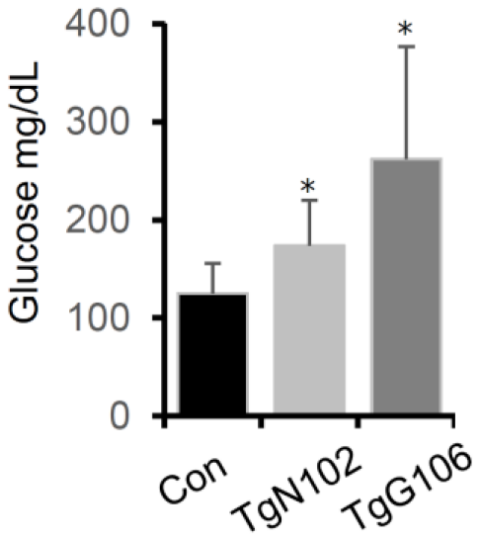
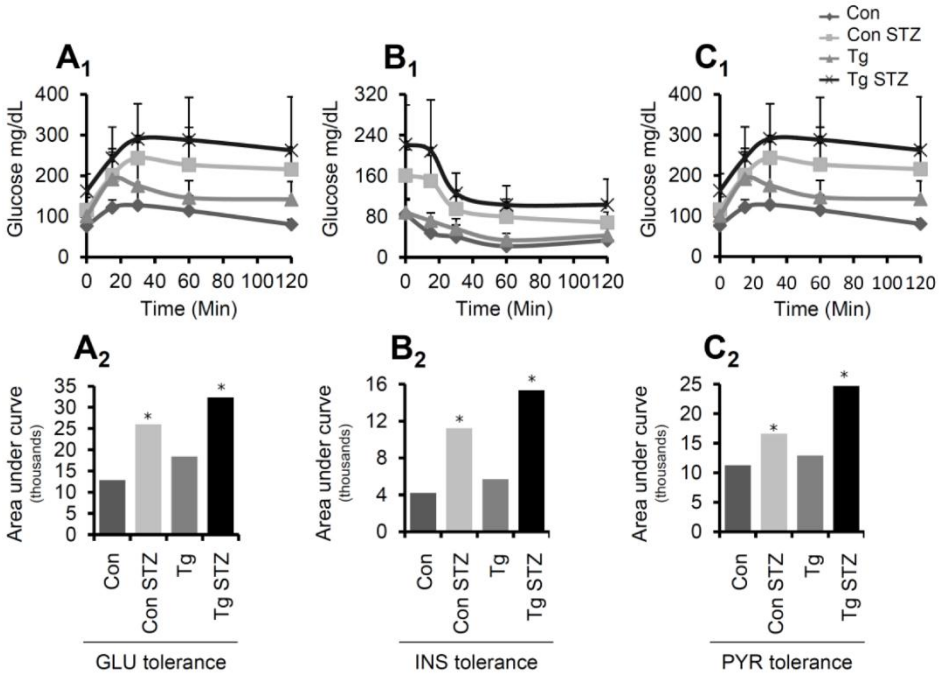
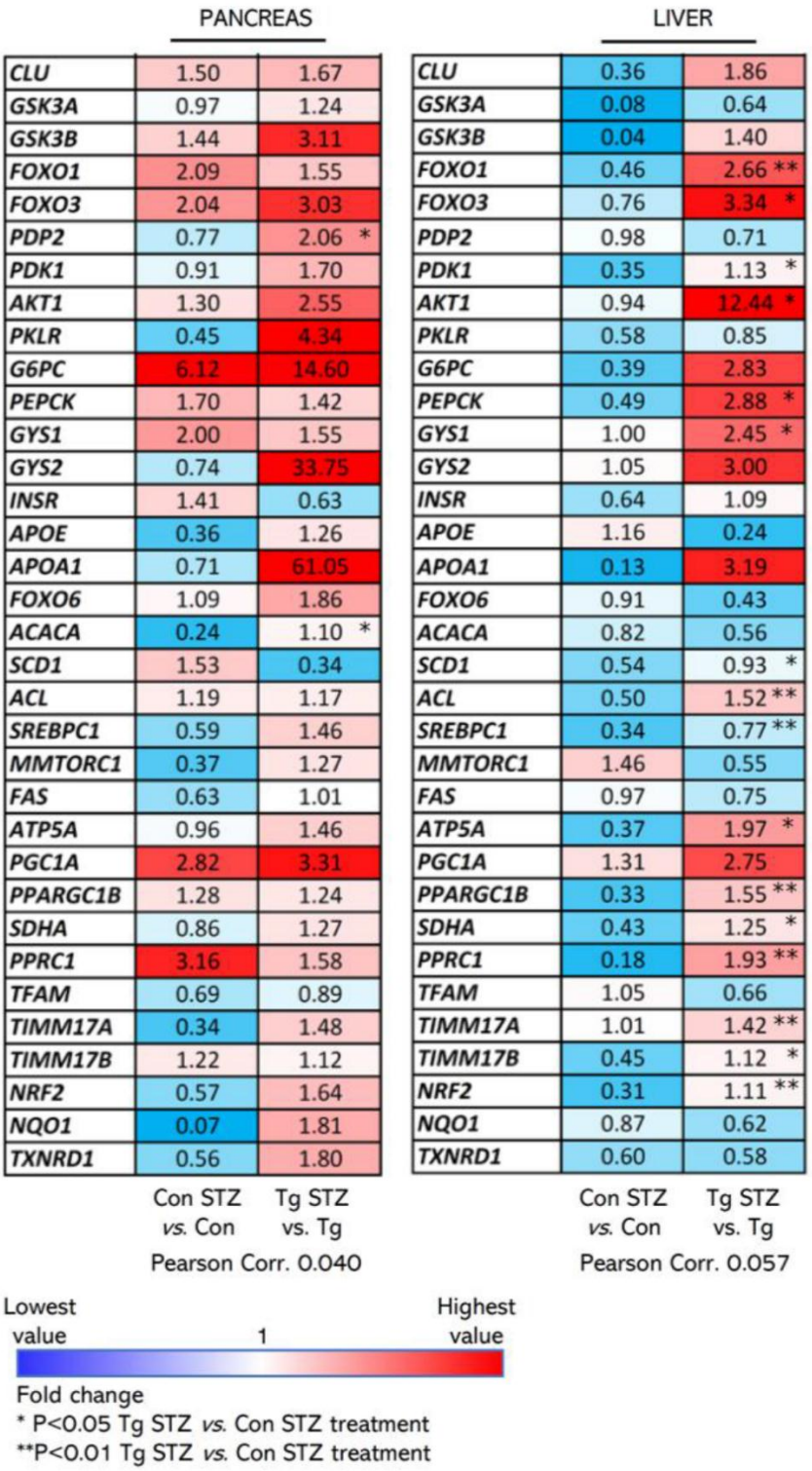
SUPPLEMENTARY FIGURES



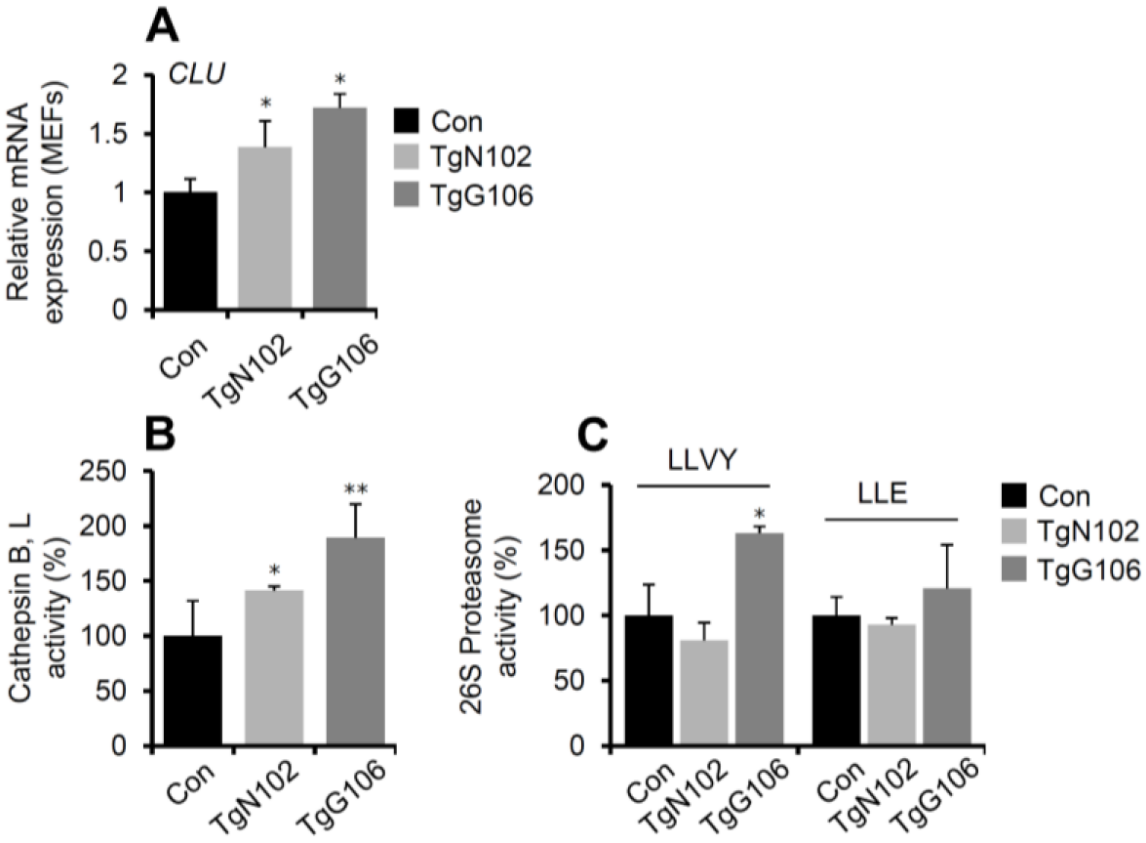
Supplementary Figure 1. Fasting GLU levels in control and CLU Tg (ubiquitous OE) male mice. GLU levels in control (littermate non-Tg) and CLU Tg male mice following fasting (n=4 per mouse genotype). Error bars, ± SD; *P<0.05.



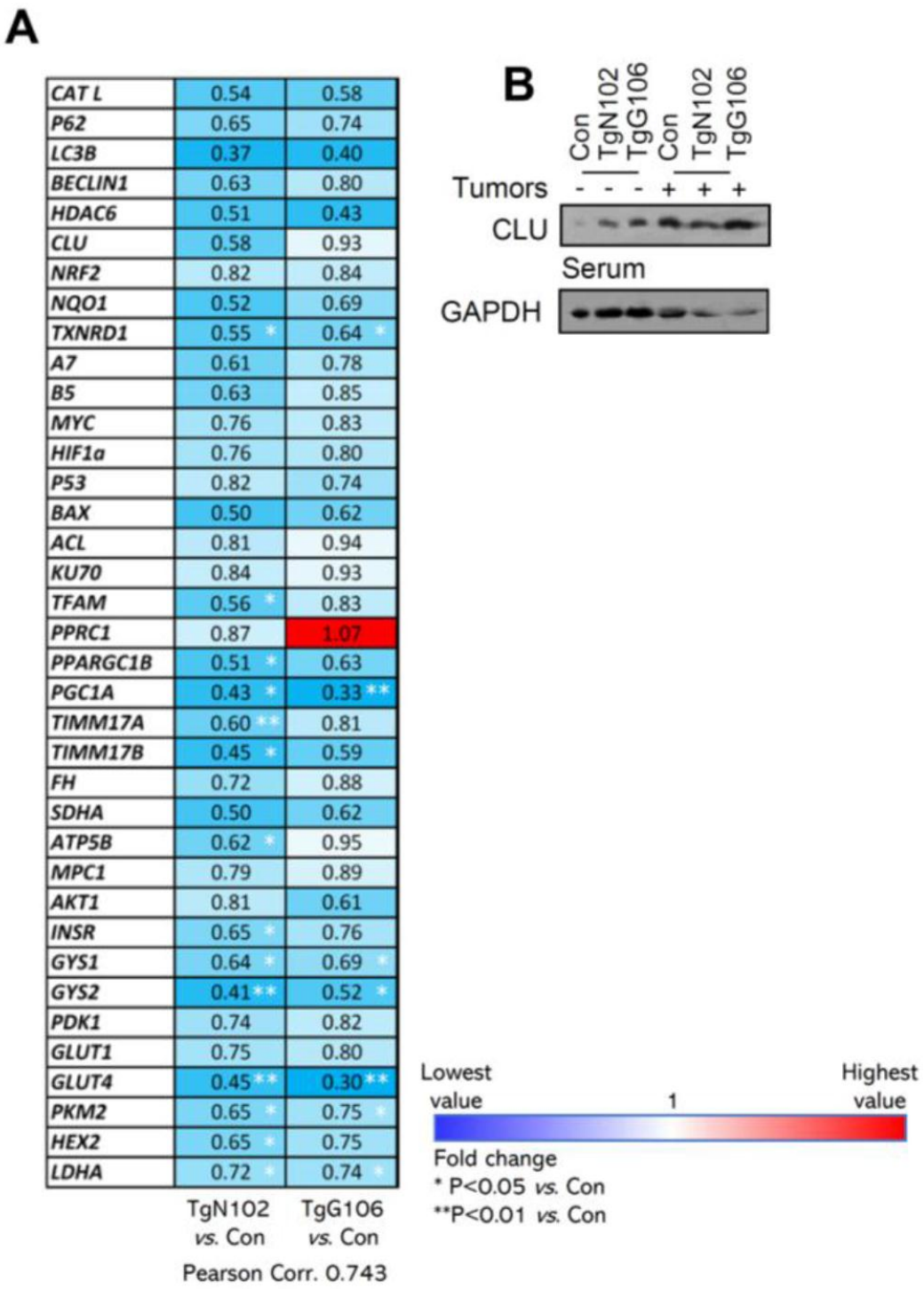
Supplementary Figure 2. GLU, INS and PYR decreased tolerance of CLU Tg (pancreas targeted OE) mice, is exacerbated in a model of STZ-mediated induction of diabetes. GLU levels (tolerance curves) in control (Con; littermate non-Tg) mice, control mice being treated with STZ (Con STZ), CLU overexpressing (Tg; pancreas-targeted) mice and CLU overexpressing mice being treated with STZ (Tg STZ). Mice were administered GLU ($\mathbf{A_1}$), INS ($\mathbf{B_1}$) or PYR ($\mathbf{C_1}$); GLU levels were measured before GLU, INS, PYR injection (see, Materials and Methods) and 15, 30, 60 and 120 minutes after. ($\mathbf{A_2}$–$\mathbf{C_2}$) Areas under respective curves ($\mathbf{A_1}$–$\mathbf{C_1}$) being calculated from the sum of the different trapeziums formed (errors bars are shown in curves). (n=5 per mouse genotype). Error bars, ± SD; *P<0.05.



Supplementary Figure 3. Expression levels (heat map) of antioxidant, mitochondrial and metabolic genes in the pancreas and liver of control or CLU Tg (pancreas-targeted OE) mice (*vs*. non STZ treated animals) after STZ administration-mediated induction of diabetes. Heat map indicating relative expression levels of shown genes following STZ treatment in control (Con; littermate non-Tg) or TgI173, TgI178 mice; differential responses among the different animal groups are also evident by shown Pearson Correlation (*r*) values (Con *vs*. Tg columns). The different groups of animals tested are control (Con; littermate non-Tg) mice, control mice being administered STZ (Con STZ), CLU overexpressing mice (Tg; pancreas-targeted) and CLU overexpressing mice being administered STZ (Tg STZ) (n=5 per mouse genotype). **P*<0.05; ***P*<0.01 (Tg STZ *vs*. Con STZ treatment).



Supplementary Figure 4. CLU OE upregulates proteostatic modules in MEFs derived from TgN102 or TgG106 (ubiquitous OE) mice. (**A**) Relative *clu* mRNA expression levels in control (Con; littermate non-Tg), TgN102 and TgG106 mice derived MEFs. (**B**) Relative (%) cathepsin B, L enzymatic activities in control, TgN102 and TgG106 MEFs. (**C**) Relative (%) proteasome enzymatic activities in control, TgN102 and TgG106 MEFs. Error bars, ± SD (n=2-4 per mouse genotype); **P*<0.05; ***P*<0.01.



Supplementary Figure 5. Differential (*vs*. controls) gene expression levels (along with CLU serum levels in Tg mice) in melanoma tumors grafted in TgN102 and TgG106 (ubiquitous OE) mice. (**A**) Heat map indicating relative expression levels (*vs*. Con; littermate non-Tg) of shown autophagic, proteasome, antioxidant, mitochondrial and metabolic genes in melanoma cells-derived tumors grafted in TgN102 or TgG106 mice (n=6 per mouse genotype); similar genomic responses in Tg mice are also evident by shown Pearson Correlation (*r*) values (TgN102 *vs*. TgG106). (**B**) CLU protein levels in the serum of shown mice bearing (or not) melanoma cells-derived tumors (n=6 per mouse genotype). GAPDH probing (tissue lysate) was used as a reference. In (A), **P*<0.05; ***P*<0.01 (Tg *vs*. Con).