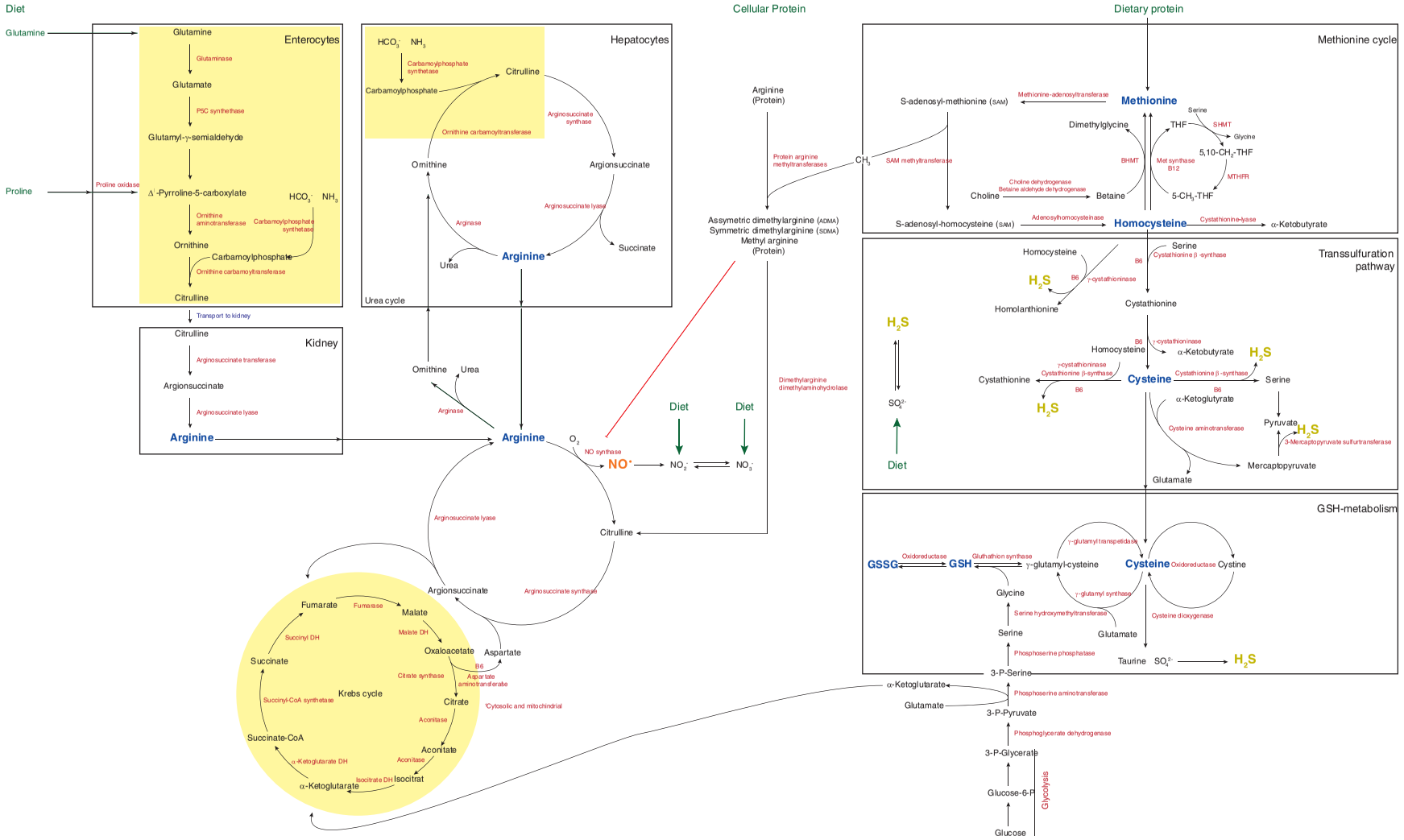
Supplementary Data



SUPPLEMENTARY FIG. S1. Metabolic pathways fueling the RSI. In adult mammals, L-arginine is formed either *via* the entero-renal axis from dietary glutamine or proline or *via* the hepatic urea cycle. Enterocyte mitochondria form citrulline from proline and glutamine *via* ornithine and carbamoylphosphate and export it to the kidney where it is converted into arginine. The hepatic urea cycle also uses ornithine and carbamoylphosphate as precursor for arginine synthesis. As in enterocytes, formation of carbamoylphosphate, from ammonia and bicarbonate, and citrulline synthesis take place in the mitochondria. Arginine used for NO synthesis can then be recycled *via* the arginine/citrulline cycle. NO synthase activity is inhibited by different methylated arginine species (ADMA, NMA), which themselves are precursors for arginine biosynthesis *via* citrulline. A key interaction between nitrogen and sulfur metabolism is the methylation of arginine using SAM-dependent methyl transferases. SAM is formed from methionine and used for the methylation of a large number of different molecules, resulting in the formation of homocysteine (Hcy). Depending on the availability of methionine, homocysteine is either recycled to methionine *via* vitamin B12 and folate-dependent methionine synthase or BHMT or is degraded to cystathionine, cysteine, and H_2S *via* the TS pathway. ADMA, asymmetric dimethylarginine; BHMT, betaine-homocysteine S-methyltransferase; H_2S, hydrogen sulfide; NO, nitric oxide; RSI, reactive species interactome; SAM, S-adenosyl-methionine; TS, transsulfuration.