

Supplementary Information for:

Title: Upregulation of reduced folate carrier (RFC) by vitamin D enhances brain folate uptake in mice lacking folate receptor alpha (Folr1)

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Table S1

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Table S1. Pharmacokinetic parameters for [¹³C₅]-5-formylTHF in WT mice estimated from plasma concentration data fitted to a two-compartment single i.v. bolus pharmacokinetic model.

Pharmacokinetic Parameters	[¹³C₅]-5-formylTHF
k_{12} (min ⁻¹)	0.055 ± 0.017
k_{21} (min ⁻¹)	0.036 ± 0.019
k_{10} (min ⁻¹)	0.221 ± 0.118
V (ml/kg)	396.34
CL (ml/min/kg)	87.76
$t_{1/2\beta}$ (min)	25.01
AUC _{0-∞} (ng/ml • min)	2,849
Analysis of model fit	
WSS	0.10
R ²	0.98
AIC	-6.13
SC	-6.96

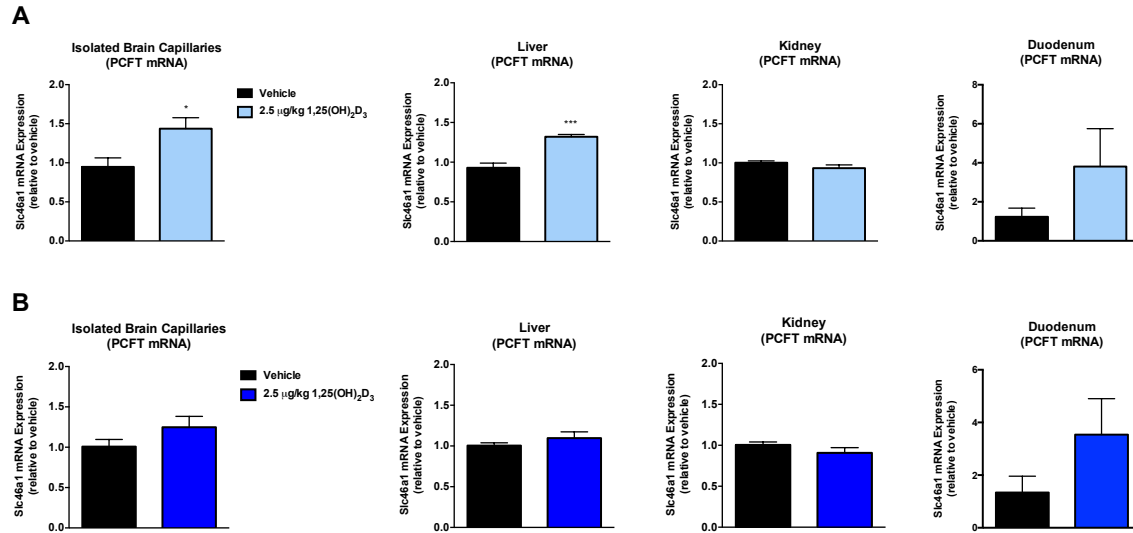


Figure S1. Effect of calcitriol treatment on PCFT expression. **(A)** Significant increases in *Slc46a1* (PCFT) mRNA was observed in isolated brain capillaries and liver of WT mice treated with calcitriol (2.5 $\mu\text{g/kg}$) compared to vehicle (corn oil). **(B)** There were no changes in *Slc46a1* (PCFT) mRNA following treatment of *Fcrl1* KO mice with calcitriol. Results are presented as mean \pm S.E.M. for $n = 3$ independent experiments (total of 8-9 animals per group). Asterisks represent data point significantly different from vehicle (*, $p < 0.05$; ***, $p < 0.001$).

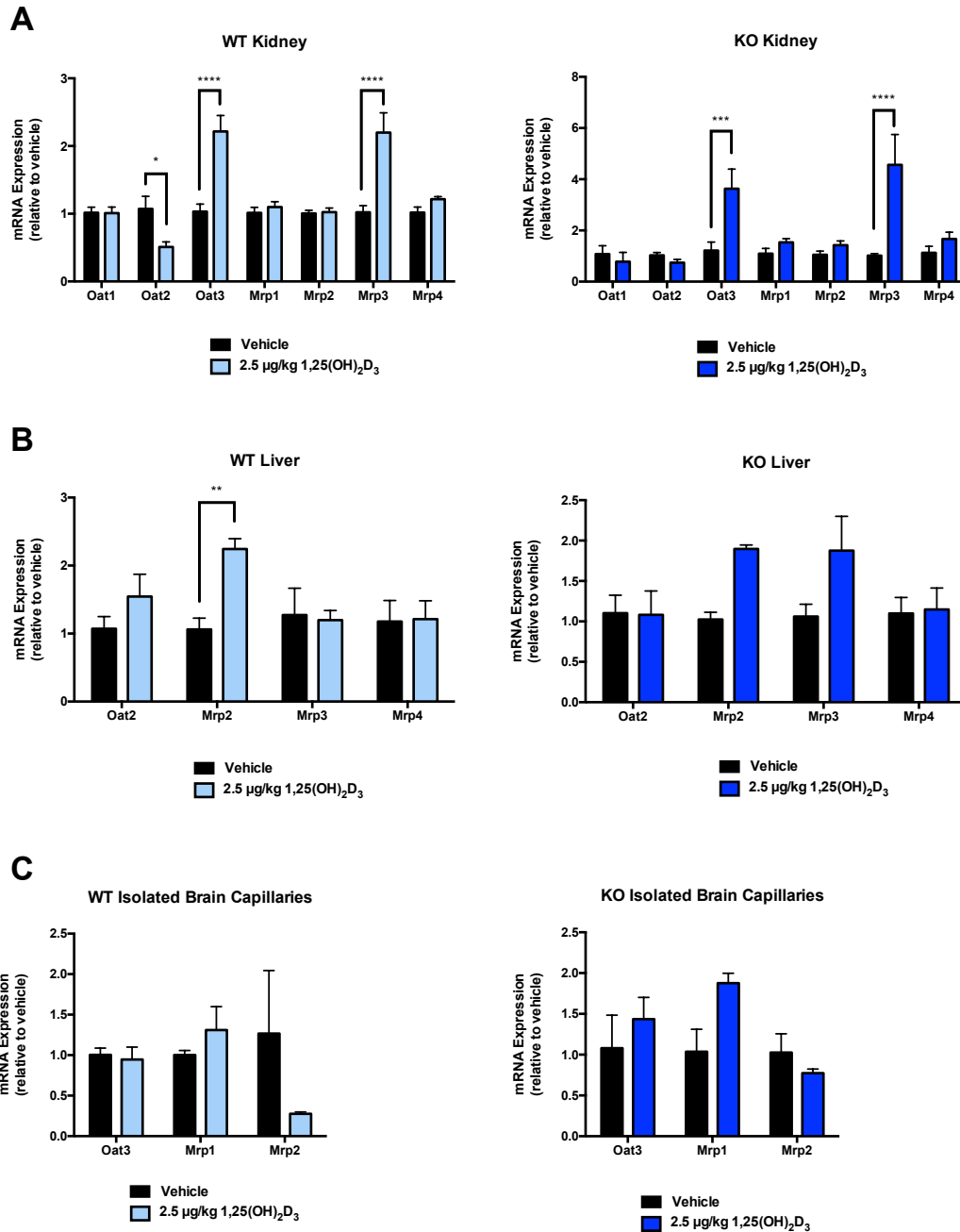


Figure S2. Effect of calcitriol treatment on Oat and Mrp expression in WT and Fcrl1 KO mice. (A) Significant increases in *Slc22a8* (Oat3) and *Abcc3* (Mrp3) mRNA were observed in kidney of WT and Fcrl1 KO mice treated with calcitriol (2.5 µg/kg) compared to vehicle (corn oil). (B) Significant induction of *Abcc2* (Mrp2) mRNA was also observed in liver of WT mice following calcitriol administration. (C) There were no significant changes in Oat or Mrp mRNA following treatment of WT and Fcrl1 KO mice with calcitriol. Results are presented as mean ± S.E.M. for $n = 3$ independent experiments (total of 5-6 animals per group). Asterisks represent data point significantly different from vehicle (*, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$).

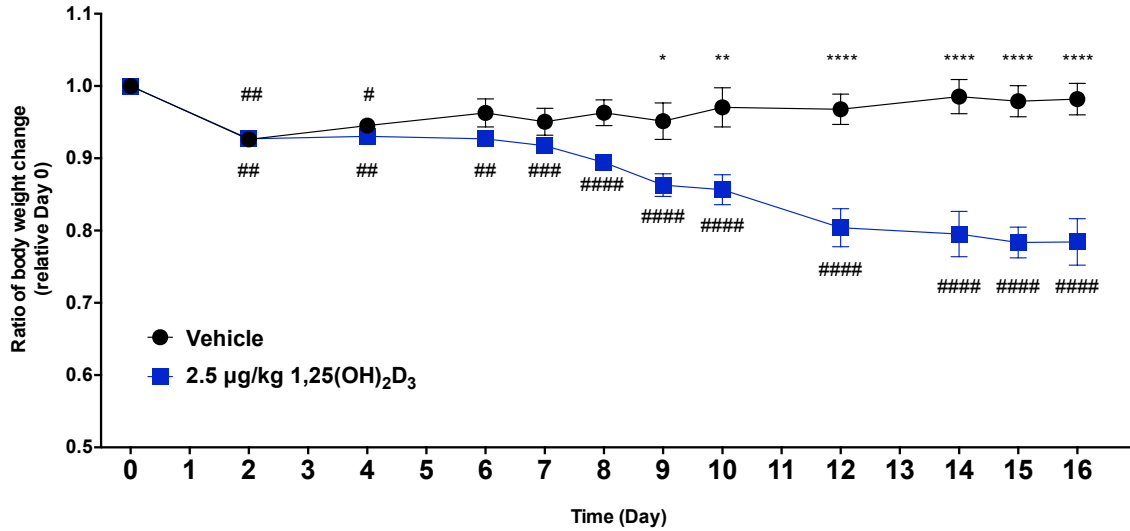


Figure S3. Long term effect of calcitriol treatment on body weight of WT mice. Significant weight loss was observed in mice treated with calcitriol (2.5 µg/kg) compared to vehicle (corn oil), but this weight loss seemed to plateau at the beginning of Day 12. Results are presented as mean ± S.E.M. (total of 3 animals per group). Asterisk and pound symbols represent data points significantly different from vehicle control and Day 0 (time before vehicle or calcitriol injections), respectively (*, $p < 0.05$; **, $p < 0.01$; ****, $p < 0.0001$; #, $p < 0.05$; ##, $p < 0.01$; ###, $p < 0.001$; #####, $p < 0.0001$).