The effect of  $\omega$ -3 polyunsaturated fatty acids on the liver lipidome, proteome and bile acid profile: parenteral *versus* enteral administration

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#### Control



ENIL: Mallory hyaline inclusions



PNIL: Mallory hyaline inclusions



PNILOV: microvesicular steatosis



ENIL: microvesicular steatosis



PNIL: microvesicular steatosis



PNIL: microvesicular steatosis and necrosis



PNILOV: Mallory hyaline inclusions



**Supplementary Figure 1** *Histological evaluation of the liver*. Black arrows: lipid droplets; red arrows: glycogen inclusion; green arrows: Mallory hyaline inclusions; yellow arrows: apoptotic bodies. Magnification 600x.







С



**Figure S2** *Effect of the route of administration on the relative content of selected lipid species in serum.* A: all groups; B: PN vs EN: Intralipid; C: PN vs EN: Intralipid + Omegaven Data are expressed as log(2) fold change over median control value. \* p < 0.05 vs control; † p < 0.05 vs PNIL;  $\ddagger < 0.05$  vs ENILOV.







Figure S3 Effect of the composition of lipid emulsions on the relative content of selected lipid species in serum. A: all groups; B: IL vs ILOV: enteral application; C: IL vs ILOV: parenteral application. Data are expressed as log(2) fold change over median control value. \* p < 0.05 vs control; # p < 0.05 vs ENIL; & p < 0.05 vs ENIL; 0.05 vs PNILOV

#### **Phosphatidylcholines**



**Figure S4** *The distribution of phosphatidylcholines containing*  $\omega$ -3 *and/or*  $\omega$ -6 *fatty acids in experimental groups.* A: PCA score plot. Each sample was determined in a doublet. B: Heatmap with the clustering dendrogram of samples. Samples are colored according to the experimental groups, individual compounds are colored according to the presence of  $\omega$ -3 FAs,  $\omega$ -6 FAs or both.

В

#### Phosphatidylethanolamines



**Figure S5** *The distribution of phosphatidylethanolamines containing*  $\omega$ -3 *and/or*  $\omega$ -6 *fatty acids in experimental groups.* A: PCA score plot. Each sample was determined in a doublet. B: Heatmap with the clustering dendrogram of samples. Samples are colored according to the experimental groups, individual compounds are colored according to the presence of  $\omega$ -3 FAs,  $\omega$ -6 FAs or both.

В

А

## Diacylglycerols



**Figure S6** *The distribution of diacylglycerols containing*  $\omega$ -3 *and/or*  $\omega$ -6 *fatty acids in experimental groups.* A: PCA score plot. Each sample was determined in a doublet. B: Heatmap with the clustering dendrogram of samples. Samples are colored according to the experimental groups, individual compounds are colored according to the presence of  $\omega$ -3 FAs,  $\omega$ -6 FAs or both.

### Lysophospholipids



**Figure S7** *The distribution of lysophospholipids containing*  $\omega$ -3 *and/or*  $\omega$ -6 *fatty acids in experimental groups.* A: PCA score plot. Each sample was determined in a doublet. B: Heatmap with the clustering dendrogram of samples. Samples are colored according to the experimental groups, individual compounds are colored according to the presence of  $\omega$ -3 FAs,  $\omega$ -6 FAs or both.

### Free fatty acids



**Figure S8** *The distribution of fatty acids in experimental groups (liver).* A: PCA score plot. Each sample was determined in a doublet. B: Heatmap with the clustering dendrogram of samples. Samples are colored according to the experimental groups, individual compounds are colored according to the presence of  $\omega$ -3 FAs,  $\omega$ -6 FAs or both.

# Triacylglycerols



**Figure S9** *The distribution of triacylglycerols containing*  $\omega$ -3 *and/or*  $\omega$ -6 *fatty acids in experimental groups.* A: PCA score plot. Each sample was determined in a doublet. B: Heatmap with the clustering dendrogram of samples. Samples are colored according to the experimental groups, individual compounds are colored according to the presence of  $\omega$ -3 FAs,  $\omega$ -6 FAs or both.

В