



Supplementary Figure S1: ^{13}C -Isotopomers of selected metabolic intermediates generated from $[U-^{13}C]$ fructose metabolism into lipogenic and glycogenic pathways. These include hepatic glucose-6-P - inferred from the analysis of newly-synthesized glycogen; triose-P recruited for gluconeogenesis (GNG-triose-P) – inferred from the analysis of indirect pathway glycogen ^{13}C -isotopomers; triose-P supplying glycerol-3-P for fatty acid esterification and acetyl-CoA units for de novo lipogenesis – inferred from the ^{13}C -isotopomer analysis of newly-synthesized triglyceride glycerol, and the acetyl-CoA pool supplying lipogenesis – inferred from the ^{13}C -isotopomer analysis of newly-synthesized fatty acids. For the metabolite carbon skeletons, the red filled and unfilled circles represent ^{13}C and ^{12}C , respectively. The shading highlights those isotopomers that form $[U-^{13}C]$ acetyl CoA and the colors indicate isotopic equivalence (same color) or non-equivalence (different colors). For simplicity, in depicting the fatty acid labeling, only the ^{13}C -isotopomers of the last two fatty acid carbons (representing the first acetyl-CoA moiety to be incorporated into DNL) are shown.

Supplementary Table S1: Liver glycogen ^{13}C -isotopomer enrichments from mice provided with $[\text{U-}^{13}\text{C}]\text{glucose}$ ($n=4$) and $[\text{U-}^{13}\text{C}]\text{fructose}$ ($n=5$). The glycogen ^{13}C -isotopomers shown in bold text are metabolized to $[\text{U-}^{13}\text{C}]\text{acetyl-CoA}$. Values are reported as means \pm S.D.

Glycogen ^{13}C-isotopomer	$[\text{U-}^{13}\text{C}]\text{Glucose}$	$[\text{U-}^{13}\text{C}]\text{Fructose}$
$[\text{U-}^{13}\text{C}]\text{glycogen}$	2.45 ± 0.84	0.56 ± 0.13
$[1,2,3\text{-}^{13}\text{C}_3]\text{glycogen}$	0.84 ± 0.54	1.84 ± 0.49
$[4,5,6\text{-}^{13}\text{C}_3]\text{glycogen}$	1.03 ± 0.43	2.03 ± 0.21
$[1,2\text{-}^{13}\text{C}_2]\text{glycogen}$	0.38 ± 0.12	0.40 ± 0.08
$[5,6\text{-}^{13}\text{C}_2]\text{glycogen}$	0.03 ± 0.04	0.11 ± 0.03
$[2,3\text{-}^{13}\text{C}_2]\text{glycogen}$	0.02 ± 0.02	0.09 ± 0.02
$[4,5\text{-}^{13}\text{C}_2]\text{glycogen}$	0.02 ± 0.03	0.11 ± 0.03

Supplementary Table S2: Newly synthesized glycogen fraction (f_{glycogen}) with direct and indirect pathway contributions to the newly synthesized glycogen (f_{direct} and f_{indirect}), and newly synthesized triglyceride glyceryl and fatty acid fractions (f_{glyceryl} and $f_{\text{fatty acid}}$) from ^2H -enrichment data of liver glycogen and triglyceride, respectively. Values are reported as means \pm S.D.

^{13}C -tracer	Glycogen			Triglyceride	
	f_{glycogen}	f_{direct}	f_{indirect}	f_{glyceryl}	$f_{\text{fatty acid}}$
[U- ^{13}C]glucose (n=4)	0.73 ± 0.11	0.62 ± 0.04	0.38 ± 0.04	0.31 ± 0.10	0.16 ± 0.05
[U- ^{13}C]fructose (n=5)	0.74 ± 0.08	0.66 ± 0.02	0.34 ± 0.04	0.30 ± 0.07	0.16 ± 0.05