### **Supplementary information**

# Exercise plasma boosts memory and dampens brain inflammation via clusterin

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## Exercise plasma boosts memory and dampens brain inflammation via clusterin

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#### **Supplementary Table 1**

Bulk RNA-sequencing hippocampal gene counts from mice injected with CP or RP.

#### Supplementary Table 2

List of redundancy depleted Gene Ontology terms. *P*-value of the enriched GO terms was provided by the authors and calculated using the Fisher Exact test on DEGs comparing mice injected with CP or RP (Wald test, P < 0.05). Semantic similarity measure was Resnik measurement (0.7 distance).

#### **Supplementary Table 3**

Bulk RNA-sequencing hippocampal gene counts from male mice (3-4 months of age) injected with LPS were treated with saline, runner plasma or control plasma (SAL – LPS, LPS – CP or LPS - RP). An additional control group received saline for all injections (SAL – SAL) (n=7-8 per group).

#### **Supplementary Table 4**

Complete list of selected DEGs (*P* <0.05 Wald test) across all comparisons (SAL – SAL vs SAL – LPS; SAL – LPS vs LPS – CP; SAL – LPS vs LPS - RP).

#### Supplementary Table 5

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#### **Supplementary Table 6**

List of redundancy depleted Gene Ontology terms. *P*-value of the enriched GO terms was provided by the authors and calculated using the Fisher Exact *t*-test on DEGs comparing mice injected with LPS and treated with saline, runner plasma or control plasma (SAL – LPS, LPS – CP or LPS - RP) and mice that received saline for all injections (SAL – SAL) (Wald test, P < 0.05). Semantic similarity measure was Resnik measurement (0.7 distance).

#### Supplementary Table 7

Abundance of plasma proteins from 28-day-runner and control male mice detected via shotgun mass spectrometry proteomic unbiased approach.

#### **Supplementary Table 8**

List of significantly changed proteins (Student's two-tailed t test, *P* <0.05) in plasma samples from 28-day-runner or control male.

#### **Supplementary Table 9**

List of redundancy depleted Gene Ontology terms. *P*-value of the enriched GO terms was provided by the authors and calculated using the Fisher Exact test on significantly changed proteins (Student's two-tailed t test, P < 0.05) between 28-day-runner and control mice. Semantic similarity measure was Resnik measurement (0.7 distance).

#### **Supplementary Table 10**

List of genes and their corresponding FC and significance (MAST test, FDR < 0.05) when comparing gene expression in BECs of mice treated with Saline, LPS, and LPS+CLU.

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List of Gene Ontology terms (Benjamini-Hochberg test, P <0.05) of BECs genes that increase with LPS inoculation and decrease with CLU treatment

#### Supplementary Table 12

List of Gene Ontology terms (Benjamini-Hochberg test, P <0.05) of BECs genes that decrease with LPS inoculation and increase with CLU treatment

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List of genes and their corresponding FC and significance (Benjamini–Hochberg adjustment test, FDR < 0.05) when comparing gene expression in BECs of APP mice treated with Saline or CLU and WT mice using a fold change of 1.1.

#### Supplementary Table 14

List of Gene Ontology terms (Benjamini-Hochberg test, P <0.05) of BECs genes that increase in APP mice and decrease with CLU treatment using a fold change of 1.1.

#### **Supplementary Table 15**

List of Gene Ontology terms (Benjamini-Hochberg test, P <0.05) of BECs genes that decrease in APP mice and decrease with CLU treatment

#### **Supplementary Table 16**

List of Gene Ontology terms (Benjamini-Hochberg test, P <0.05) of BECs genes that are commonly changed by LPS or APP and reversed by CLU using a fold change cutoff of 1.05.

#### **Supplementary Table 17**

Gene identification of significantly changed plasma proteins (paired Student's two-tailed *t*-test, P < 0.05) in humans before and after 6 months of exercise intervention.

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#### Supplementary Table 20

Description of patient's demographic information