**Supplementary Information**

# Pivotal role of inter-organ aspartate metabolism for treatment of mitochondrial aspartate-glutamate carrier 2 (citrin) deficiency, based on the mouse model

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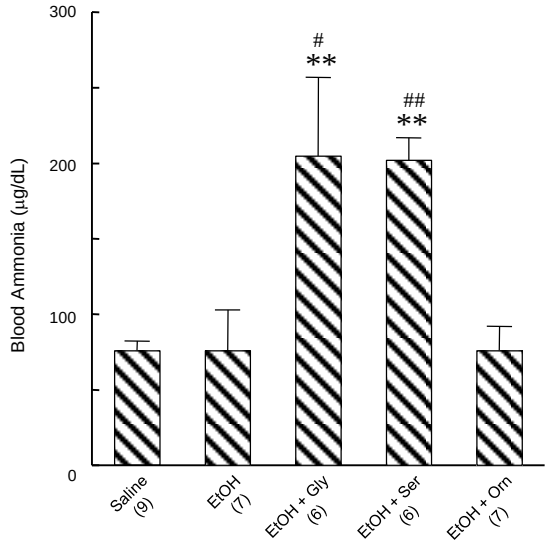
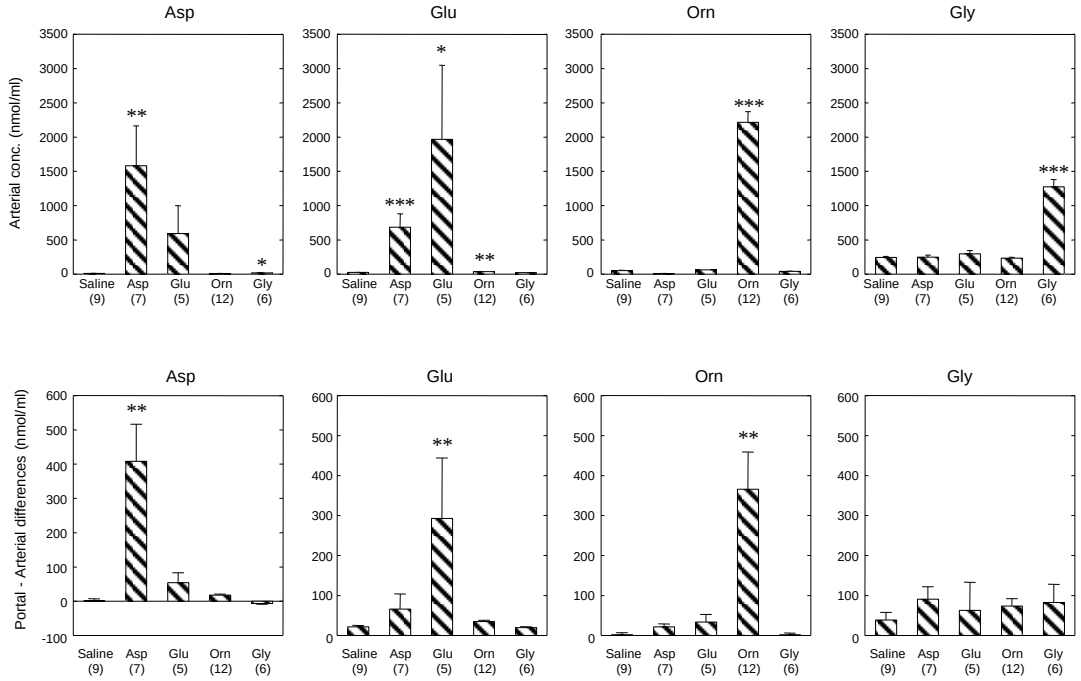



**Supplementary Figure S1.** Effect of administration of 5% ethanol (EtOH) and further addition of 1M glycine, serine or ornithine (20 ml/kg) on blood ammonia in mGPD-KO mice.
Experimental procedures are the same as described in Fig. 2(a). Data are presented as mean ± SEM. Asterisks (**P<0.01) and ($^{\#}$P<0.05 and $^{\#\#}$P<0.01) denote statistical differences from the levels when administered saline and ethanol, respectively. Number of mice are shown in parenthesis.

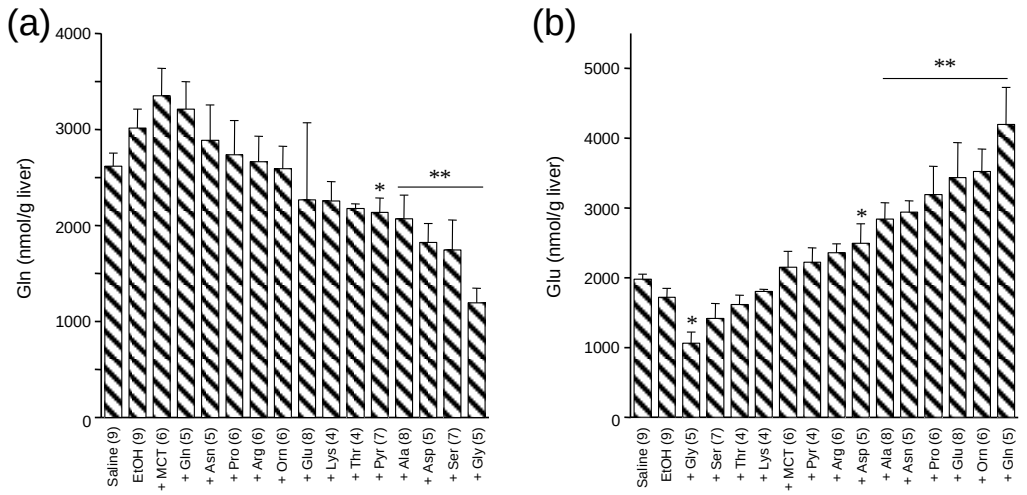
Blood ammonia level was increased by enteral administration of 1M glycine plus 5% ethanol (EtOH) (20ml/kg bw) and 1M serine plus 5% ethanol, but not by 1M ornithine plus ethanol, or ethanol alone in mGPD-KO mice.




**Supplementary Figure S2.** Arterial concentrations (upper figures) and porta – arterial differences (lower figures) of amino acids indicated above the figures following enteral administration of amino acids listed below the figures.

Experimental procedures are the same as described in Fig. 4(a). Data are presented as mean ± SEM. Asterisks (*P<0.05, and **P<0.01) denote statistical differences from the levels when administered saline. Number of mice are shown in parenthesis.

Arterial concentrations of aspartate, glutamate, ornithine and glycine were highly increased when the corresponding amino acids were administered, and the portal – arterial differences were similarly highly increased except that administration of glycine did not increase the difference at all.




**Supplementary Figure S3.** Effects of amino acids on hepatic glutamine (*A*) and glutamate (*B*) in mGPD-KO mice administered 5% ethanol.

Experimental procedures are the same as described in Fig. 1. Data are presented as mean ± SEM. Asterisks (*P<0.05, **P<0.01, and ***P<0.001) denote statistical differences from the levels when administered ethanol.

Hepatic glutamine shown in Supplementary Fig. S3(a) was not affected by 5% ethanol, but decreased significantly by enteral administration of glycine, serine, aspartate, alanine and pyruvate.

Hepatic glutamate was not significantly decreased by enteral administration of 5% ethanol in mGPD-KO mice (Supplementary Fig. 3(b)). It was significantly increased by administration of glutamine, ornithine, glutamate. proline, asparagine, alanine and aspartate, while it was decreased by administration of glycine.