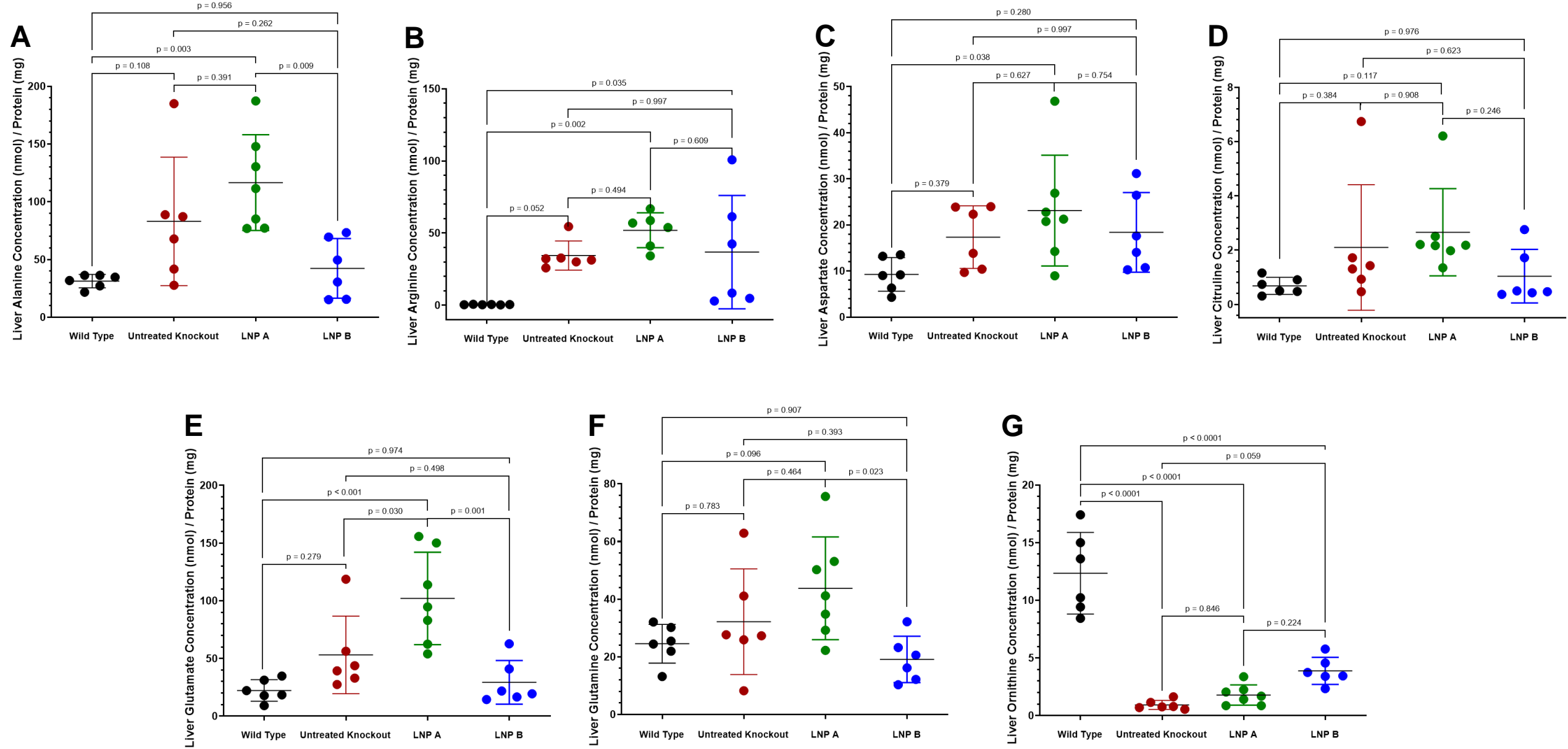


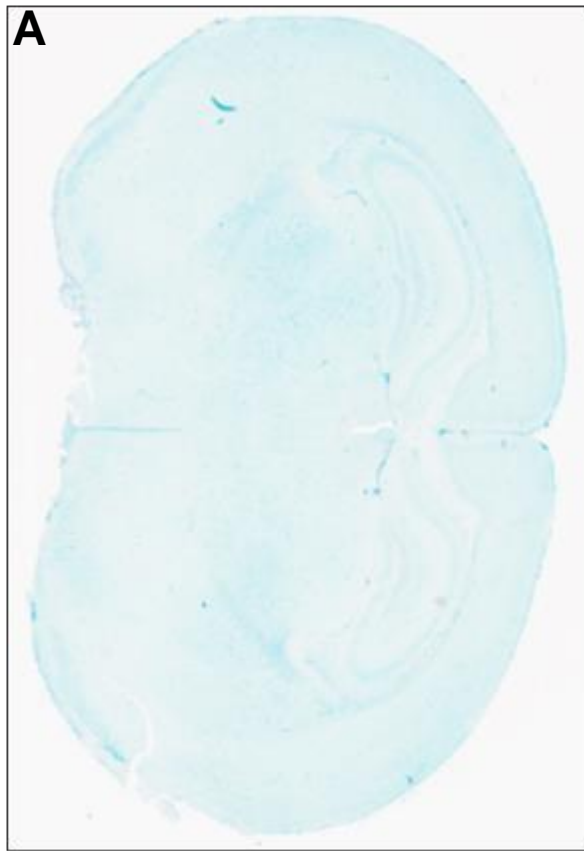
**Supplemental information**

**Intermittent lipid nanoparticle mRNA  
administration prevents cortical dysmyelination  
associated with arginase deficiency**

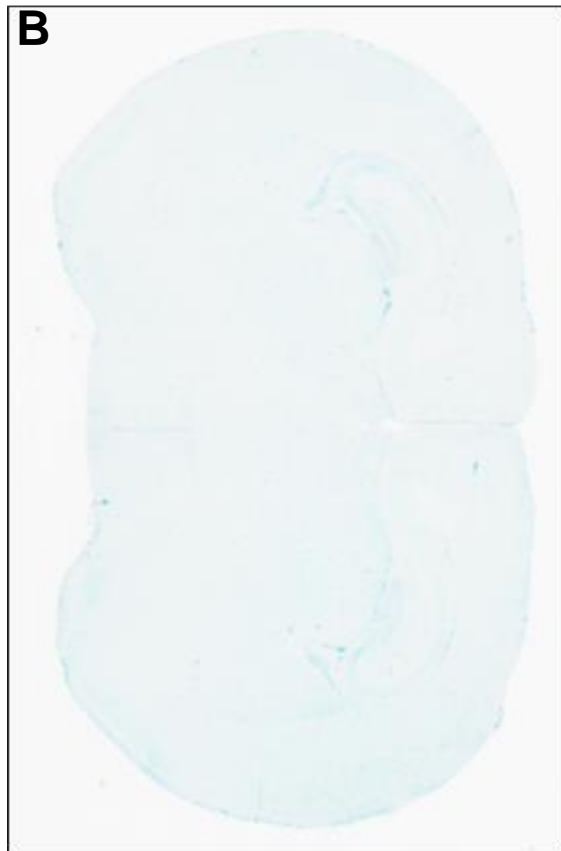
**Suhail Khoja, Xiao-Bo Liu, Brian Truong, Matthew Nitzahn, Jenna Lambert, Adam Eliav, Eram Nasser, Emma Randolph, Kristine E. Burke, Rebecca White, Xuling Zhu, Paolo G.V. Martini, Itzhak Nissim, Stephen D. Cederbaum, and Gerald S. Lipshutz**



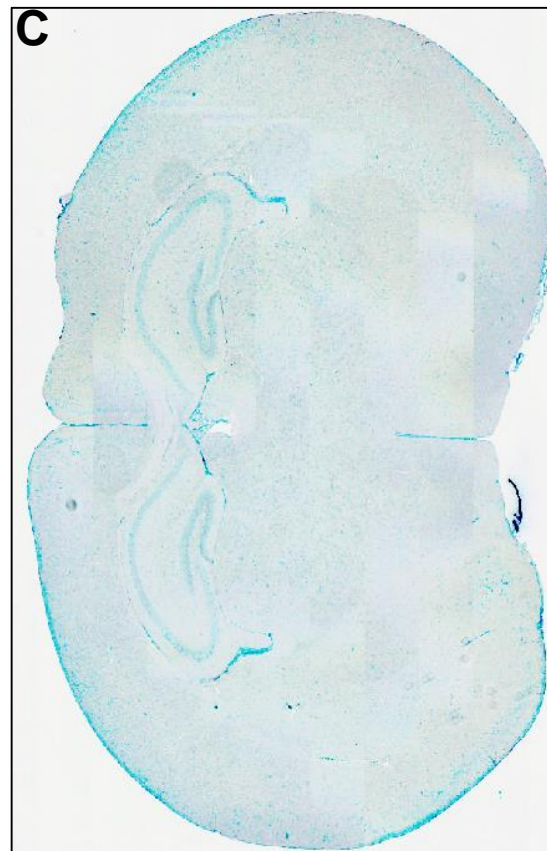
**Supplementary Figure 1: Abnormalities of Hepatic Amino Acids are Improved with *ARG1* mRNA delivered by Lipid Nanoparticle B.** Derangements of the urea cycle related hepatic amino acids of **A**) alanine, **B**) arginine, **C**) aspartate, **D**) citrulline, **E**) glutamate, and **F**) glutamine are improved with the LNP B *ARG1* for mRNA delivery; ornithine (**G**) remains reduced. (n=6-7 per group) (*ARG1*, arginase 1; LNP, lipid nanoparticle) Data are represented as mean  $\pm$  SD.



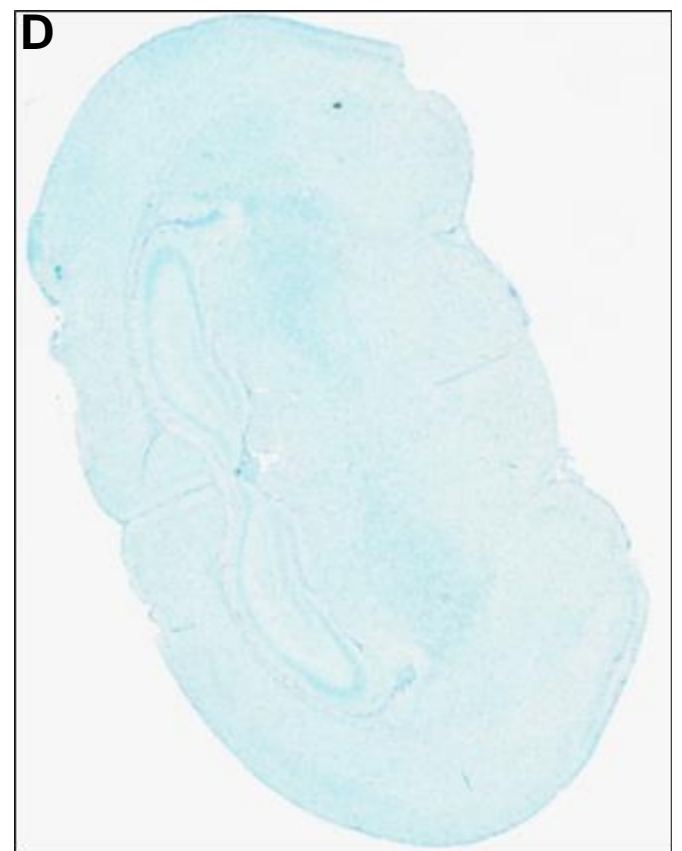
Wild Type



Untreated Knockout



LNP A



LNP B

**Supplementary Figure 2: Myelin Detection with Luxol Fast Blue Demonstrates Generalized CNS Reduction in Arginase Deficiency that is Restored with mRNA Therapy.** Representative images of the copper phthalocyanine dye Luxol Fast Blue staining to detect myelin in P14 mice: **A)**  $Arg1^{+/+}$ , **B)** untreated  $Arg1^{-/-}$ , **C)** LNP A *ARG1* mRNA treated  $Arg1^{-/-}$ , and **D)** LNP B *ARG1* mRNA treated  $Arg1^{-/-}$ . (CNS, central nervous system; mRNA, messenger ribonucleic acid; P, postnatal day; *ARG1*, arginase 1; Arg1, arginase 1; LNP, lipid nanoparticle)