

Supporting Information for

In Vivo Performance of a Novel Fluorinated
Magnetic Resonance Imaging Agent for Functional
Analysis of Bile Acid Transport

*Diana Vivian[†], Kunrong Cheng[‡], Sandeep Khurana[‡], Su Xu[§], Edwin H. Kriel^{||}, Paul A. Dawson[⊥],
Jean-Pierre Raufman^{‡,*} and James E. Polli^{†,*}*

[†]Department of Pharmaceutical Sciences, University of Maryland School of Pharmacy, Baltimore, Maryland 21230, United States.

[‡]Department of Medicine, University of Maryland School of Medicine, Baltimore, Maryland 21230, United States.

[§]Department of Diagnostic Radiology and Nuclear Medicine, University of Maryland School of Medicine, Baltimore, Maryland 21230, United States.

^{||} Department of Pathology, University of Maryland School of Medicine, Baltimore, Maryland 21230, United States.

[⊥]Department of Internal Medicine, Wake Forest School of Medicine, Winston-Salem, North Carolina 27157, United States.

Correspondence should be addressed to J-P.R. (jraufman@medicine.umaryland.edu) or J.E.P. (jpolli@rx.umaryland.edu).

Figure S1 ^{19}F MRI of ex-vivo phantoms of 10 mM CA-lys-TFA dissolved in different solvents. Average ROI signal intensities relative to human bile were 94.2, 83.5, and 109.4 in methanol, DMSO, and 1:1 PEG:DPBS, respectively.

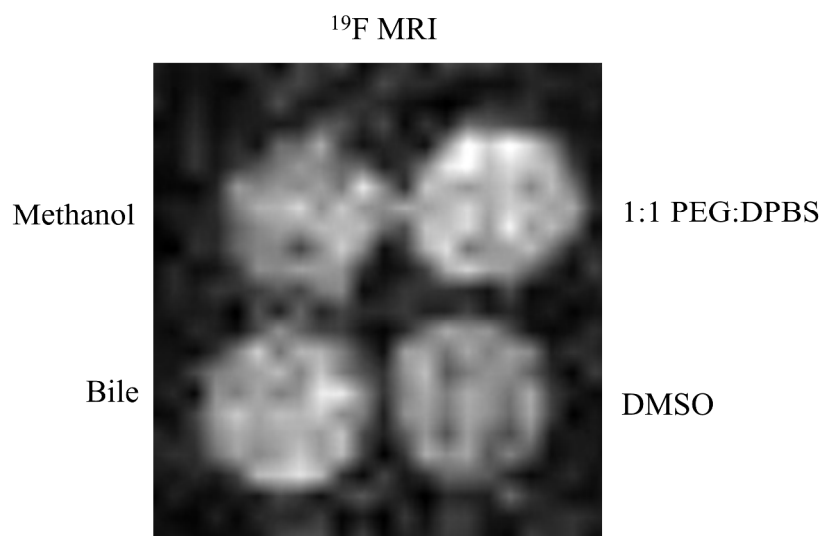


Figure S2 Comparison of gallbladder CA-lys-TFA concentrations calculated from ^{19}F MRI signal intensity to those measured by LC/MS/MS. This figure similar to Figure 4, but where data at the origin (0,0) has been excluded and where an intercept is not fitted. (A) Calculation of ^{19}F MRI signal intensity in the gallbladders of live, anesthetized mice was accomplished by comparison to the ^{19}F MRI signal intensity of a 30-mM CA-lys-TFA phantom. ^{19}F image acquisition was 1.5 h. CA-lys-TFA content in gallbladder bile by LC/MS/MS was measured after MRI. Each data point represents results from one mouse; MRI-based and LC/MS/MS-based measurements are paired ($n = 10$ mice). Linear regression analysis (solid line) yielded $R^2 = 0.896$, $P = 0.00003$, indicating association between MRI-based and LC/MS/MS-determined values. The line of unity is dashed. (B) Comparison of CA-lys-TFA measurements obtained from MRI and LC/MS/MS after applying a 2.7-correction factor to LC/MS/MS values to account for a post-MRI effect. The line of unity is dashed, while the line from regression is solid ($R^2=0.896$). The slope from linear regression is 1.12, i.e. 2.7-fold lower than the regressed slope in Fig. S2A.

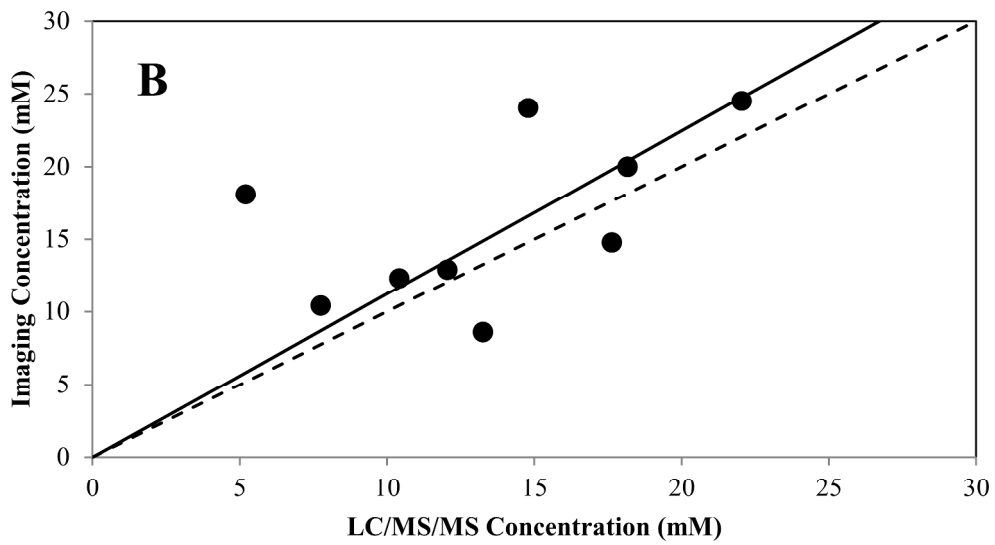
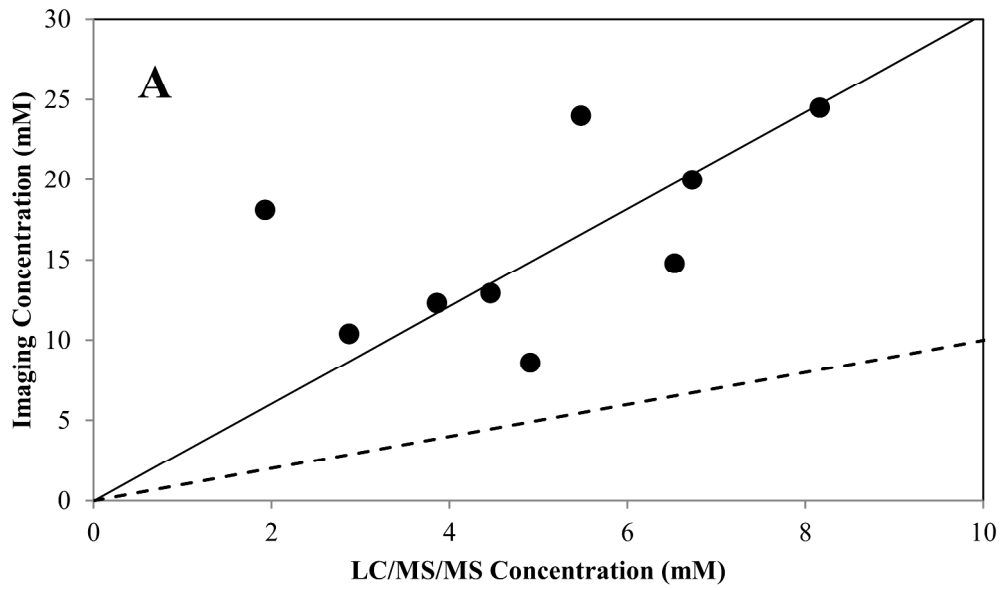


Table S1 T1 relaxation times and Relative signal intensity compared to human bile of 10 mM CA-lys-TFA dissolved in methanol, DMSO, 1:1 PEG:DPBS, and human bile.

Solvent	Signal Intensity (% Compared to Bile)	T1 (s)
Methanol	94.2	1.046 ± 0.100
DMSO	83.5	0.667 ± 0.102
1:1 PEG: DPBS	109.4	0.629 ± 0.059
Bile	100	0.380 ± 0.013

Table S2 Liver and plasma CA-lys-TFA concentrations in mice 1-14, measured by LC/MS/MS after euthanasia.

Mouse	Dose	Time of Euthanasia (h)	Liver [CA-lys-TFA] (μ M)	Plasma [CA-lys-TFA] (μ M)
1	150 mg/kg	5.0	3.83	0.10
2	150 mg/kg	51.4	0.76	0.02
3	150 mg/kg	2.8	7.40	15.90
4	150 mg/kg	8.6	8.99	16.56
5	150 mg/kg	8.5	1.97	0.07
6	150 mg/kg	53.0	0.71	0.04
7	150 mg/kg	8.4	3.73	1.28
8	50 mg/kg 7x	4	10.66	0.05
9	50 mg/kg 7x	3.5	14.02	0.02
10	50 mg/kg 7x	8.9	1.63	0.02
11	150 mg/kg	8.5	22.97	0.20
12	150 mg/kg	8.5	7.92	0.18
13	150 mg/kg	8.5	6.96	0.09
14	150 mg/kg	8.5	6.55	0.42

Table S3 Gallbladder, liver and plasma concentrations of CA-lys-TFA in WT and *Slc10a2*^{-/-} mice. Mice 15-18 and 20-23 were euthanized without imaging 7 h after gavage, whereas mice 19 and 24 were imaged and euthanized 8.5 h after oral gavage with 150 mg/kg CA-lys-TFA. In general, CA-lys-TFA concentrations in WT mice were substantially greater than those in *Slc10a2*^{-/-} mice.

	Mouse	Gallbladder [CA-lys-TFA] (mM)	Liver [CA-lys-TFA] (μ M)	Plasma [CA-lys-TFA] (μ M)
WT	15	4.36	7.95	0.78
	16	12.32	10.28	0.23
	17	13.95	18.83	0.25
	18	8.61	17.21	0.42
	19	4.81	4.49	0.69
<i>Slc10a2</i> ^{-/-}	20	0.30	0.61	0.00
	21	0.42	0.61	0.17
	22	0.27	0.63	0.05
	23	0.28	0.46	0.22
	24	0.27	1.26	0.52