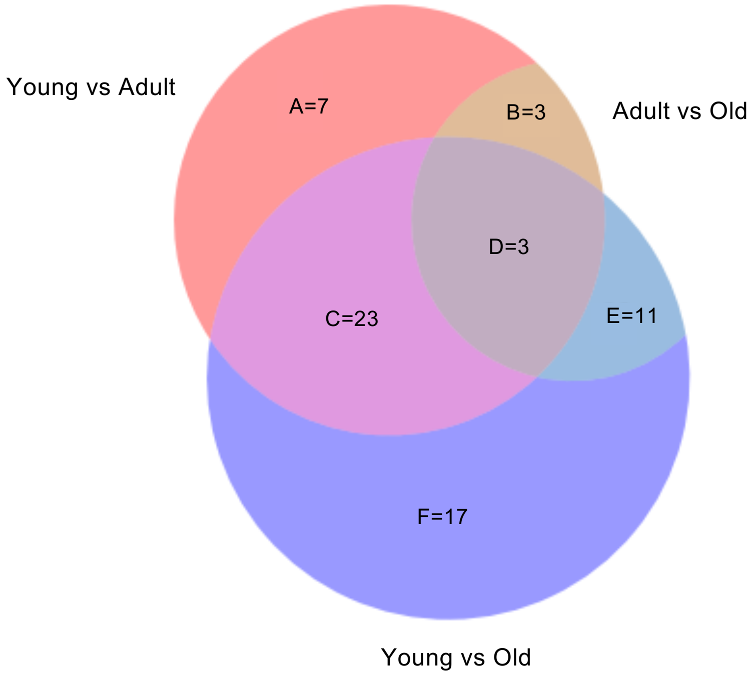
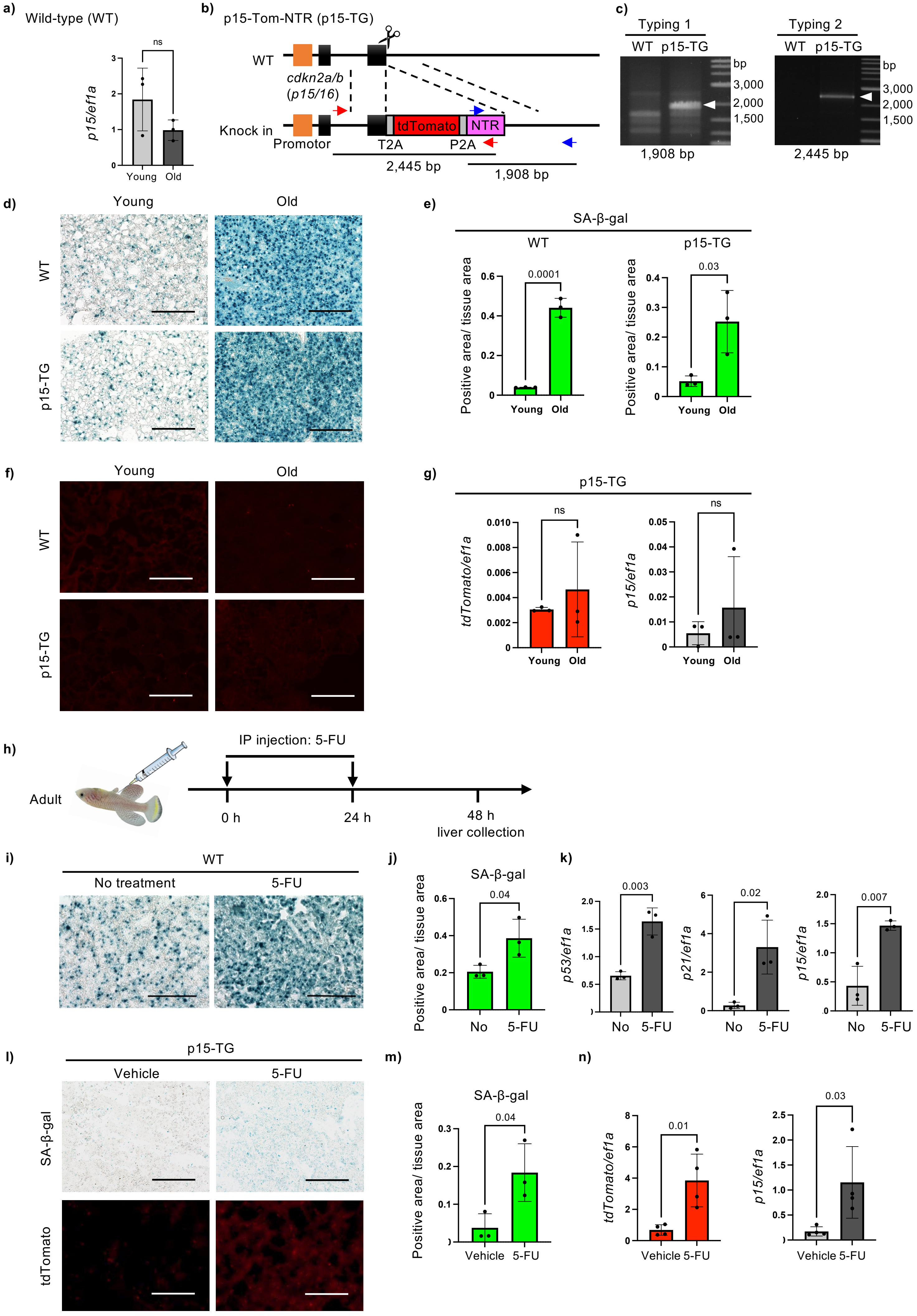


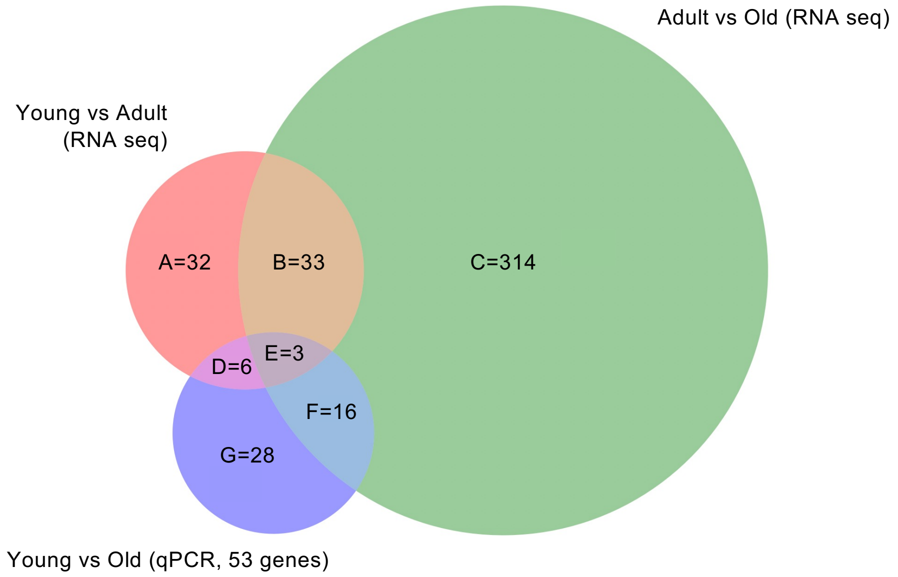
Supplementary Fig. 1 Chen *et al*.

Supplementary Fig. 2 Chen *et al*.

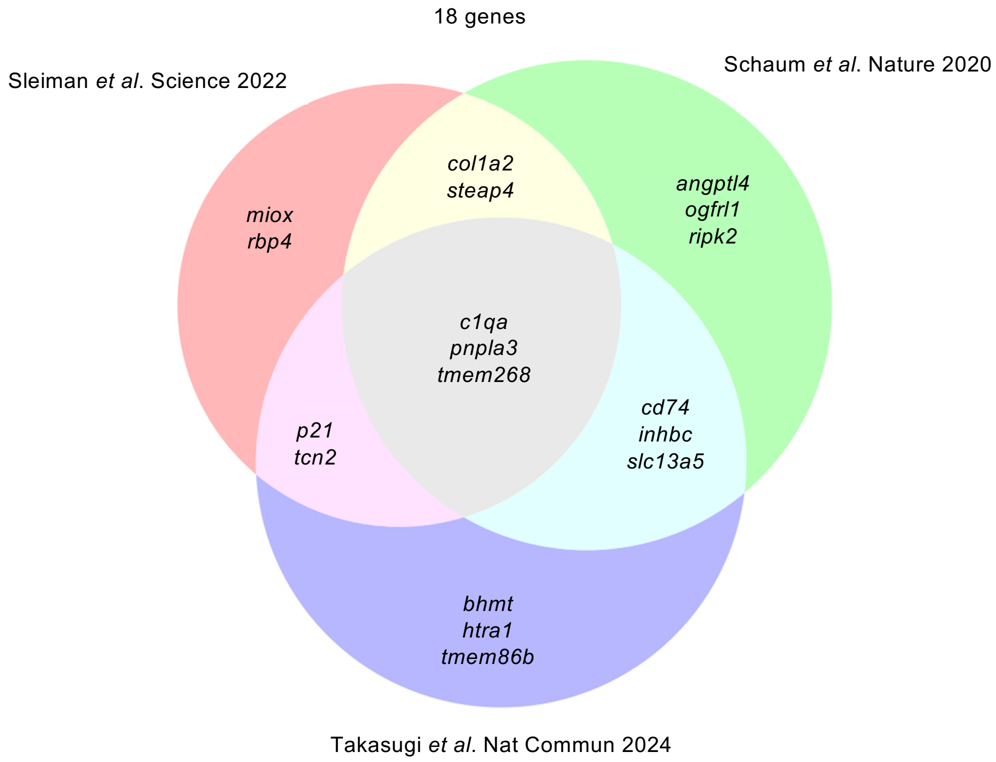


Supplementary Fig. 3 Chen *et al.*

a)



b)



Supplementary Fig. 4 Chen *et al*.

Supplementary Figure 1. Commonality in altered metabolites in *N. furzeri* livers.

Venn diagram of metabolites whose levels changed significantly between the two indicated stages.

Supplementary Figure 2. Transcriptomic analysis in *N. furzeri* livers.

qPCR analysis of 53 differentially expressed genes in young (6 weeks old) and old (24 to 25 weeks old) livers. Data were normalized to *ef1a* levels. Data are mean±SD. Two-tailed unpaired Student's *t*-test was performed.

Supplementary Figure 3. p15 is a stress-response marker but not an aging change or senescence marker in *N. furzeri*.

a) qPCR analysis of *p15* expression of the liver of young (6 weeks old) and old (24 weeks old) *N. furzeri*. Data were normalized to *ef1a* levels. Data are mean±SD. Two-tailed unpaired Student's *t*-test was performed. **b)** Gene targeting of p15-TG-transgenic fish. **c)** Genotyping results of transgenic fish. **d)** SA-β-gal staining of young (6 weeks old) and old (18 weeks old) WT and p15-TG livers. Scale bar: 50 µm. **e)** Quantification of d). Data are mean±SD. Two-tailed unpaired Student's *t*-test was performed. **f)** Fluorescence of tdTomato in young (6 weeks old) and old (18 weeks old) WT and p15-TG livers. Scale bar: 50 µm. **g)** qPCR analysis of gene expression in young (6 weeks old) and old (24 weeks old) WT and p15-TG livers. Data were normalized to *ef1a* levels. Data are mean±SD. Two-tailed unpaired Student's *t*-test was performed. **h)** Experimental design of 5-FU treatment. **i)** SA-β-gal staining of the 12-week-old no treatment (No) or 5-FU-injected (5-FU) livers. Scale bar: 50 µm. **j)** Quantification of i). Data are mean±SD. Two-tailed unpaired Student's *t*-test was performed. **k)** qPCR analysis of gene expression in no treatment or 5-FU-injected livers. Data were normalized to *ef1a* levels. Data are mean±SD. Two-tailed unpaired Student's *t*-test was performed. **l)** SA-β-gal staining of the liver and fluorescence of tdTomato in the 13-14-week-old vehicle or 5-FU-injected p15-TG livers. Scale bar: 50 µm. **m)** Quantification of SA-β-gal-positive signals of l). Data are mean±SD. Two-tailed unpaired Student's *t*-test was performed. **n)** qPCR analysis of expression of the *tdTomato* gene and the *p15* gene in vehicle or 5-FU-injected livers. Data were normalized to *ef1a* levels. Data are mean±SD. Two-tailed unpaired Student's *t*-test was performed. Each group contains 3 biologically independent samples.

Supplementary Figure 4. Commonality in altered expression of genes between *N. furzeri* and mice.

a) Venn diagram of metabolites whose levels changed significantly between the two indicated stages. **b)** Venn diagram of genes whose levels changed significantly between mice and fish.

Supplementary Table 1: Raw data of the metabolomic analysis.

Supplementary Table 2: Metabolites whose levels were significantly changed.

Supplementary Table 3: Metabolites belonging to each part of the Venn diagram related to Supplementary Fig.1.

Supplementary Table 4: 10,947 genes used for RNA-seq analysis.

Supplementary Table 5: 231 Genes whose levels were significantly changed between Young and Old.

Supplementary Table 6: 154 genes with human's orthologs.

Supplementary Table 7: 53 genes whose expression changes were confirmed by qPCR.

Supplementary Table 8: Gene list which was used for Venn diagram analysis derived from RNA-seq.

Supplementary Table 9: Genes belonging to each part of the Venn diagram related to Supplementary Fig.4a