**Supporting Information** 

## Glucagon-like peptide-1 analog liraglutide leads to multiple metabolic alterations in diet-induced obese mice

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## Figure S1. Comparative metabolite analysis between the groups

*A*–*C*, Principal component analysis (PCA) plots for (*A*) DIO saline vs. Chow saline, (*B*) DIO liraglutide vs. DIO saline, and (*C*) DIO liraglutide vs. Chow saline. *D*–*F*, Orthogonal partial least squares discriminant analysis (OPLS-DA) scores plots for (*D*) DIO saline vs. Chow saline, (*E*) DIO liraglutide vs. DIO saline, and (*F*) DIO liraglutide vs. Chow saline. *G*–*I*, Variable influence on projection (VIP) scores plots (top 10) for (*G*) DIO saline vs. Chow saline, (*H*) DIO liraglutide vs. DIO saline, and (*I*) DIO liraglutide vs. Chow saline. In *G*–*I*, colors show the number of tissue-specific metabolites up- or down-regulated in the volcano plot in Figure 2D.



Figure S2. OPLS-DA and volcano plots for the hypothalamus

A, C, E, OPLS-DA scores plots for (A) DIO saline vs. Chow saline, (C) DIO liraglutide vs. DIO saline, and (E) DIO liraglutide vs. Chow saline. B, D, F, Volcano plots for (B) DIO saline vs. Chow saline, (D) DIO liraglutide vs. DIO saline, and (F) DIO liraglutide vs. Chow saline. In B, D, F, non-significant metabolites are shown in gray.



Figure S3. OPLS-DA and volcano plots for the plasma

*A*, *C*, *E*, OPLS-DA scores plots for (*A*) DIO saline vs. Chow saline, (*C*) DIO liraglutide vs. DIO saline, and (*E*) DIO liraglutide vs. Chow saline. *B*, *D*, *F*, Volcano plots for (*B*) DIO saline vs. Chow saline, (*D*) DIO liraglutide vs. DIO saline, and (*F*) DIO liraglutide vs. Chow saline. In *B*, *D*, *F*, non-significant metabolites are shown in gray.



Figure S4. OPLS-DA and volcano plots for the liver

A, C, E, OPLS-DA scores plots for (A) DIO saline vs. Chow saline, (C) DIO liraglutide vs. DIO saline, and (E) DIO liraglutide vs. Chow saline. B, D, F, Volcano plots for (B) DIO saline vs. Chow saline, (D) DIO liraglutide vs. DIO saline, and (F) DIO liraglutide vs. Chow saline. In B, D, F, non-significant metabolites are shown in gray.



Figure S5. OPLS-DA and volcano plots for the skeletal muscle

*A*, *C*, *E*, OPLS-DA scores plots for (*A*) DIO saline vs. Chow saline, (*C*) DIO liraglutide vs. DIO saline, and (*E*) DIO liraglutide vs. Chow saline. *B*, *D*, *F*, Volcano plots for (*B*) DIO saline vs. Chow saline, (*D*) DIO liraglutide vs. DIO saline, and (*F*) DIO liraglutide vs. Chow saline. In *B*, *D*, *F*, non-significant metabolites are shown in gray.





Chow saline

Chow

saline





saline



## Figure S6. Tissue-specific correlations among the three groups

Correlations plots based on Pearson's correlation coefficients analysis: A, hypothalamus; B, plasma; *C*, liver; and *D*, skeletal muscle.