Figure s1

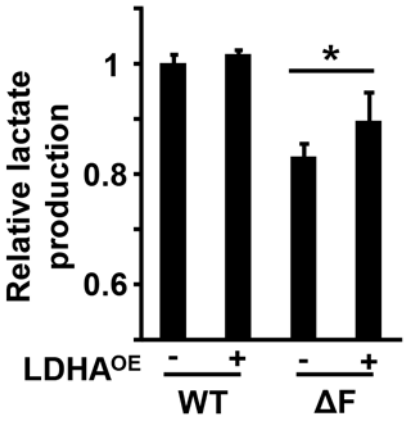

Fig. S1. Overexpression of LDHA partially restores lactate production in MEF$^{\Delta F}$ cells.

Relative lactate production. Data represent mean and standard deviation from triplicate samples. WT, wildtype MEF; ΔF, MEF$^{\Delta F}$; LDHA^{OE}, LDHA overexpression; *, P<0.05.

Figure s2

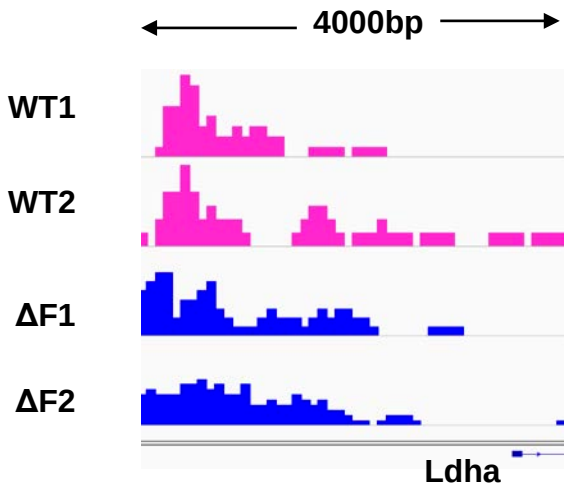

Fig. S2. Ablation of FGF signaling does not affect DNA methylation in the *Ldha* promoter. The same high-throughput sequencing of immunoprecipitated DNA as in Fig. 3 was analyzed and the level of methylation at CpG islands in the *Ldha* promoter region is shown. WT, wildtype MEF; ΔF, MEF$^{\Delta F}$.

Figure s3

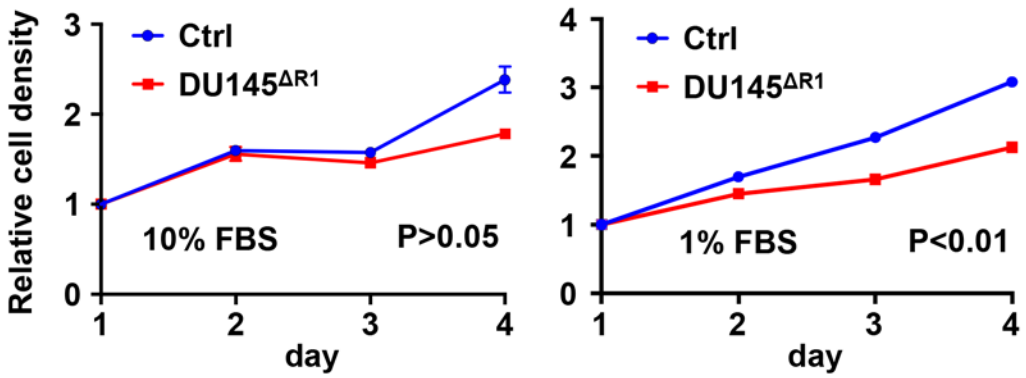

Fig. S3. Effect of Fgfr1 ablation on the growth of DU145 cells. DU145 cells (1.0 x 10^3 per well) were seeded in 96 well plates in the DMEM medium with 10% or 1% FBS as indicated. The cell density was assessed daily after the inoculation with the CCK-8 kit as described in the Materials and Methods. No significant difference were observed in the 10% FBS group. However, in the 1% FBS group, control DU145 cells grew faster than $FGFR1^{null}$ DU145 cells. Ctrl, DU145 cells, ΔR1, $Fgfr1^{null}$ DU145 cells

Figure s4

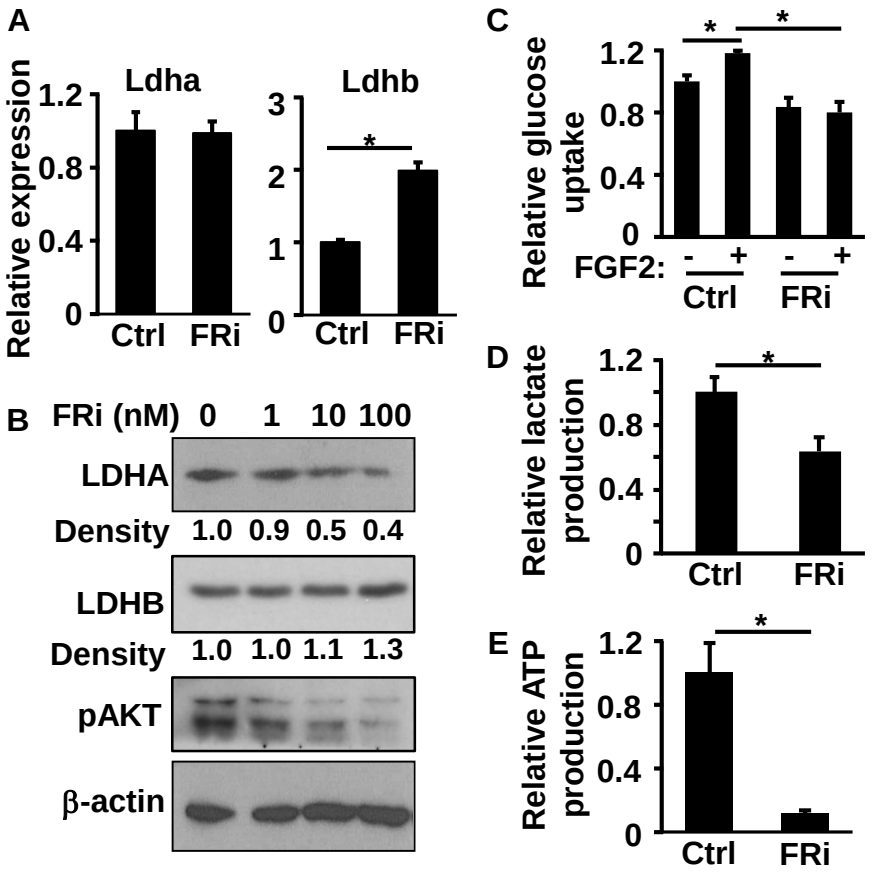

Fig. S4. Inhibition of FGF signaling suppresses aerobic glycolysis in DU145 cells. **A.** DU145 cells were treated with 100 nM AZD4547 for 24 hours and the expression of LDH mRNA was analyzed by Real-time RT-PCR. **B.** DU145 cells were treated with the indication concentration of AZD4547 for 24 hours and expression of LDH isoforms were analyzed with western blot analyses. **C-E.** DU145 cells were treated AZD4547 for 24 hours and the glucose uptake (**C**), lactate production (**D**), and ATP production (**E**) were measured. Ctrl, solvent only; FRi, FGFR inhibitor AZD4547.

Figure s5

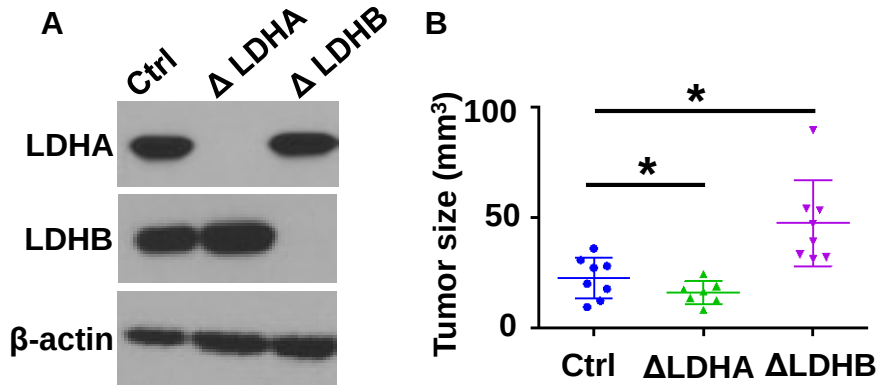

Fig. S5. LDHA ablation reduces, and LDHB ablation enhances, the tumorigenicity of PC3 cells. A, Western blot of the expression of LDHA and LDHB. **B.** Xenografts derived from control PC3, PC3$^{\Delta Ldha}$, or PC3$^{\Delta Ldhb}$ cells. The sizes of the xenografts were measured two weeks after the inoculation. The average xenograft size was calculated from all individual xenografts and is presented as mean $\pm$ sd. ΔLDHA, PC3$^{\Delta Ldha}$; ΔLDHB, PC3$^{\Delta Ldhb}$; Ctrl, control PC3 cells.

Figure s6

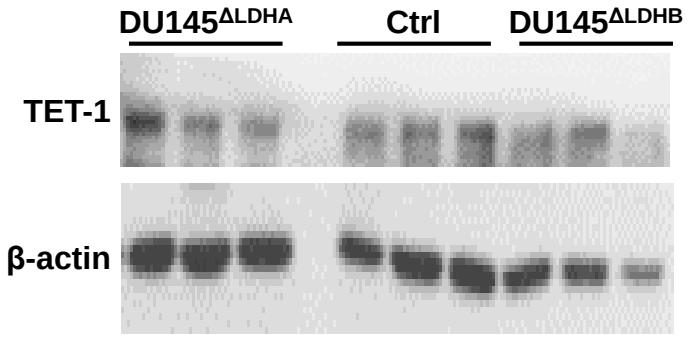

Fig. S6. Expression of TET1 in DU145$^{\Delta Ldha}$ and DU145$^{\Delta ldhb}$ xenografts. Western blot of the expression of TET1 in xenografts derived from the indicated DU145 cells. β-actin was used as loading controls; Ctrl, DU145 cells.

Figure s7

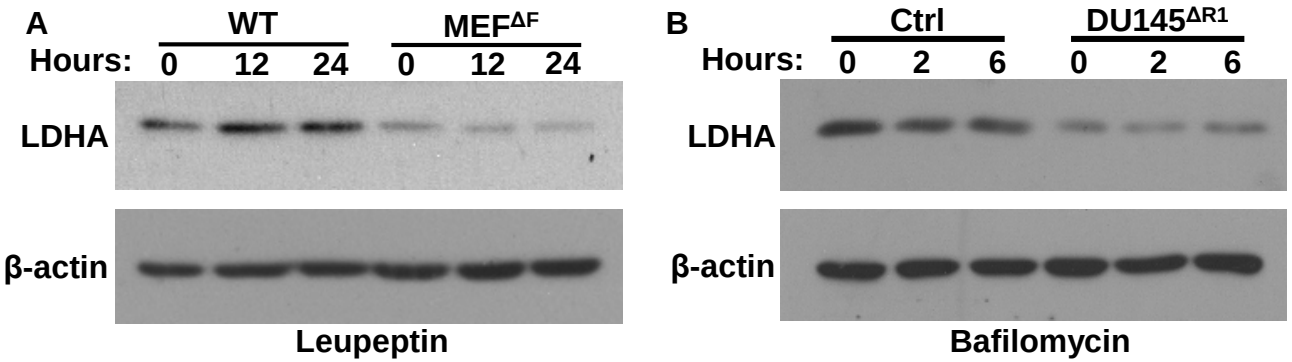

Fig. S7. Suppression of protease or autophagy does no change LDHA degradation in cells with or without FGFR1. MEF (**A**) or DU145 (**B**) cells were treated with leupeptin or bifilobyin, respectively for the indicated hours and the abundance of LDHA was assessed by western blot. β-actin was used as a loading control; WT, wildtype MEF; Ctrl, DU145 cells.

Figure s8

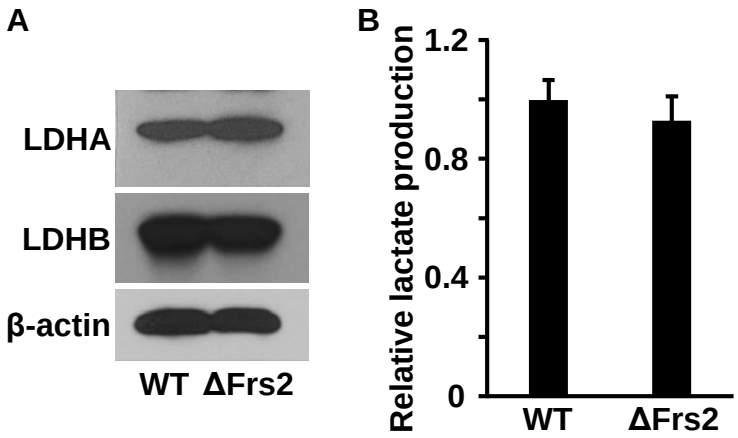

Fig. S8. *Frs2α* ablation does not affect LDH isoform expression and lactate production in MEFs. A, Western blot of LDHA and LDHB expression. **B.** Relative lactate production of the indicated MEF was measured as described in the Material and Method section. β-actin was used as loading controls. WT, wildtype MEF; ΔFrs2, $Frs2^{null}$ MEF.