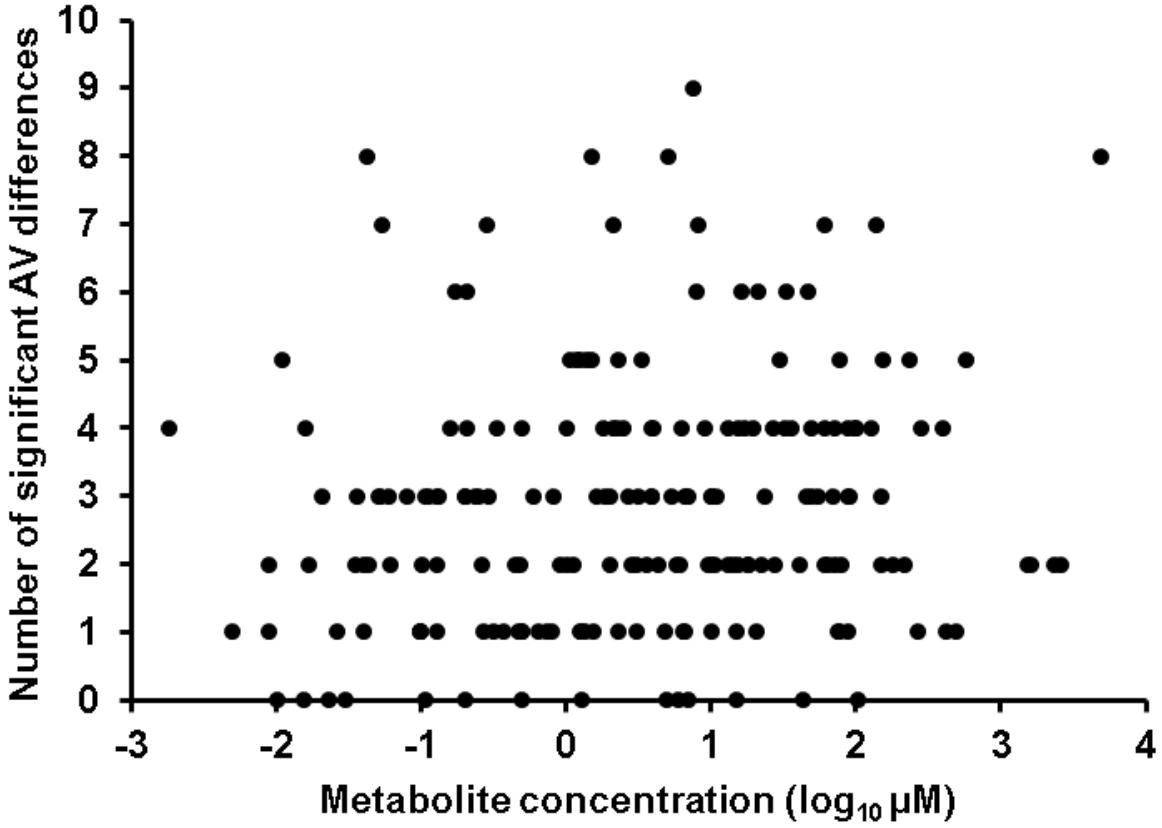

Figure S1. The correlation between the number of significant AV differences detected per metabolite and the metabolite's absolute concentration. Related to Fig.1.

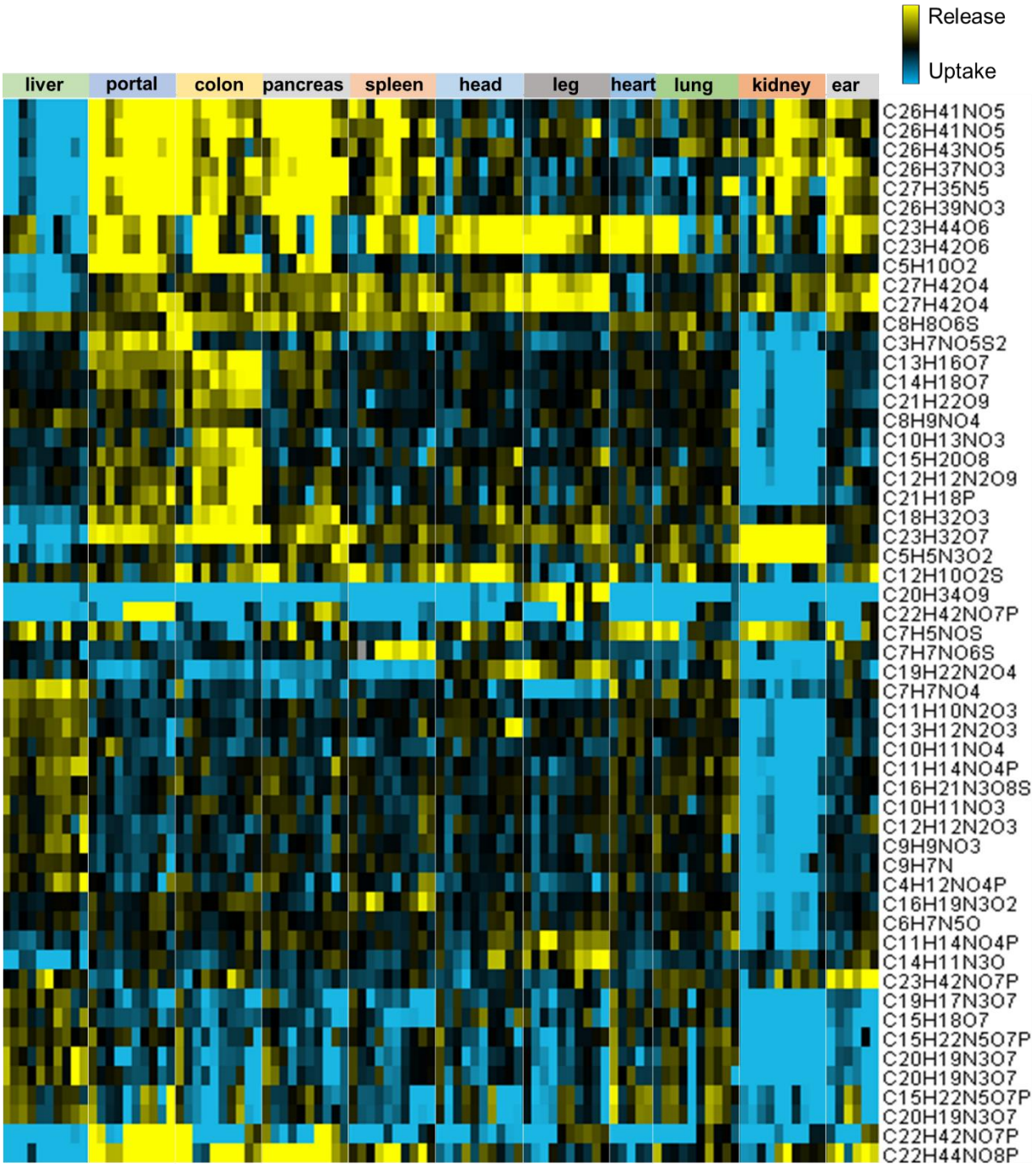

Figure S2. Unknown metabolites showing significant inter-organ exchange. Related to Fig.1.

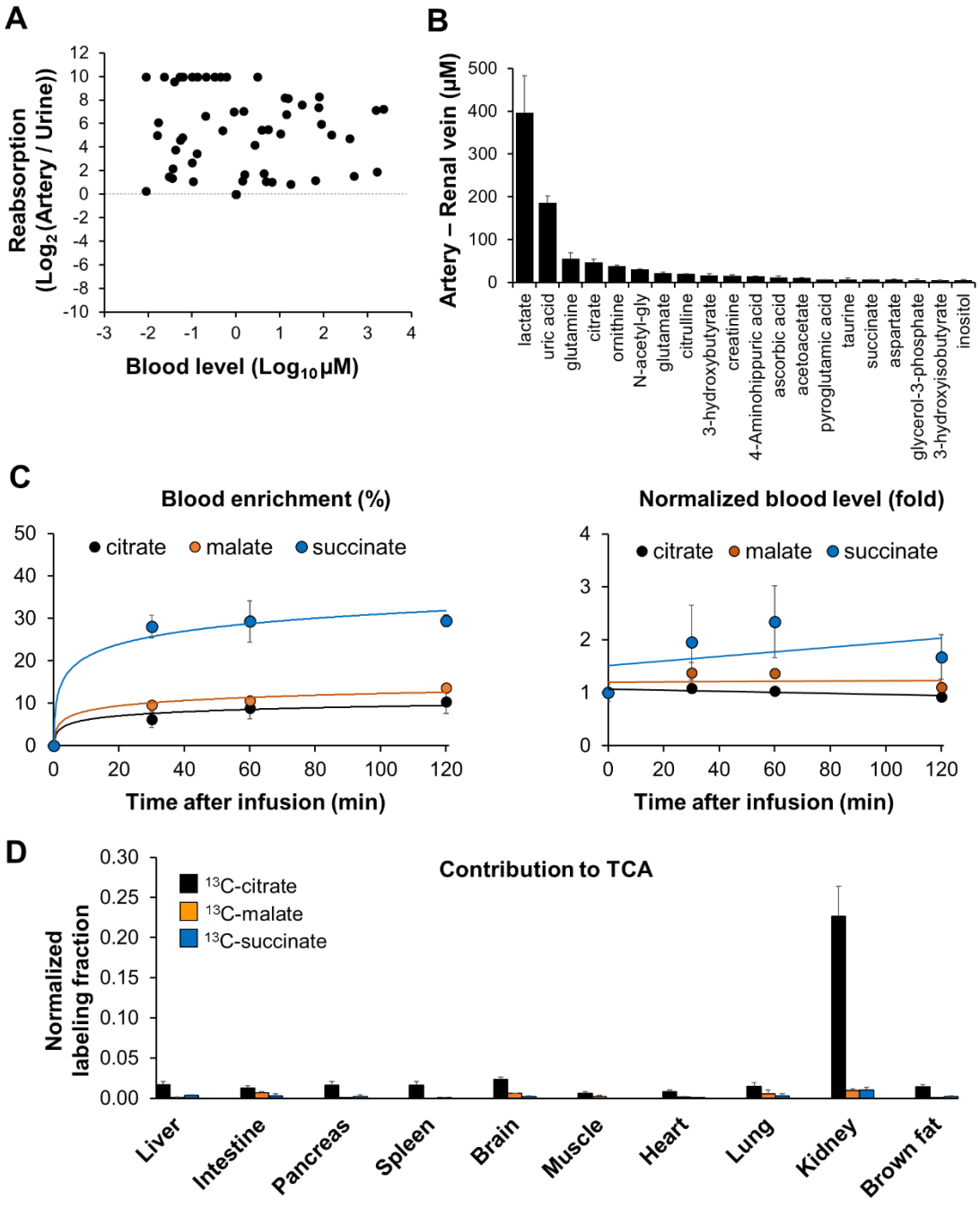

Figure S3. Renal metabolite uptake in pigs (A and B) and steady-state infusion of ^{13}C-labeled TCA intermediate tracers in mice (C and D). The reporter metabolite (measured to determine TCA labeling) was selected to be distinct from the tracer metabolite, to avoid misinterpreting extracellular tracer as TCA labeling (in practice, we observe an additional 1% to 8%. TCA contribution, depending on the tissue, when the reporter metabolite and tracer are the same). Specifically, for ^{13}C-citrate and ^{13}C-malate infusions, tissue succinate labeling was used to determine their TCA contribution. For ^{13}C-succinate infusion, tissue malate labeling was used. Data are means and error bars are standard errors. N = 4 for citrate, and N = 3 for malate and succinate. Related to Fig.2.

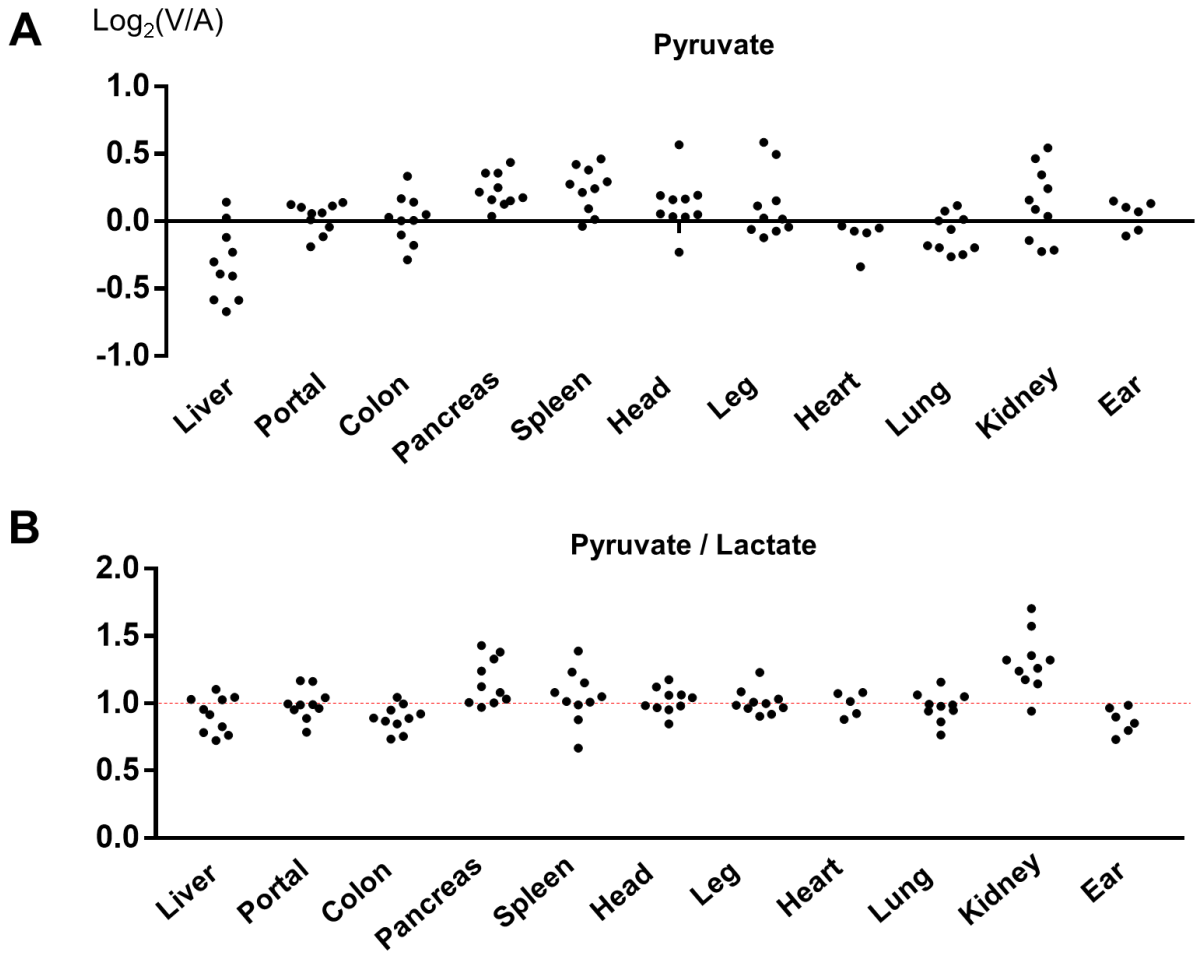

Figure S4. Kidneys oxidize circulating lactate into circulating pyruvate in pigs. Related to Fig. 3.

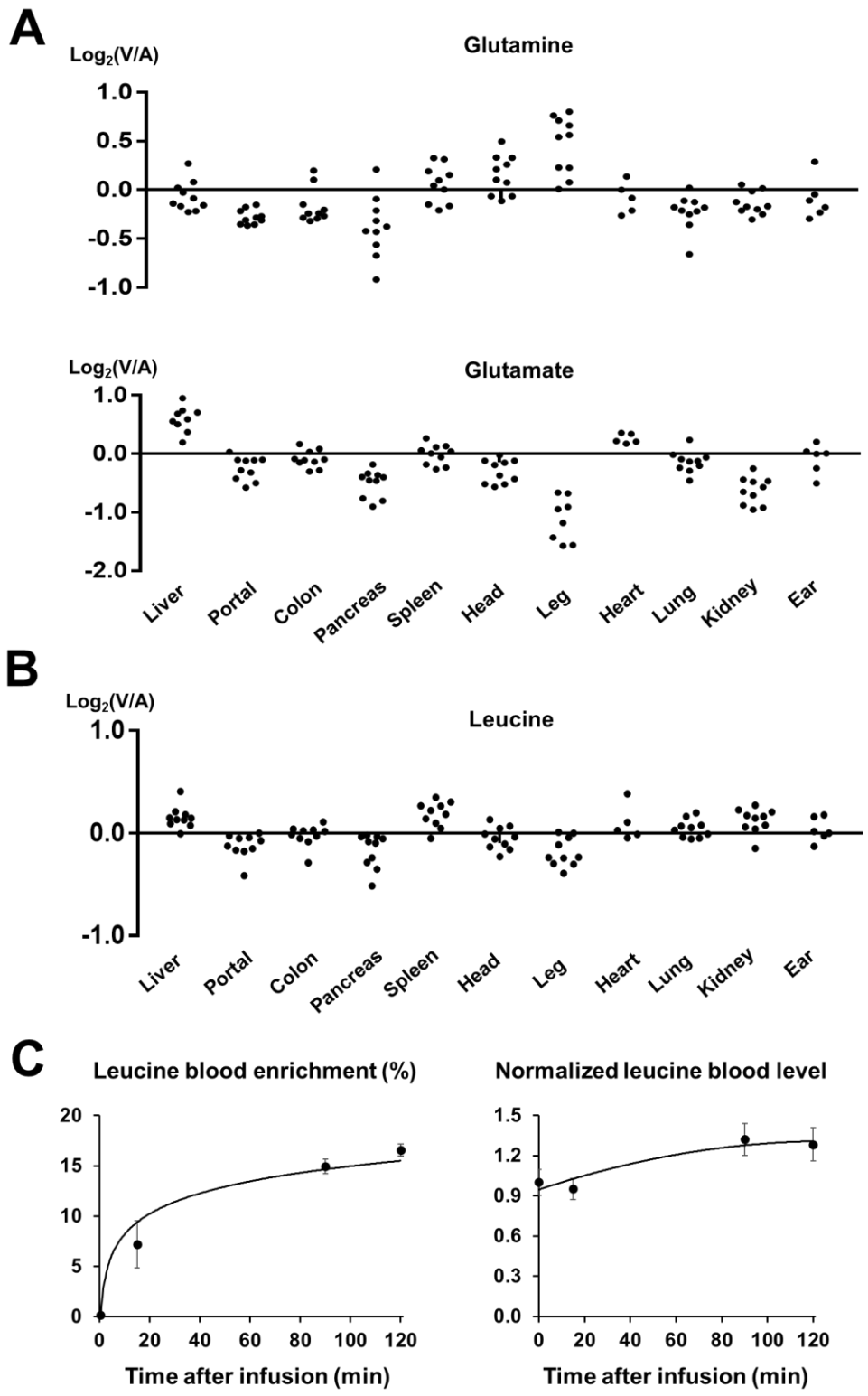

Figure S5. Exchange of amino acids in pigs (A and B), and steady-state infusion of a ^{13}C-leucine tracer in mice (C). Data are means and error bars are standard errors (N = 4 mice). Related to Fig. 4.

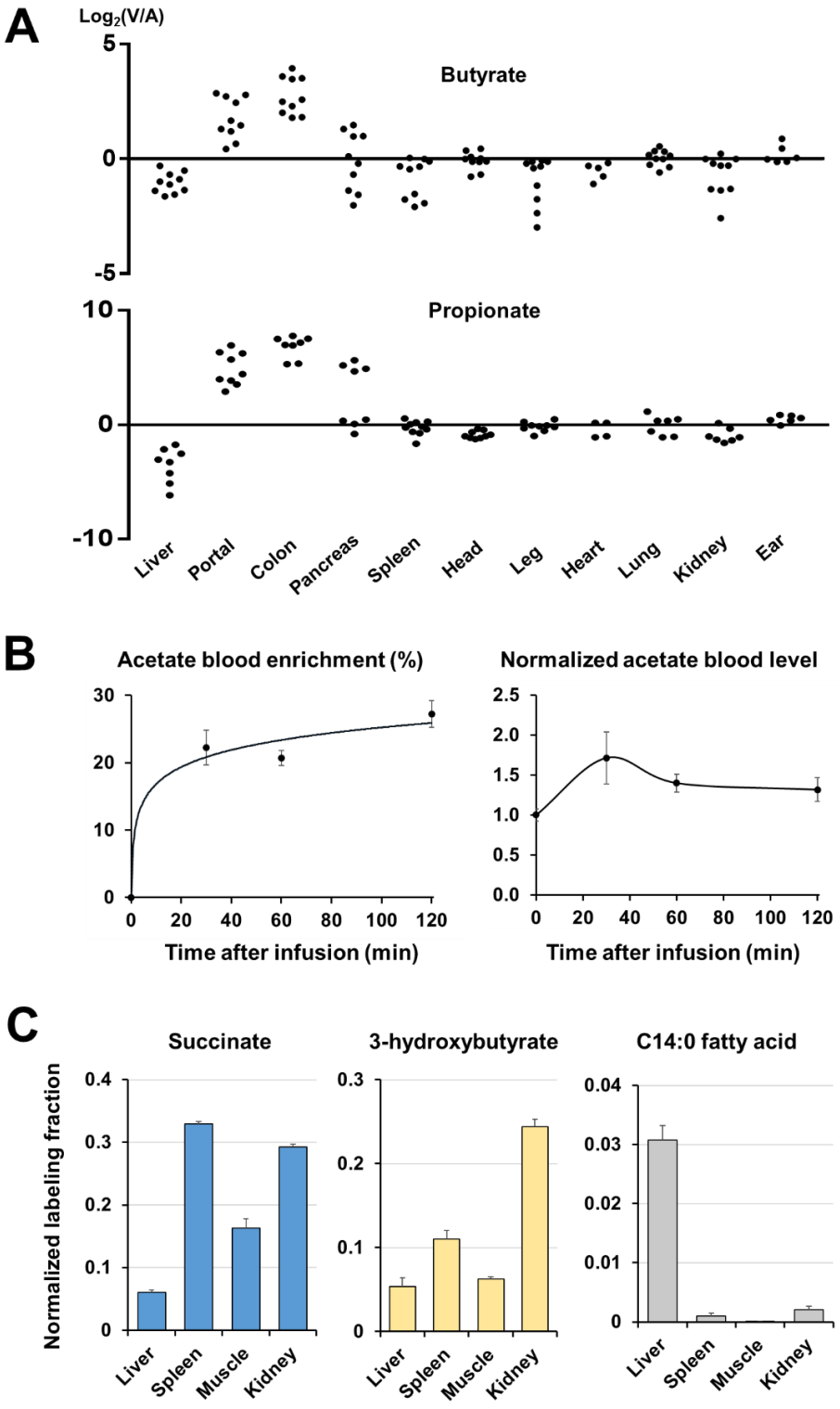

Figure S6. Short chain fatty acid exchange in pigs (A) and steady-state infusion of a ^{13}C-acetate tracer in mice (B and C). Data are means and error bars are standard errors (N = 3 mice). Related to Fig. 5.

Metabolites	Produced	Consumed
Secondary bile acids	Intestine, Colon	Liver
Acetate	Intestine, Colon, Head	Liver, Spleen, Leg
Butyrate, Propionate	Intestine, Colon	Liver
Ribonucleosides	Spleen	Kidneys
Deoxyribonucleosides	Colon, Spleen	Kidneys
Glucose	Liver, Kidneys	Intestine, Colon, Pancreas, Spleen, Head, Leg
Lactate	Spleen, Ear	Liver, Kidneys
Pyruvate	Pancreas, Spleen	Heart
3-hydroxybutyrate	Colon	Leg, Lung, Kidneys
Acetoacetate	Liver	Pancreas, Spleen, Leg, Lung, Kidneys
Malate, Fumarate, α-KG	Intestine, Colon, Pancreas, Spleen, Leg, Ear	Liver, Kidneys
Succinate	Intestine, Colon, Pancreas, Leg	Liver, Kidneys
Citrate	Pancreas, Head, Leg	Kidneys
Indole metabolites	Intestine, Colon	Kidneys
Taurine	Liver, Spleen, Ear	-
Inositol	Liver, Spleen	Kidneys
Serine	Kidneys, Liver	Intestine, Pancreas, Head, Leg, Ear
Aspartate	Liver, Spleen	Leg, Kidneys
Asparagine	Spleen	Intestine, Pancreas
Glutamate	Liver, Heart	Intestine, Pancreas, Head, Leg, Kidneys
Glutamine	Leg	Intestine, Pancreas, Lung, Kidneys
Alanine	Leg	Colon
Branched-chain amino acids	Liver	Intestine, Leg
Other essential amino acids	Liver, Kidneys	Intestine, Pancreas
Branched-chain α-keto acids	Leg	Intestine, Colon, Spleen
Branched-chain α-hydroxy acids	Leg	Kidneys
N-acetyl-amino acids	Liver, Spleen	Kidneys
Unsaturated fatty acids (C14-C20)	Intestine, Colon, Pancreas, Spleen, Head, Leg	Liver, Heart
Unsaturated fatty acids (C22)	Intestine, Spleen, Leg	Liver, Heart
Unsaturated fatty acids (C24)	Spleen	Liver, Heart
Saturated fatty acids (C14-C20)	-	Heart
Saturated fatty acids (C22-C24)	-	Head, Leg, Lung
Carnitine	-	Intestine, Colon, Spleen
Short-chain carnitines (C2-C5)	Colon, Heart	Spleen, Leg, Kidneys
Medium-chain carnitines (C6-C12)	Pancreas, Leg	Kidneys
Long-chain carnitines (C14-C20)	Intestine, Pancreas, Leg, Ear	Heart, Kidneys

Table S1. Sources and sinks of metabolites (continued). Related to Fig. 1.

Metabolites	Produced	Consumed
Nicotinamide	Spleen	Leg, Colon
Ornithine, Citrulline	Intestine	Spleen, Leg, Kidneys
Creatine	Liver, Heart	Intestine, Leg
Creatinine	Liver, Leg	Intestine, Colon, Kidneys
D-gluconate	Colon, Pancreas, Spleen, Brain	Leg
Allantoin	Liver	Intestine, Colon, Pancreas, Spleen, Kidneys, Ear
Allantoate	Kidneys	Head
Benzoic acid	Colon, Ear	-
Biotin	Spleen, Heart	Intestine, Kidneys
Capryloyl glycine	Liver, Pancreas	Kidneys
Carnosine	Liver	Kidneys, Ear
Citramalic acid	Colon, Pancreas, Head, Leg	Liver, Kidneys
Dihydroxymandelic acid	Intestine, Colon	Spleen, Head, Kidneys
Gluconolactone	Brain	-
Glycerate	Liver, Lung	Kidneys
Glycerol-3-phosphate	Liver, Pancreas, Spleen	Leg, Kidneys
Glycyl-L-proline	Leg	-
Guanine	Spleen, Leg, Ear	Kidneys
Glycocyamine	Kidneys	Liver
Homocysteine	Liver	Intestine, Colon
Homogentisic acid	Liver, Leg	Kidneys
Hypotaurine	Colon, Spleen, Leg, Heart	Liver
L-Threonic acid	Liver, Lung	Kidneys
m-Coumaric acid	Intestine, Colon	Brain
Methylcysteine	Liver	Intestine, Colon
Methylmalonic acid	Intestine, Colon, Pancreas, Leg	Liver, Kidneys
m-Hydroxyhippuric acid	Liver	Leg, Kidneys, Ear
N-Tiglylglycine	Liver, Spleen	Kidneys
O-Phosphorylethanolamine	Pancreas, Spleen	Leg, Kidneys
Phenol sulphate	Liver	Intestine, Colon, Pancreas, Spleen, Kidneys
Phenylacetate	Intestine, Colon, Kidneys	Liver
Phenylpropionylglycine	Lung	Leg, Kidneys
Propionyl-glycine	Liver	Intestine, Colon, Pancreas, Spleen, Leg, Kidneys
S-methyl-5'-thioadenosine	Pancreas	Kidneys
Synephrine	Colon, Head	Liver, Leg, Kidneys

Table S1. Sources and sinks of metabolites (continued). Related to Fig. 1.

Metabolites	Produced	Consumed
Thymine	Intestine, Colon, Pancreas, Spleen, Head	Liver, Kidneys
Triethanolamine	Liver	Leg, Kidneys
Uracil	Leg	Kidneys
Uric acid	Head, Skin	Spleen, Kidneys
Xanthine	Intestine, Colon	Liver
1-methyl-histidine	Liver	Intestine, Colon, Pancreas
3-hydroxyanthranilic acid	Liver, Lung, Ear	Kidneys
3-hydroxyphenyllactate	Leg	Kidneys
Phenylpropionic acid	Intestine, Colon	Liver, Kidneys
2-hydroxybutyrate	Liver, Ear	-
3-hydroxyisobutyrate	Liver	Intestine, Pancreas, Spleen, Leg, Kidneys
2-Isopropylmalic acid	Liver	Colon, Head
3-4-dihydroxyhydrocinnamic acid	Leg	Kidneys
4-pyridoxic acid	Liver	Kidneys, Ear
5-aminolevulinic acid	Leg	Colon, Spleen, Kidneys
Beta-aminoisobutyric acid	Liver	Intestine, Pancreas, Ear
Cinnamoylglycine	Colon, Ear	Leg, Kidneys
Dehydroascorbic acid	Spleen, Lung	-
D-Galactonic acid	Colon, Pancreas, Spleen	Kidneys
Dimethylglycine	Liver	Intestine, Colon, Spleen
5-Hydroxylysine	Ear	Intestine, Colon, Pancreas
L-Rhamnose	Liver	Intestine, Colon, Pancreas
Pipecolic acid	Liver	Intestine, Colon, Spleen
Sorbitol	Spleen, Leg, Ear	Kidneys
Ureidopropionic acid	-	Liver, Kidneys

Table S1. Sources and sinks of metabolites. Related to Fig. 1.