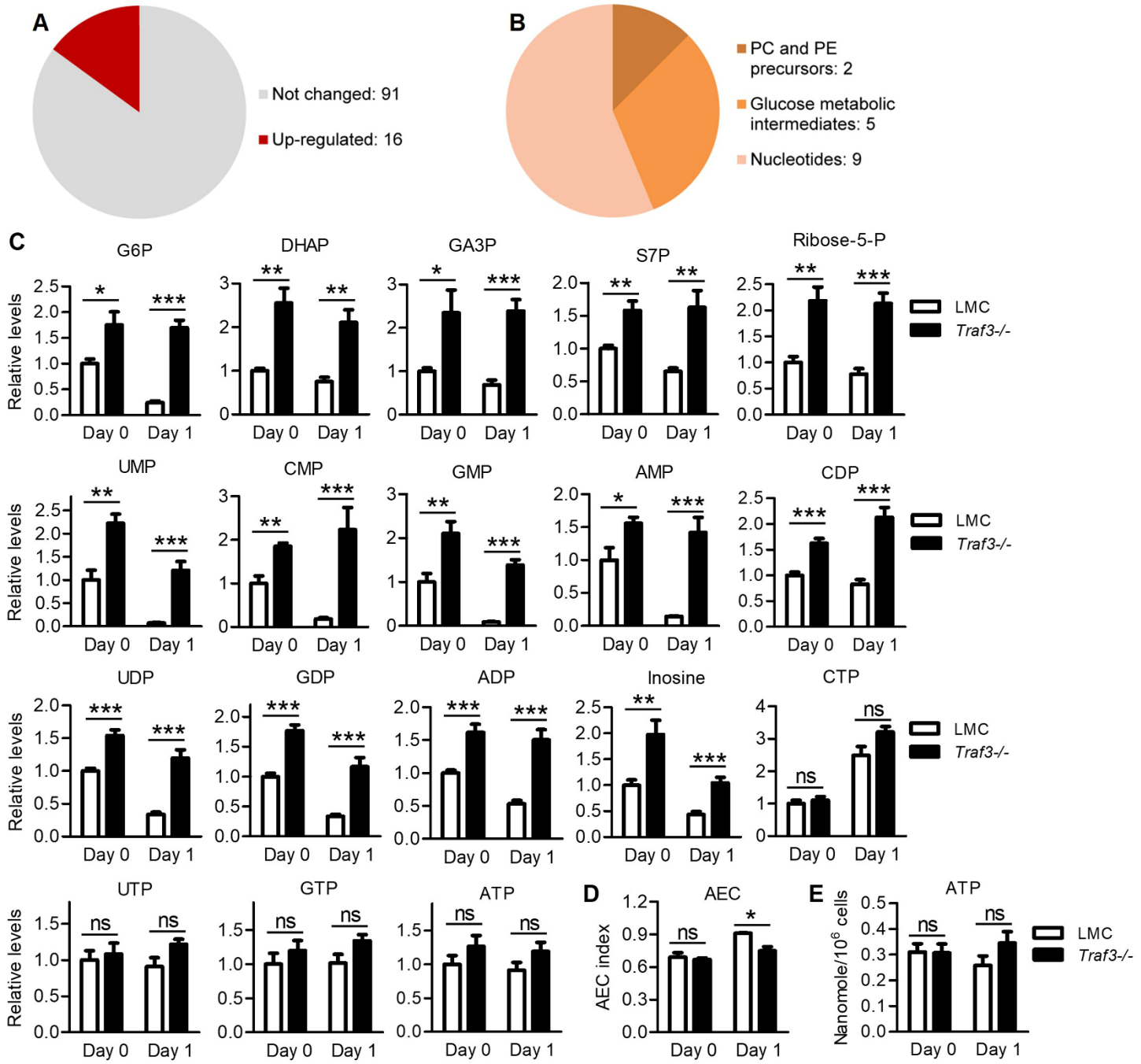
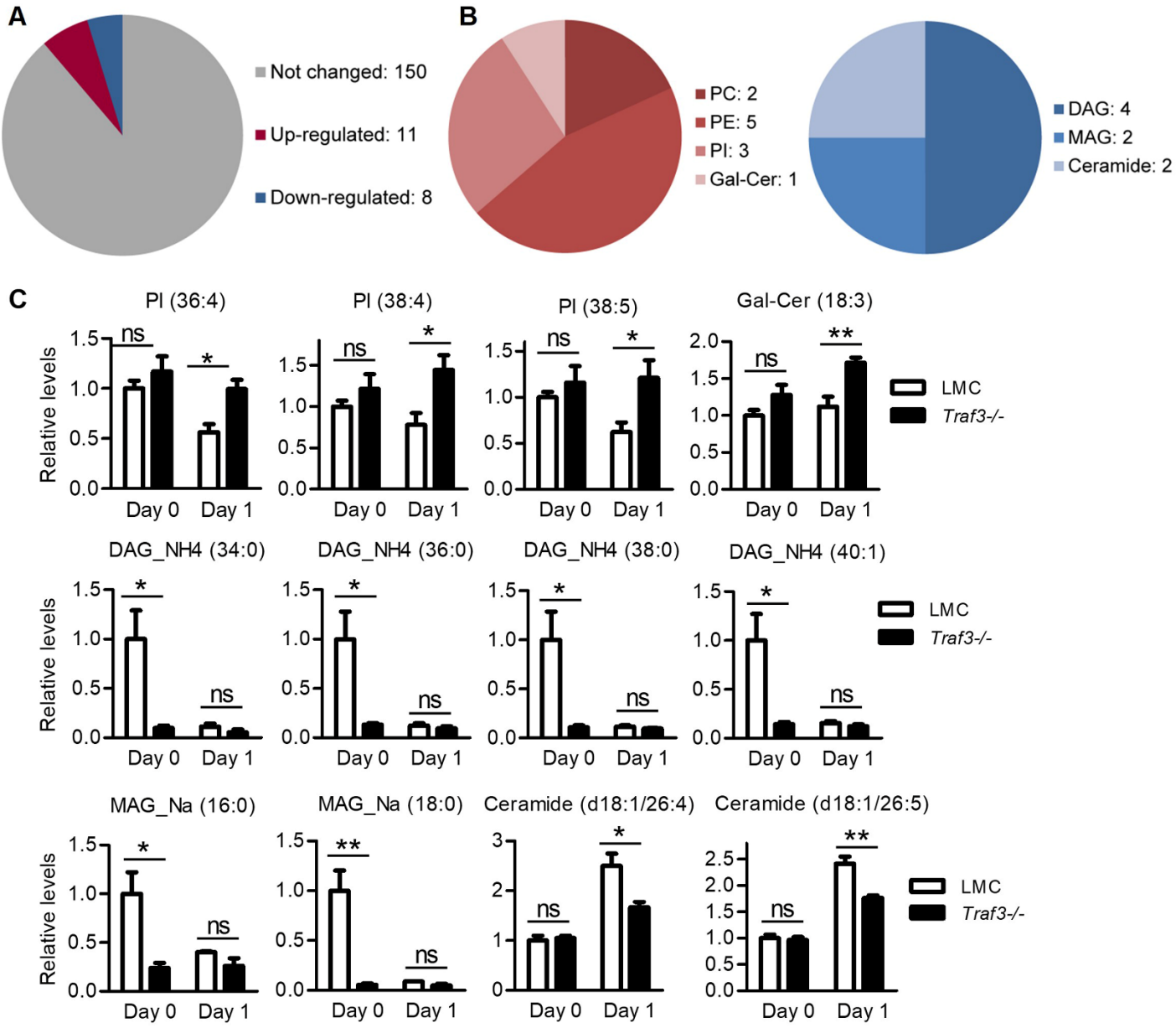
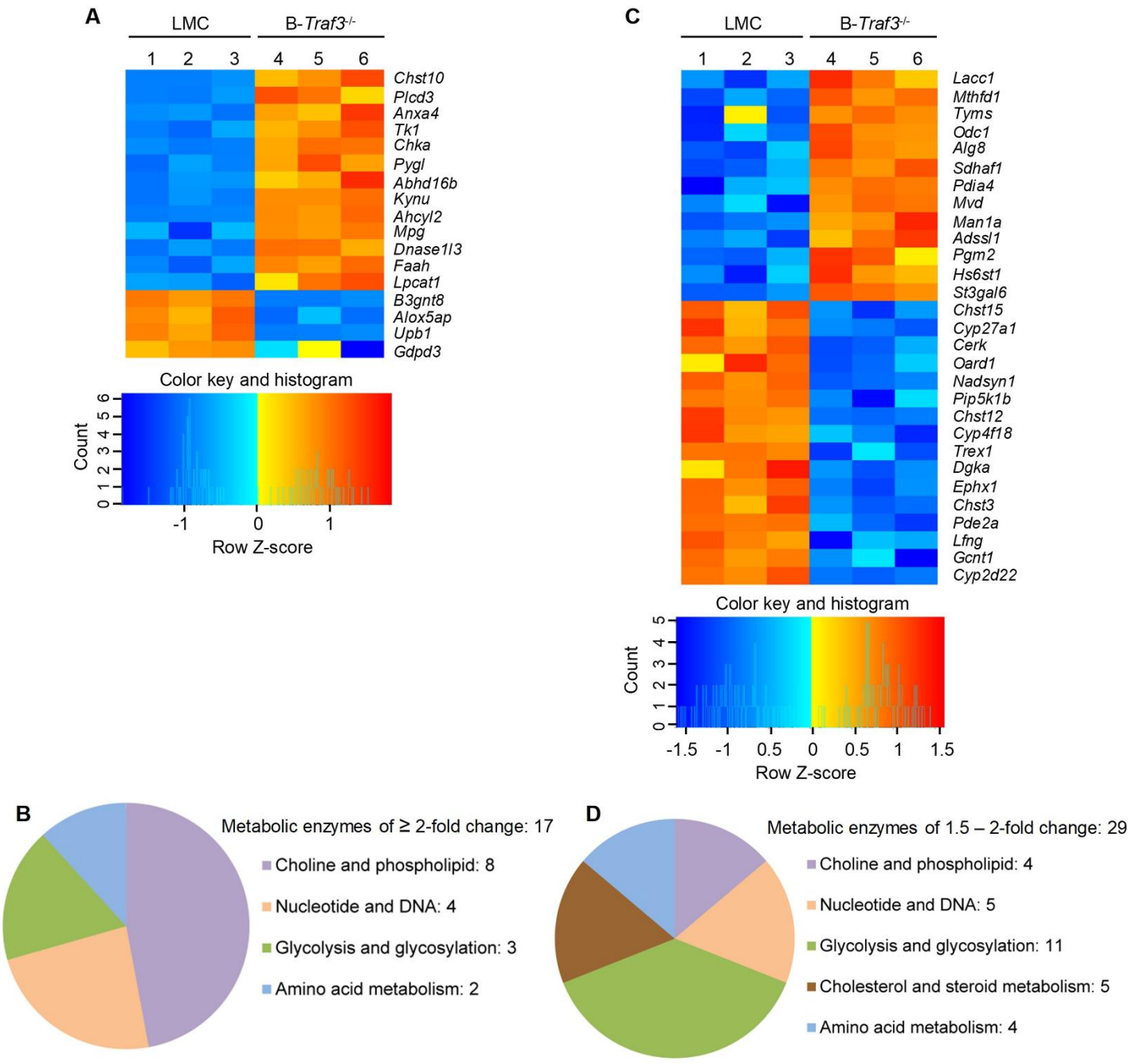


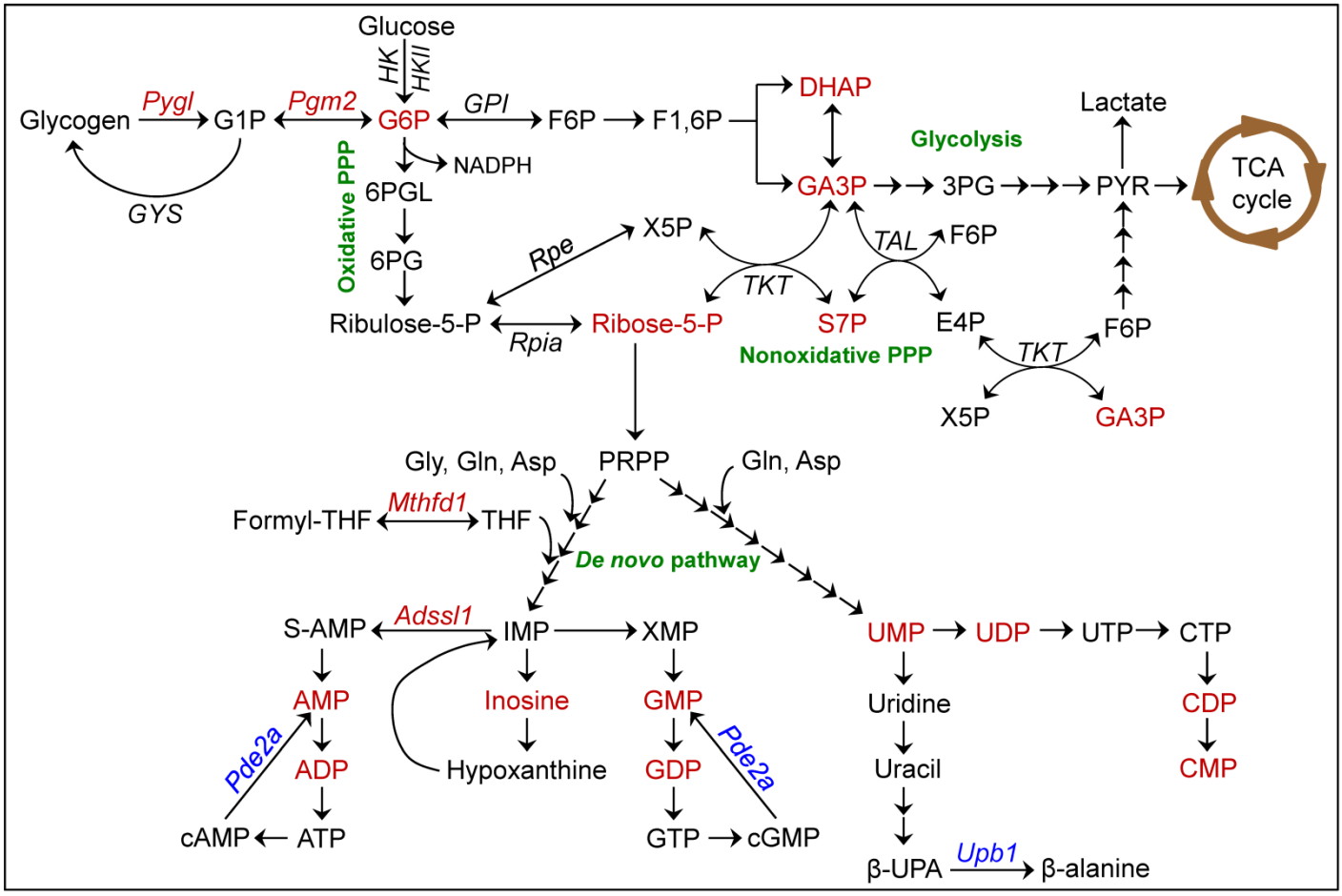
Supplementary Figure 1. Metabolomic screening of splenic B cells by LC-MS. Splenic B cells were purified from gender-matched, young adult (8-12-week-old) LMC and B-*Traf3*$^{-/-}$ mice. Water-soluble polar metabolites were extracted from cells directly *ex vivo* (day 0) or after cultured *in vitro* in mouse B cell medium for 1 day, and then analyzed by LC-MS. Totally, 107 metabolites were detected in resting splenic B cells. (**A**) Numbers of metabolites that were not changed or up-regulated in *Traf3*$^{-/-}$ B cells. (**B**) Distribution of the metabolites that were significantly increased in *Traf3*$^{-/-}$ B cells. (**C**) The graphic results of glucose metabolic intermediates and ribonucleotides that were significantly increased in *Traf3*$^{-/-}$ B cells. The 4 NTP graphs are also included for comparison to the NMP and NDP data. (**D**) AEC index calculated based on the LC-MS data of ATP, ADP and AMP using the formula: AEC = ([ATP]+0.5[ADP])/([ATP]+[ADP]+[AMP]). (**E**) Cellular ATP concentration measured by a Luciferase-Luciferin-based ATP Determination Kit (Molecular Probes). Results shown are mean ± SD (n=6, including 3 female and 3 male samples for each genotype). *, significantly different (*t* test, $p < 0.05$); **, very significantly different (*t* test, $p < 0.01$); ***, highly significantly different (*t* test, $p < 0.001$); ns, not significantly different between LMC and *Traf3*$^{-/-}$ B cells (*t* test, $p \geq 0.05$).



Supplementary Figure 2. Lipidomic screening of splenic B cells by LC-MS. Splenic B cells were purified from gender-matched, young adult (8-12-week-old) LMC or B-*Traf3*$^{-/-}$ mice. Lipids were extracted from cells directly *ex vivo* (day 0) or after cultured *in vitro* for 1 day, and then analyzed by LC-MS. Totally, 169 lipid molecules were detected in resting splenic B cells. (**A**) Numbers of lipids that were not changed, up-regulated or down-regulated in *Traf3*$^{-/-}$ B cells. (**B**) Distribution of lipid molecules that were elevated (red) or decreased (blue) in *Traf3*$^{-/-}$ B cells. (**C**) The graphic results of PI, DAG, MAG and ceramide species that were significantly altered in *Traf3*$^{-/-}$ B cells. DAGs were detected as $NH4^+$ adducts and MAGs were detected as Na^+ adducts. Results shown are mean ± SD (n=6, including 3 female and 3 male samples for each genotype). *, significantly different (*t* test, $p < 0.05$); **, very significantly different (*t* test, $p < 0.01$); ***, highly significantly different (*t* test, $p < 0.001$); ns, not significantly different between LMC and *Traf3*$^{-/-}$ B cells (*t* test, $p \geq 0.05$).



Supplementary Figure 3. Transcriptomic screening of splenic B cells by microarray analysis. Total cellular RNA was prepared from splenic B cells purified from gender-matched, young adult LMC and B-*Traf3*$^{-/-}$ mice, and processed for the microarray analysis to identify genes differentially expressed between the two genotypes of B cells. (**A** and **B**) Heatmap representation (A) and functional clustering (B) of the 17 metabolic enzymes that were up- or down-regulated at least 2-fold in *Traf3*$^{-/-}$ B cells. (**C** and **D**) Heatmap representation (C) and functional clustering (D) of additional 29 metabolic enzymes identified by the microarray analysis that were up- or down-regulated by 1.5 to 2-fold in *Traf3*$^{-/-}$ B cells.



Supplementary Figure 4. Pathway schematics depicting TRAF3-mediated regulation of glucose and ribonucleotide metabolism in B cells. Enzymes are denoted in *Italic* font in the schematics. Glucose metabolic intermediates, ribonucleotides and metabolic enzymes that were regulated by TRAF3 are indicated in red (for those up-regulated in *Traf3*$^{-/-}$ B cells) or blue (for those down-regulated in *Traf3*$^{-/-}$ B cells). Abbreviations: G1P, glucose-1-phosphate; G6P, glucose-6-phosphate; F6P, fructose-6-phosphate; F1,6P, fructose-1,6-biphosphate; DHAP, dihydroxyacetone phosphate; GA3P, glyceraldehyde 3-phosphate, 3PG, 3-phosphoglycerate; PYR, pyruvate; TCA cycle, the tricarboxylic acid cycle or the Krebs cycle; NADPH, dihydronicotinamide-adenine dinucleotide phosphate; 6PGL, 6-phospho-D-glucono-1,5-lactone; 6PG, 6-phosphogluconate; Ribulose-5-P, ribulose-5-phosphate; Ribose-5-P, ribose-5-phosphate; X5P, xylulose-5-phosphate; E4P, erythrose-4-phosphate; S7P, sedoheptoluse-7-phosphate; PRPP, 5-phospho-alpha-D-ribose 1-diphosphate; PPP, pentose phosphate pathway; Formyl-THF, formyltetrahydrofolate; THF, tetrahydrofolate; S-AMP, adenylosuccinate; Gly, glycine; Gln, glutamine; Asp, aspartic acid; IMP, inosine monophosphate; AMP, adenosine monophosphate; XMP, xanthosine monophosphate; GMP, guanosine monophosphate; UMP, uridine monophosphate; CMP, cytidine monophosphate; ADP, adenosine diphosphate; GDP, guanosine diphosphate; UDP, uridine diphosphate; CDP, cytidine diphosphate; ATP, adenosine triphosphate; GTP, guanosine triphosphate; UTP, uridine triphosphate; CTP, cytidine triphosphate; β-UPA, β-ureidopropionate; cAMP, cyclic adenosine monophosphate; cGMP, cyclic guanosine monophosphate; Pygl, glycogen phosphorylase, liver form; Pgm2, phosphoglucomutase 2; GYS, glycogen synthase; GPI, glucose-6-phosphate isomerase; HK, hexokinase; HKII, hexokinase II; TKT, transketolase; TAL, transaldolase; RPE, D-ribulose-5-phosphate 3-epimerase; Rpia, ribose-5-phosphate isomerase A; Mthfd1, methylenetetrahydrofolate dehydrogenase 1; ADSSL1, adenylosuccinate synthase like 1; Upb1, β-ureidopropionase 1; Pde2a, cGMP-dependent 3',5'-cyclic phosphodiesterase 2A