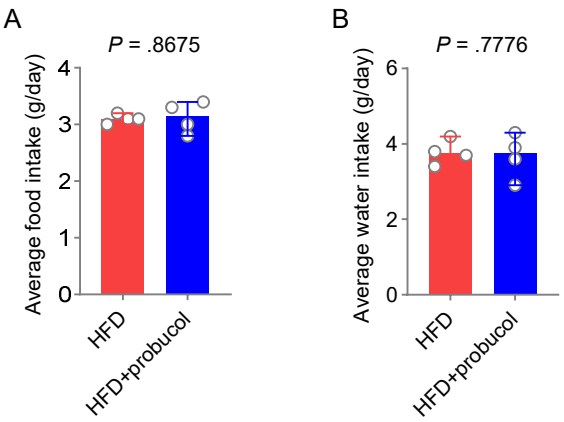
| | Normal chow diet | | High-fat diet | |
|---|---|---|---|---|
| | g % | kcal % | g % | kcal % |
| Protein | 19.2 | 20 | 26.2 | 20 |
| Carbohydrate | 67.3 | 70 | 26.3 | 20 |
| Fat | 4.3 | 10 | 34.9 | 60 |
| Total | | | | 100 |
| kcal/gram | 3.85 | | 5.24 | |

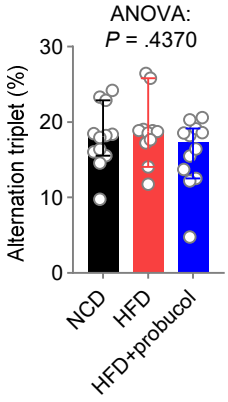
| Ingredient | gram | kcal | gram | kcal |
|---|---|---|---|---|
| Casein, 80 mesh | 200 | 800 | 200 | 800 |
| L-Cystine | 3 | 12 | 3 | 12 |
| Cornstarch | 315 | 1260 | 0 | 0 |
| Maltodextrin 10 | 35 | 140 | 125 | 500 |
| Sucrose | 350 | 1400 | 68.8 | 275.2 |
| Cellulose, BW200 | 50 | 0 | 50 | 0 |
| Soybean Oil | 25 | 225 | 25 | 225 |
| Lard* | 20 | 180 | 245 | 2205 |
| Mineral Mix, S10026 | 10 | 0 | 10 | 0 |
| Dicalcium Phosphate | 13 | 0 | 13 | 0 |
| Calcium Carbonate | 5.5 | 0 | 5.5 | 0 |
| Potassium Citrate, 1 $H_2O$ | 16.5 | 0 | 16.5 | 0 |
| Vitamin Mix, V10001 | 10 | 40 | 10 | 40 |
| Choline Bitartrate | 2 | 0 | 2 | 0 |
| FD and C Dye | 0 | 0 | 0.05 | 0 |
| Total | 1055.05 | 4057 | 773.85 | 4057 |

*Estimated Lard Cholesterol: 300.8 mg/kg high-fat diet

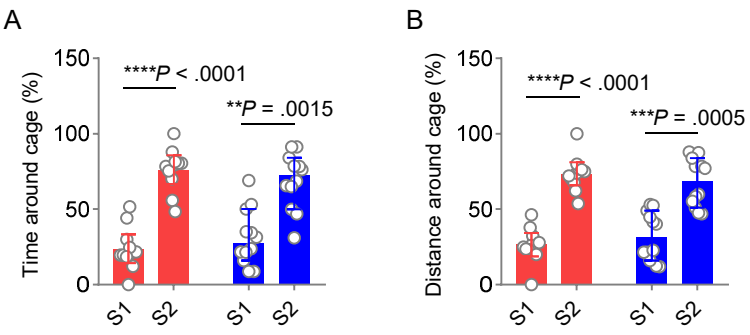
**Supplementary Figure S1**
Diet formulas.



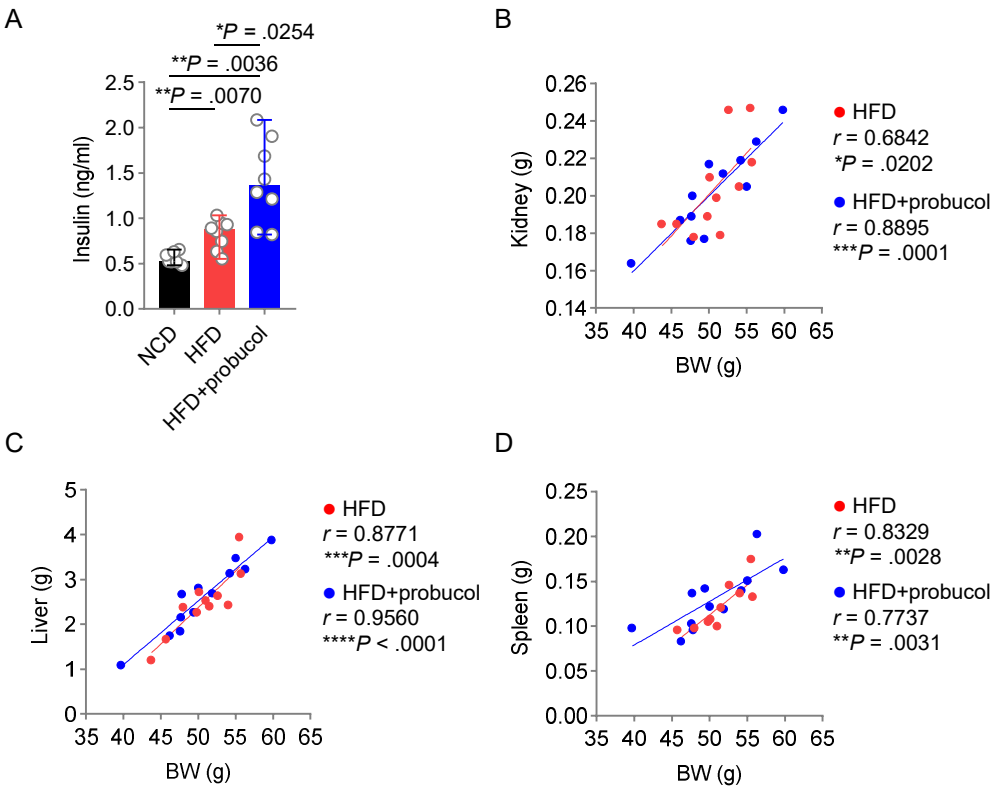

**Supplementary Figure S2**
Probucol did not significantly affect the consumption of food or water by mice. **(A, B)** After 12 weeks of probucol treatment, the intake of food **(A)** and water **(B)** in HFD-fed mice was recorded for each cage. The average daily consumption of food and water per mouse was calculated and presented as individual values with median ± 95% CI (two cages and two days for each group). Two-tailed unpaired Student's t test was used (food, $t = 0.1741$, $p = 0.8675$; water, $t = 0.2954$, $p = 0.7776$). $p < 0.05$ was indicative of statistical significance.




**Supplementary Figure S3**
HFD-feeding and probucol treatment did not display any discernible impact on the Y maze performance of mice.




**Supplementary Figure S4**
HFD did not impair social preference of the mice for a stranger mouse over a familiar one. **(A, B)** Social preference test was performed following sociability test using the three-chamber social approach task. S1 and S2 indicate the cage with a familiar mouse introduced in the preceding social interaction phase and a new stranger mouse introduced in this social preference phase, respectively. The percentages of time spent around the cage **(A)** and the percentages of distance around the cage **(B)** are shown as individual values with median ± 95% CI (n = 11 or 12 mice for each group). Time around cage, two-way RM ANOVA (cage, $p < 0.0001$; group, $p = 0.5034$), followed by Sidak's multiple comparisons test. Distance around cage, two-way RM ANOVA (cage, $p < 0.0001$; group, $p > 0.9999$), followed by Sidak's multiple comparisons test. $p < 0.05$ was indicative of statistical significance.




**Supplementary Figure S5**
Probucol exhibited no effect on the metabolic parameters of HFD-fed mice. **(A)** Serum insulin level of mice. Blood samples of mice were collected after 6-h fasting. Data are expressed as individual values with median ± 95% CI (n = 7-8 mice for each group). The difference in serum insulin level among groups was compared by Brown-Forsythe ANOVA ($p$ = 0.0007), followed by Tamhane's T2 multiple comparisons test. **(B-D)** The correlations between body weights and the weights of kidney, liver and spleen of the HFD-fed mice and probucol treated mice. The degree of correlations was measured by Pearson $r$ correlation. $p < 0.05$ was indicative of statistical significance.

Figure 5A

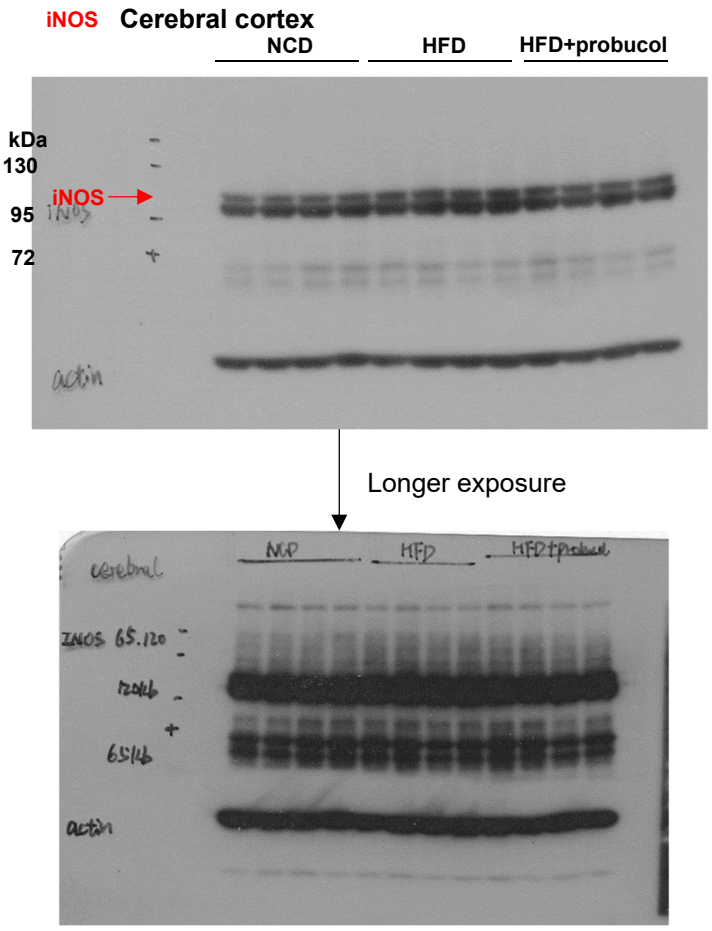
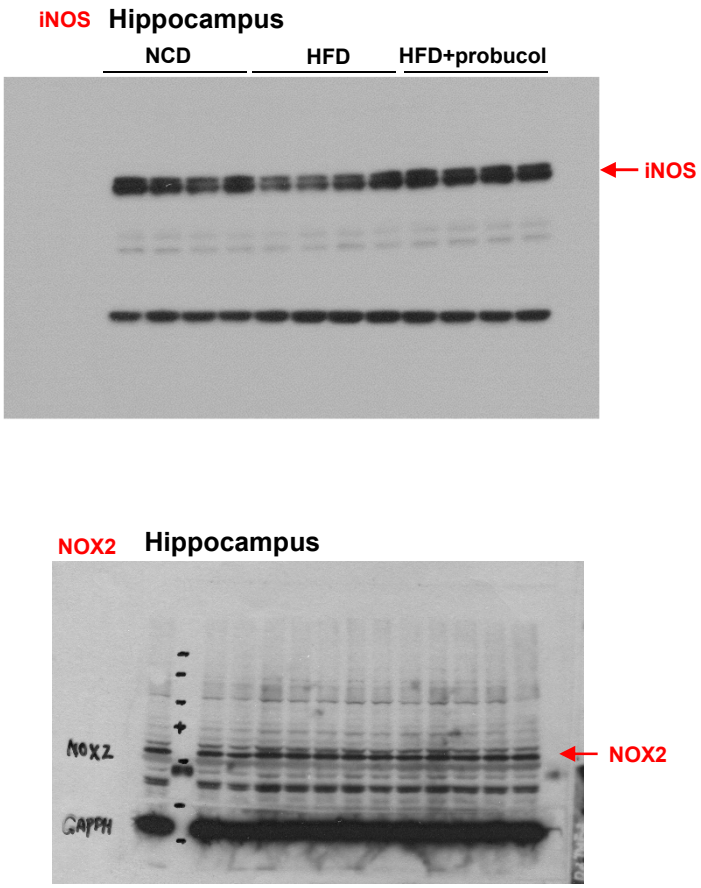
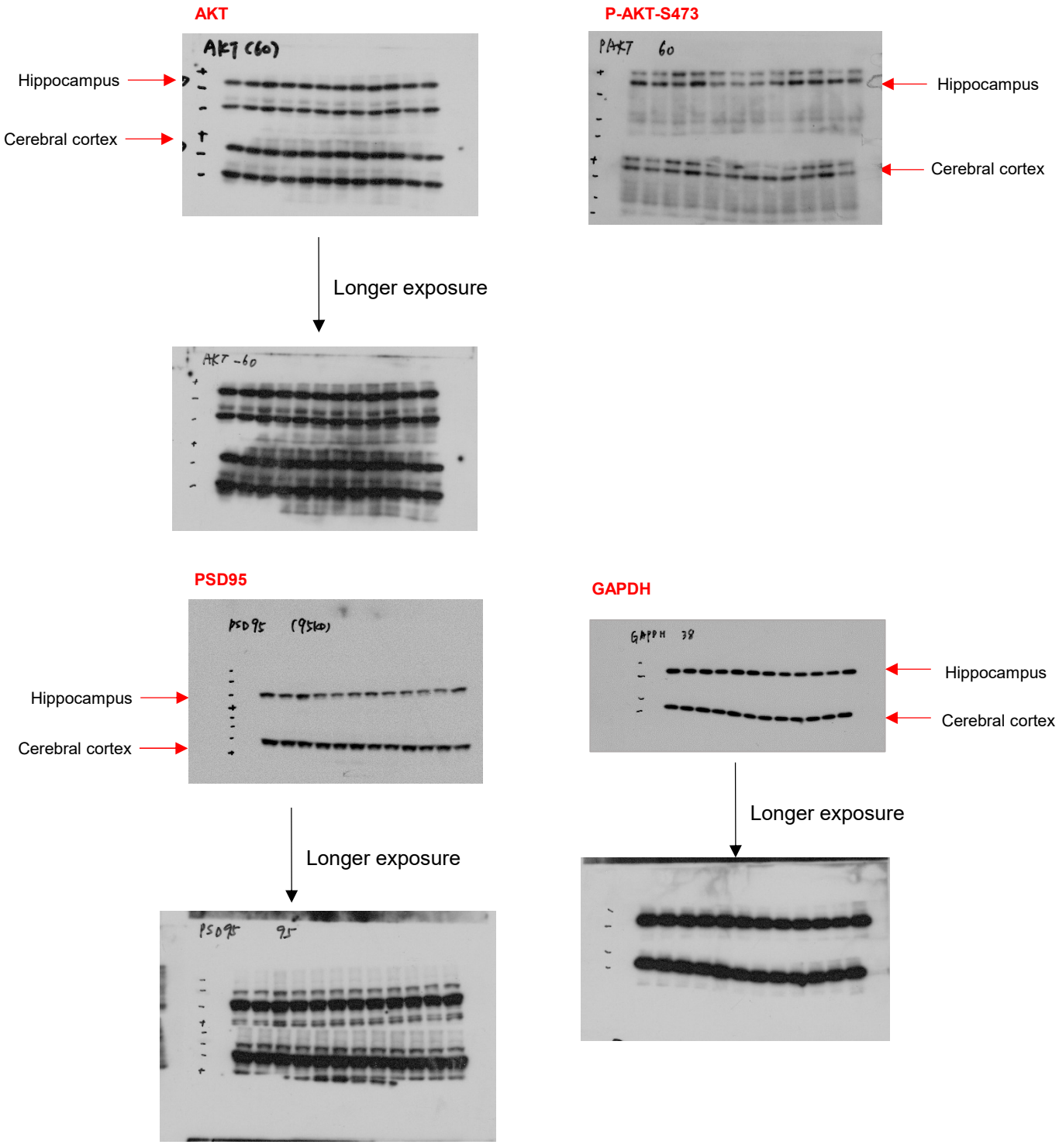



Figure 5B




**Supplementary Figure S6**
Raw blots for Figure 5, A and D.

**Figure 5, C and D**




**Supplementary Figure S7**
Raw blots for Figure 5, G and J.