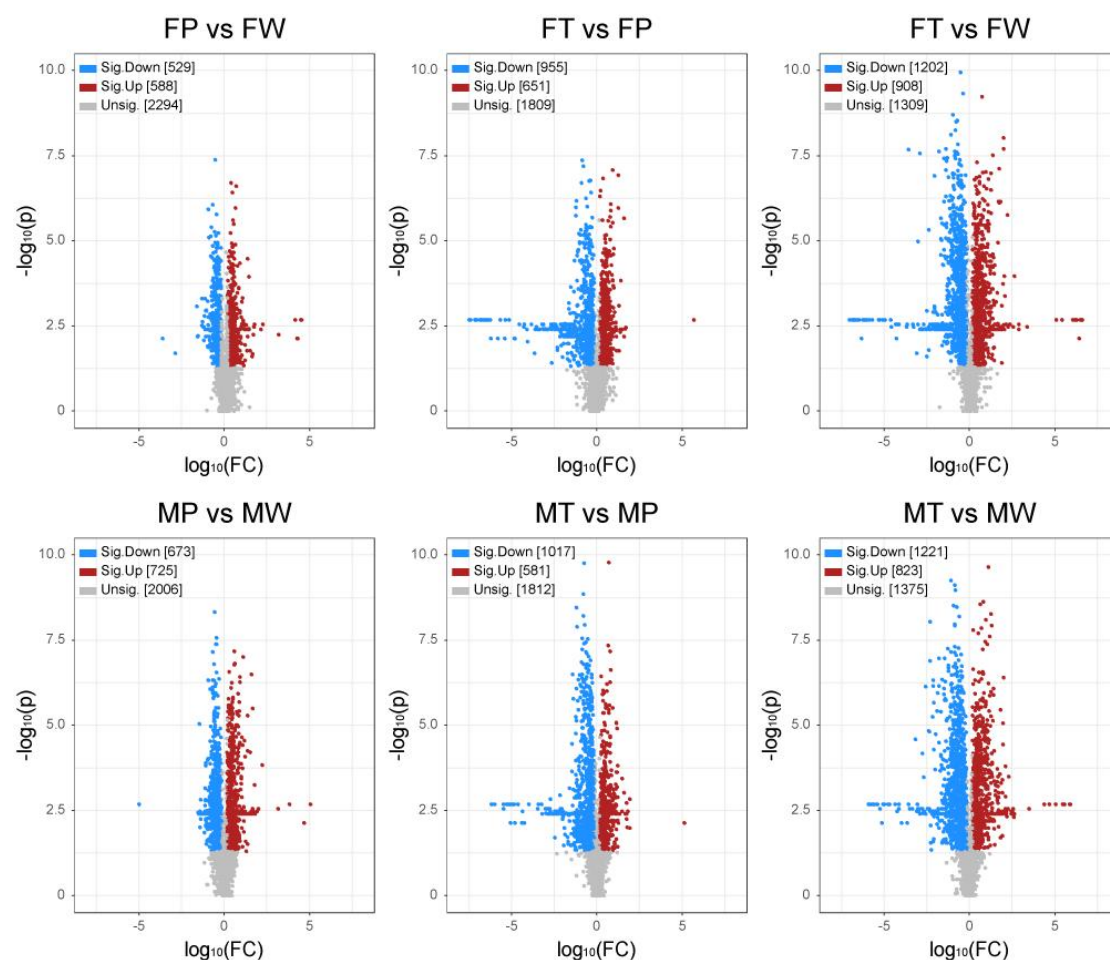
Supplementary Figure S1. Quality control of positive and negative ion mode experiments in this study. (A) Density distribution of the percentage of RSD values for metabolic mass spectrometry features in QC samples. (B) RSD distribution of metabolic mass spectrometry features in QC samples. Curves are cumulative values of percentages within different coefficient of variation intervals. (C) Extent of variation in metabolic mass spectrometry features in QC samples. (D) Extent of variation in metabolic mass spectrometry features in actual samples compared to QC samples. (E) PCA analysis of actual and QC samples. (F) Species of lipids detected in this experiment and their quantity. n=6.



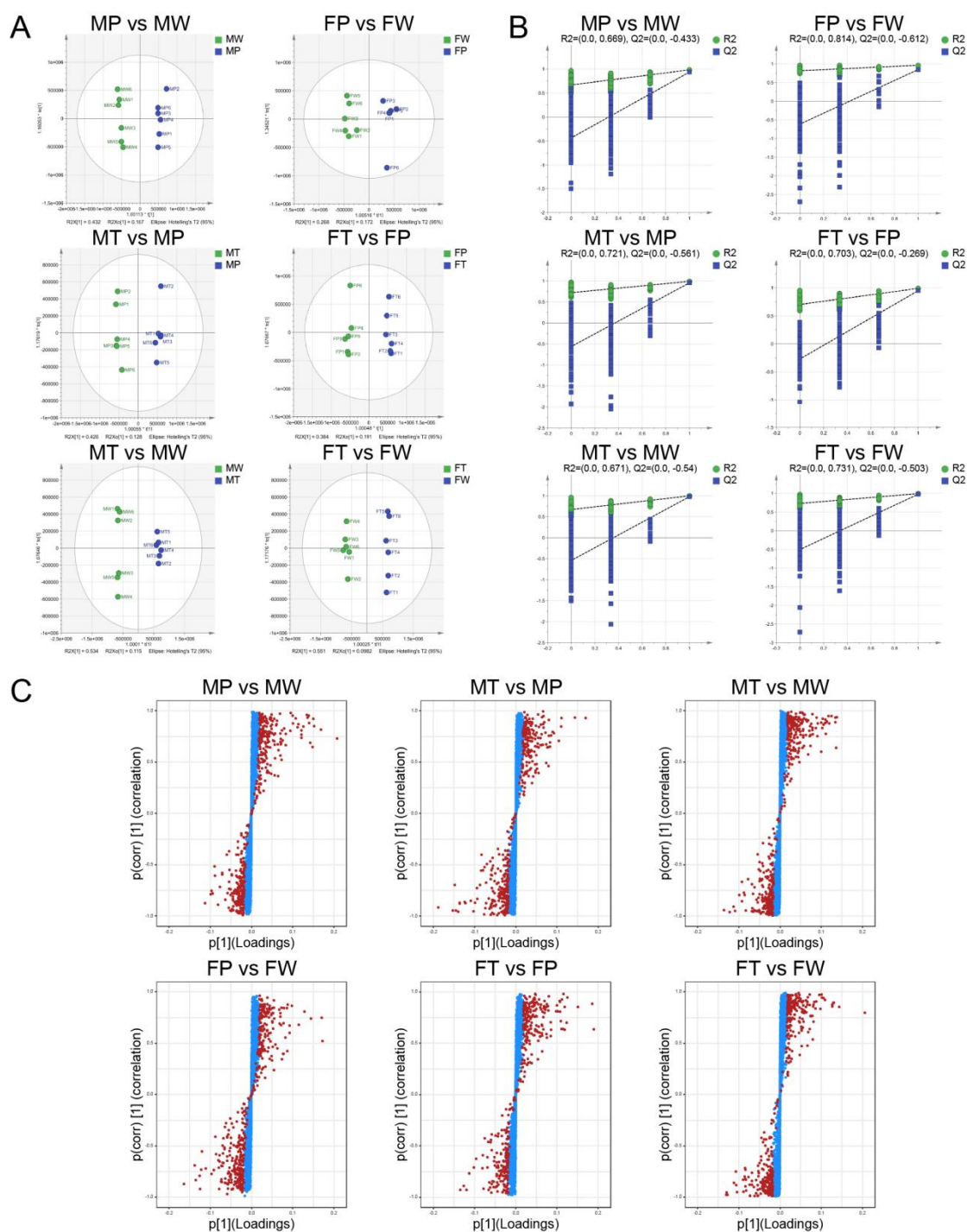
Supplementary Figure S2. Percentage changes in major lipid species during hepatocarcinogenesis. F, female; M, male; Wt, wild-type mice; Ras-Tg, Hras12V transgenic mice; W, liver tissues of Wt; P, peri-tumor tissues of Ras-Tg; T, HCC tissues of Ras-Tg.



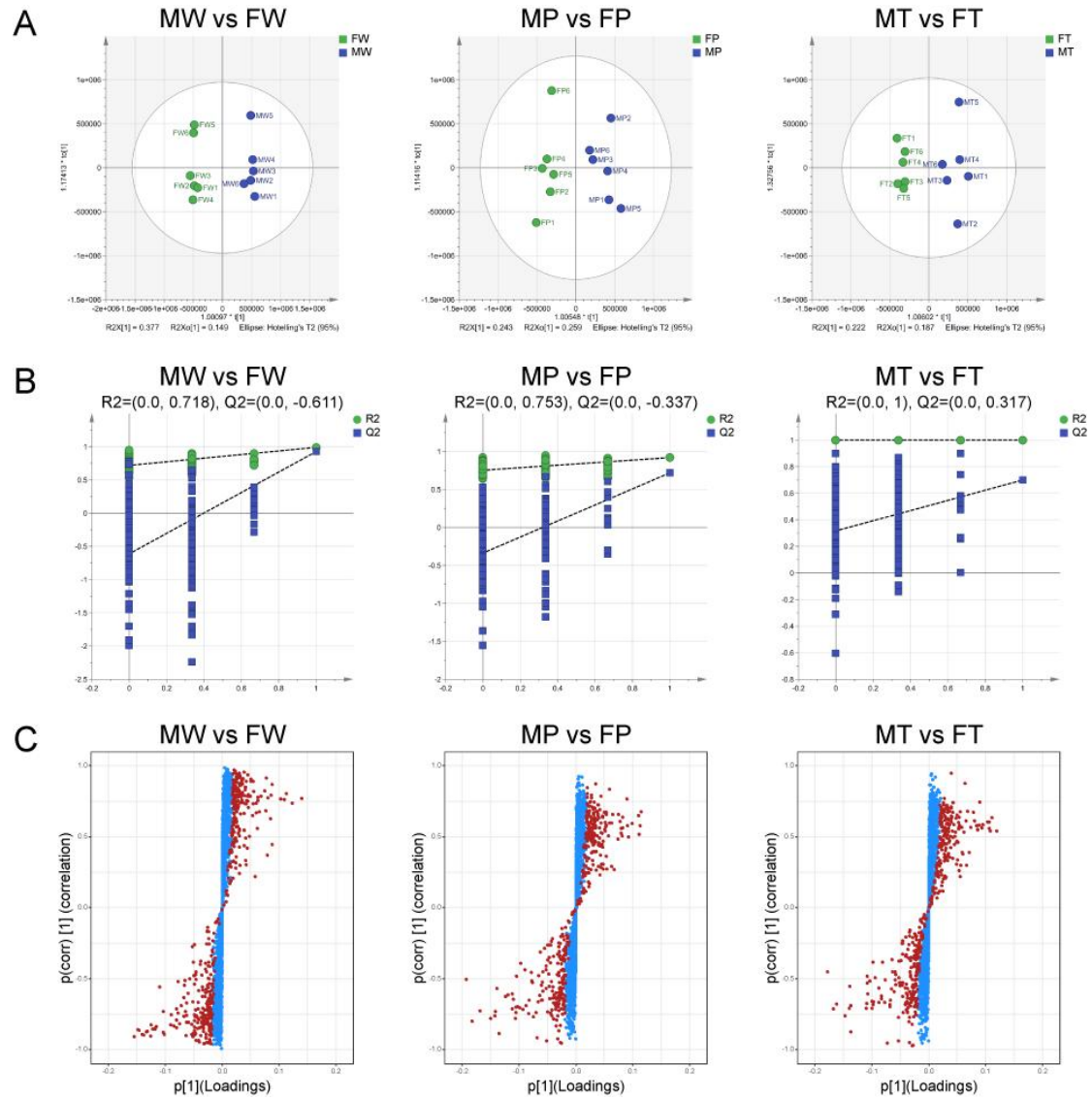
Supplementary Figure S3. Fatty acid analysis of the major lipid species identified, DG, TG, TG-O, PC, LPC and PE. **(A)** Altered levels of SFA, MUFA and PUFA in lipid species without normalization with total concentration. **(B)** Changes in fatty acid ratios in lipid species. The abbreviation as well as descriptions are the same as those in the caption for [Figure S2](#). The data are expressed as the mean \pm SD. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$. $n = 6$.



Supplementary Figure S4. Volcano plots of longitudinally paired comparisons. The abbreviation as well as descriptions are the same as those in the caption for [Figure S2](#). The data are expressed as the mean \pm SD. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$. The abbreviation as well as descriptions are the same as those in the caption for [Figure S2](#). n = 6.



Supplementary Figure S5. Orthogonal projections to latent structures discriminant analysis (OPLS-DA) for longitudinal comparisons. **(A)** OPLS-DA score plots. **(B)** Permutation tests for the OPLS-DA models. **(C)** S-plots. Red dots represent lipid metabolites with VIP > 1. The abbreviation as well as descriptions are the same as those in the caption for [Figure S2](#). n = 6.



Supplementary Figure S6. OPLS-DA analysis for lateral comparisons between sexes. **(A)** OPLS-DA score plots. **(B)** Permutation tests for the OPLS-DA models. **(C)** S-plots. Red dots represent lipid metabolites with VIP > 1. The abbreviation as well as descriptions are the same as those in the caption for [Figure S2](#). n = 6.