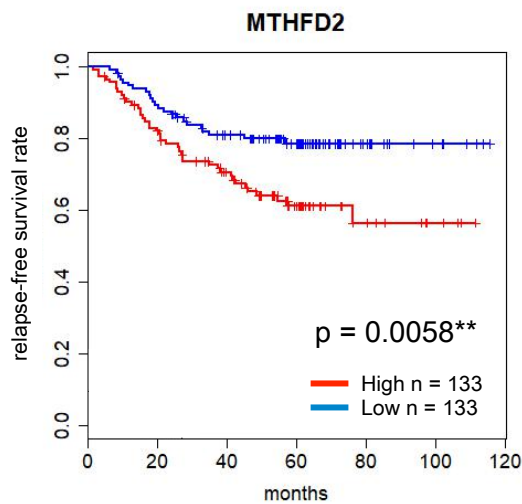
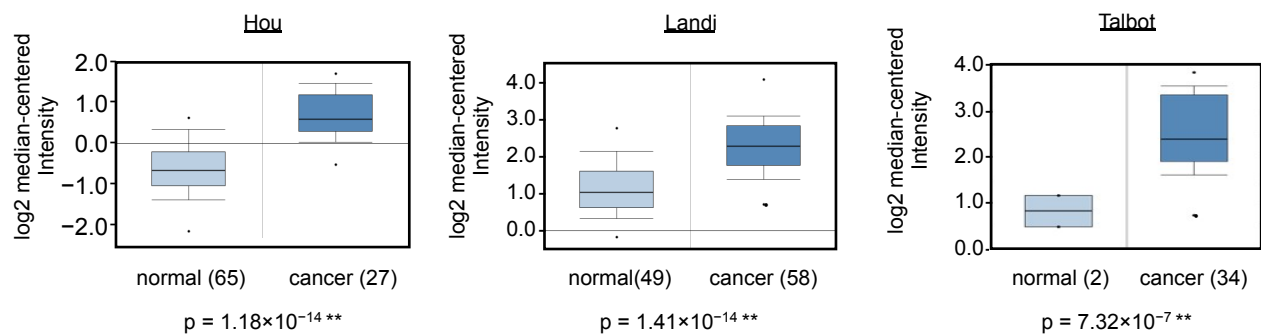


Supplementary Figure 1

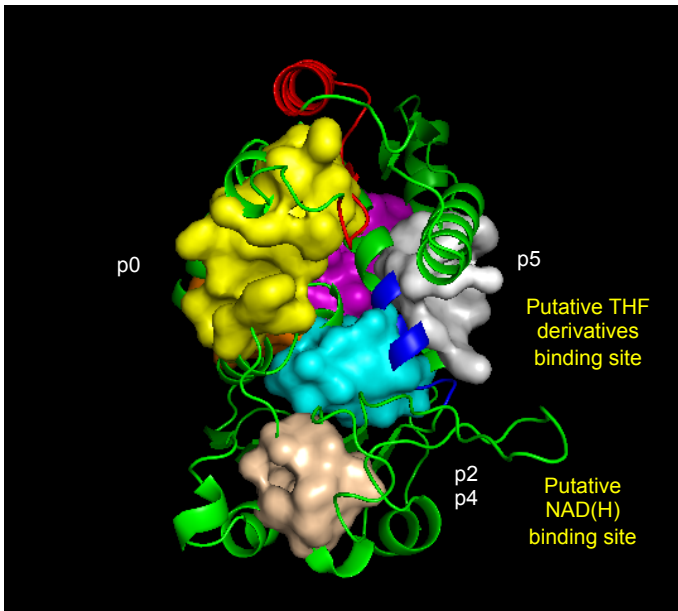
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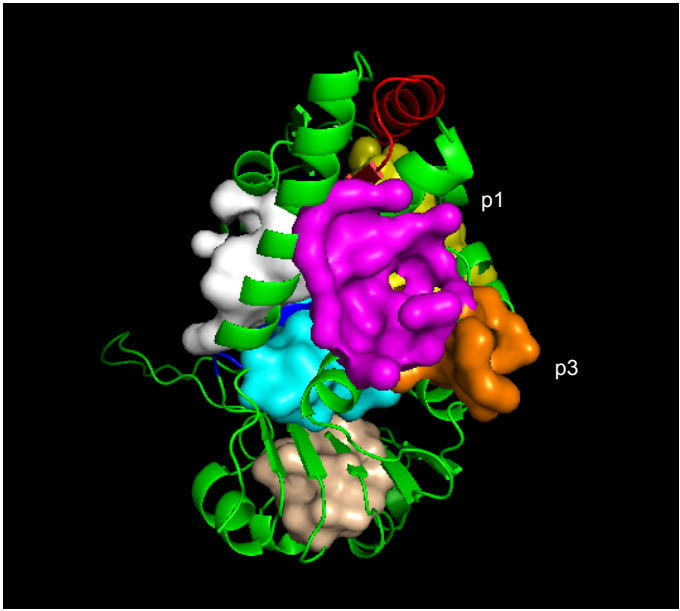
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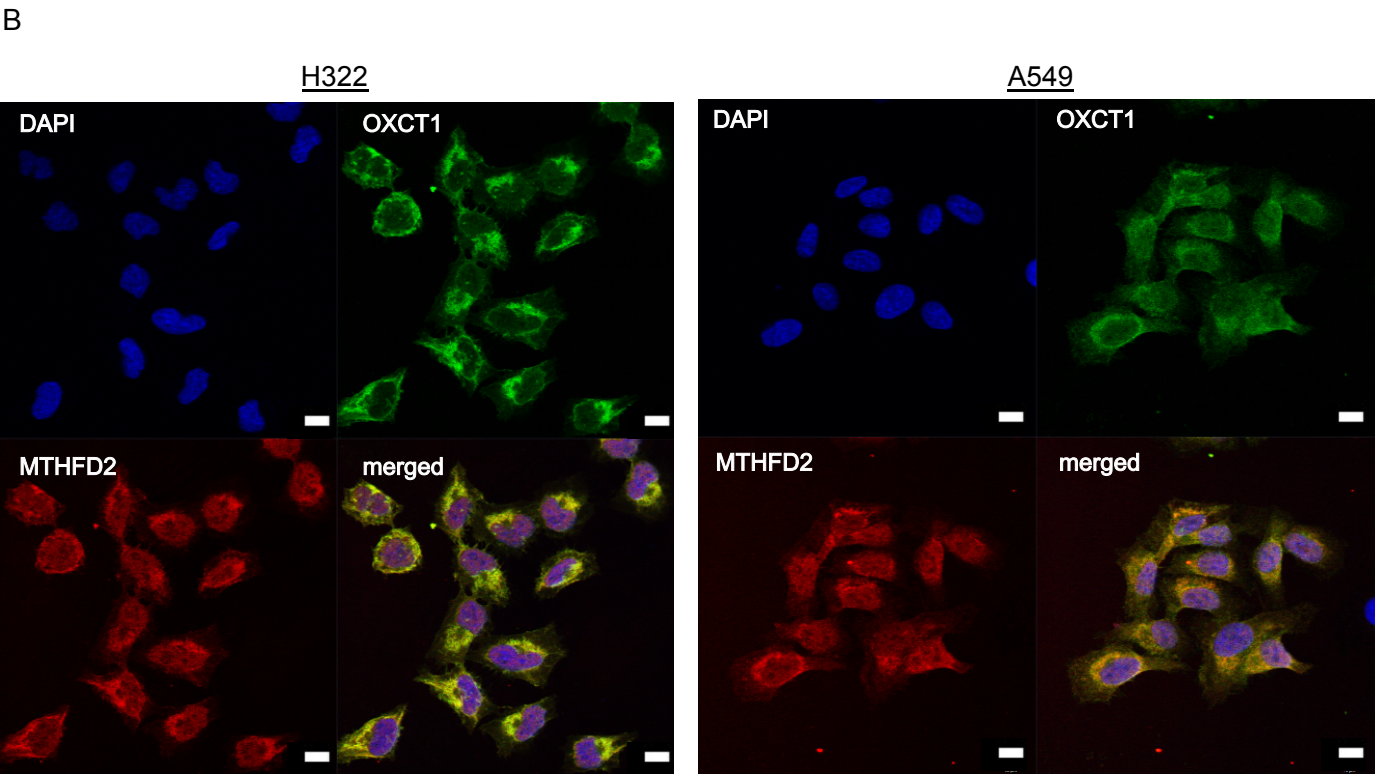
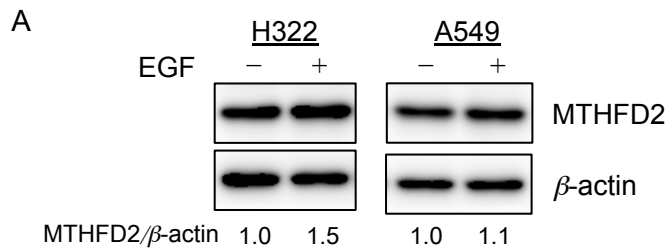
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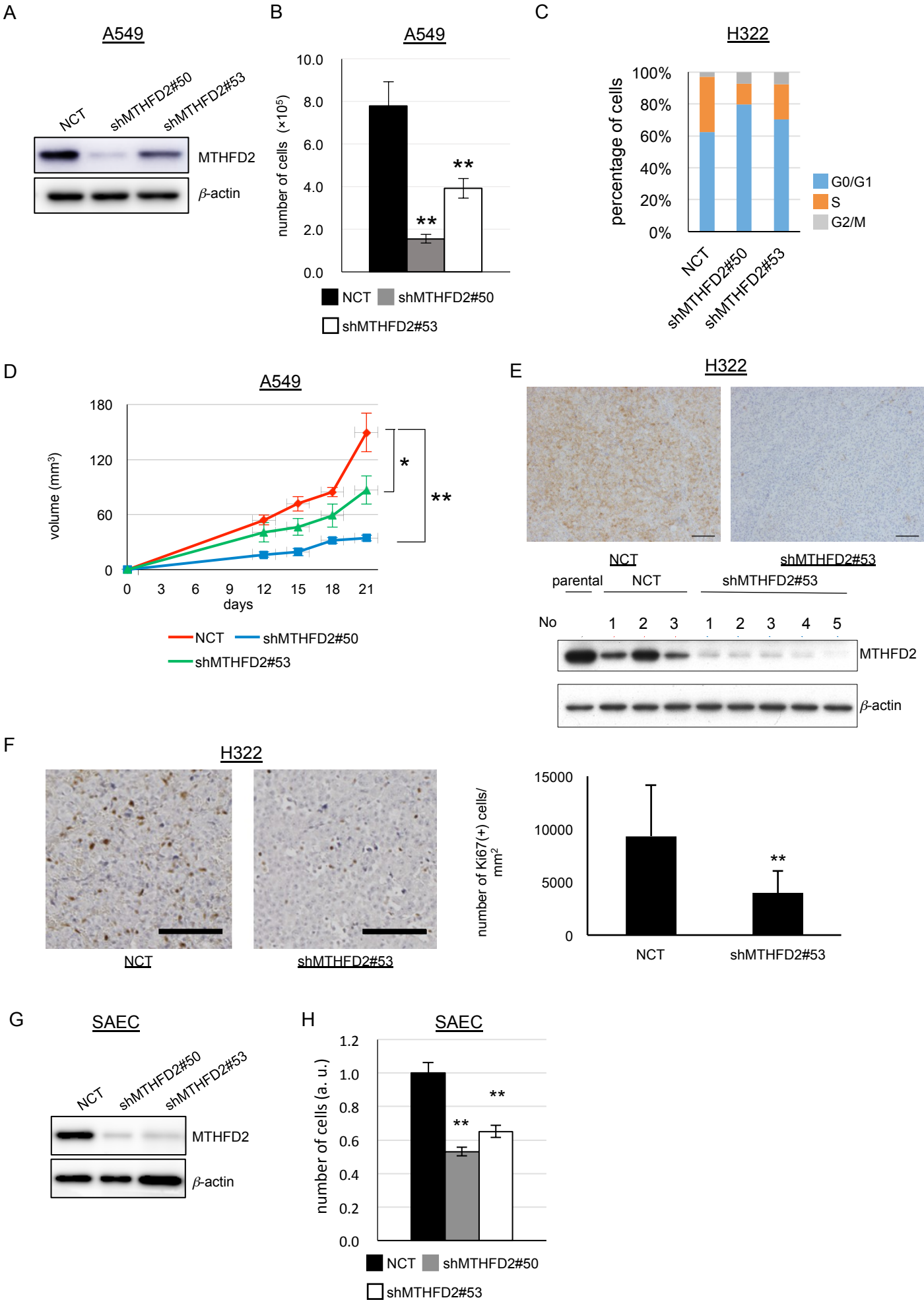
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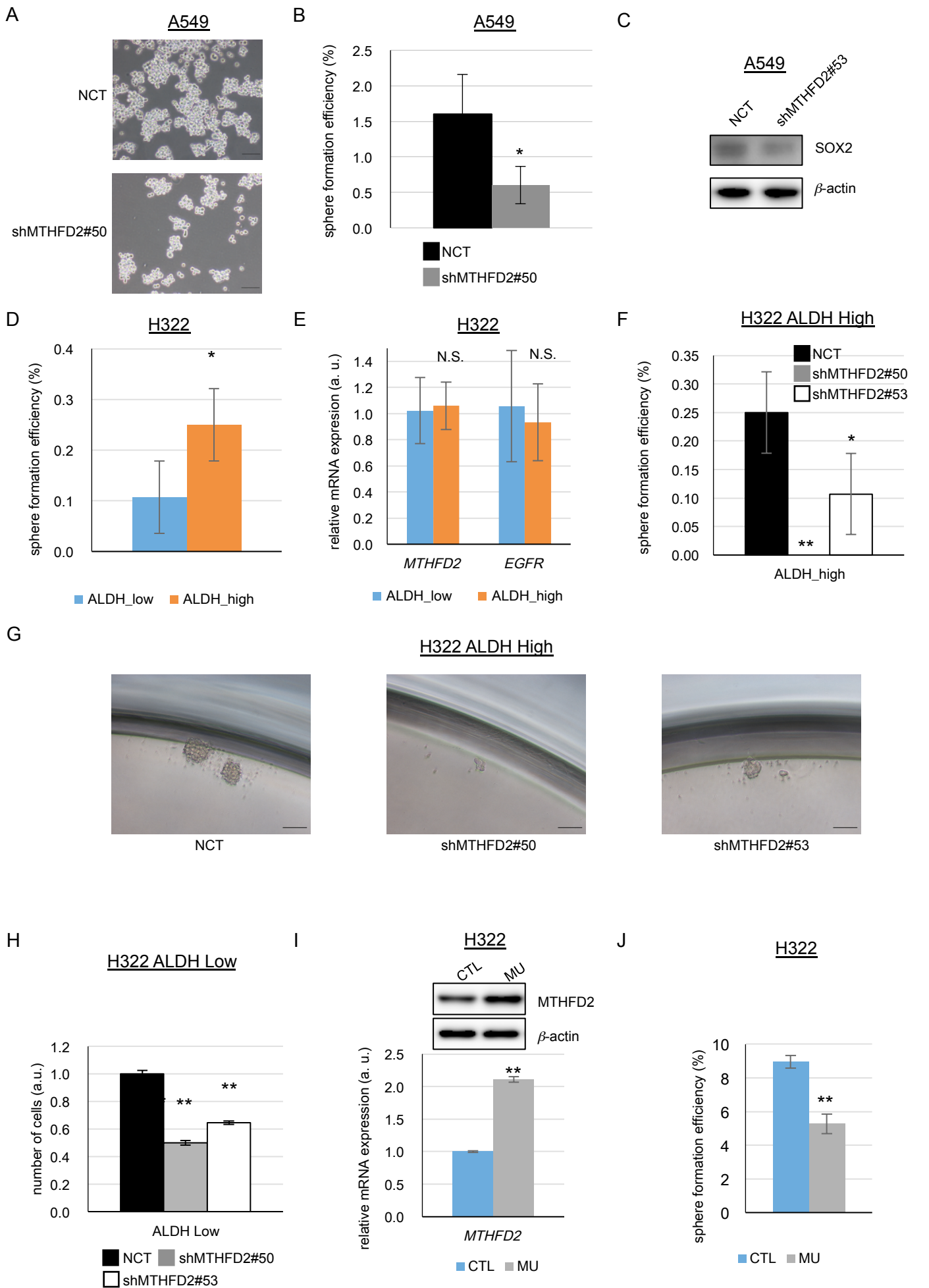
Supplementary Figure 2



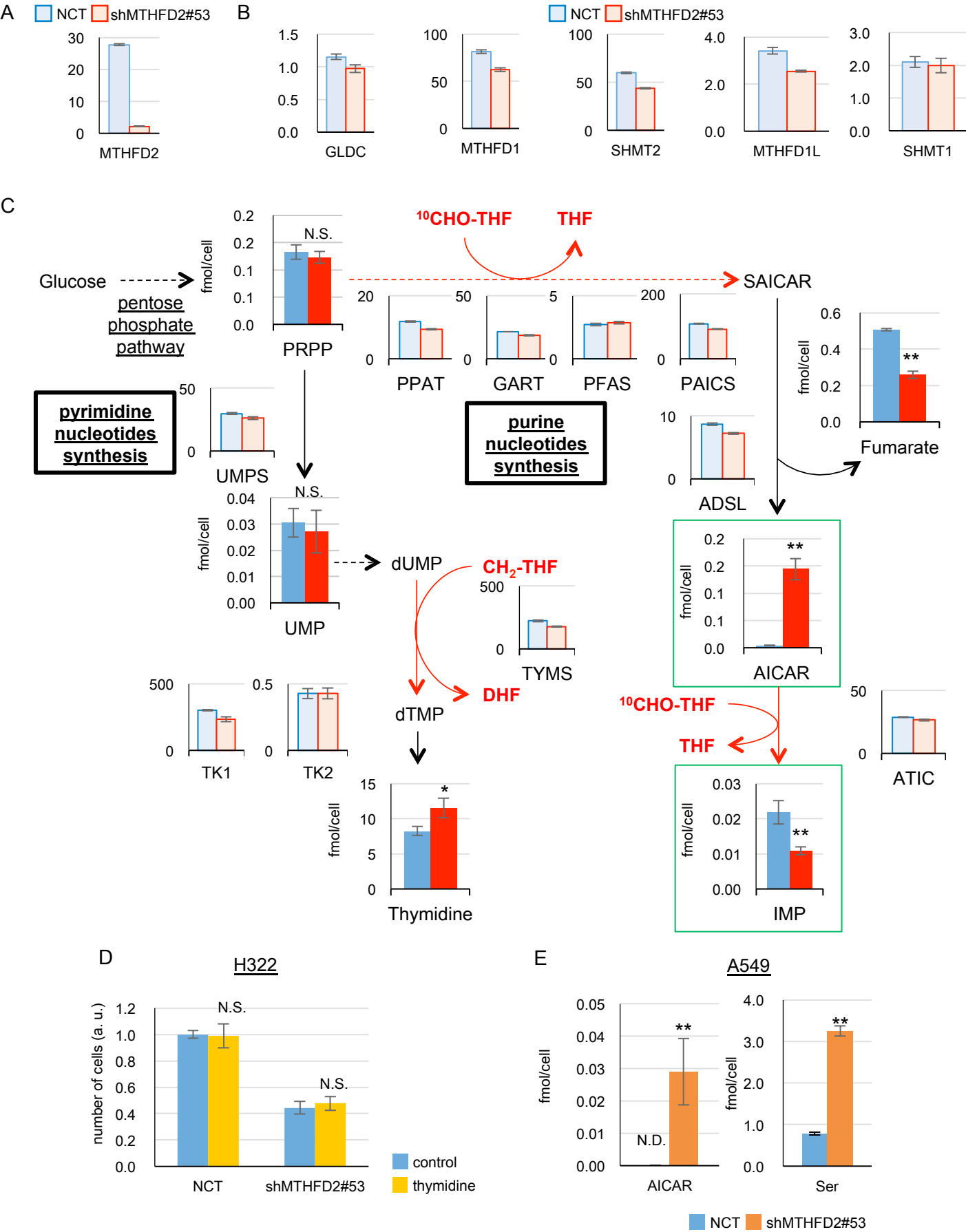
Supplementary Figure 3



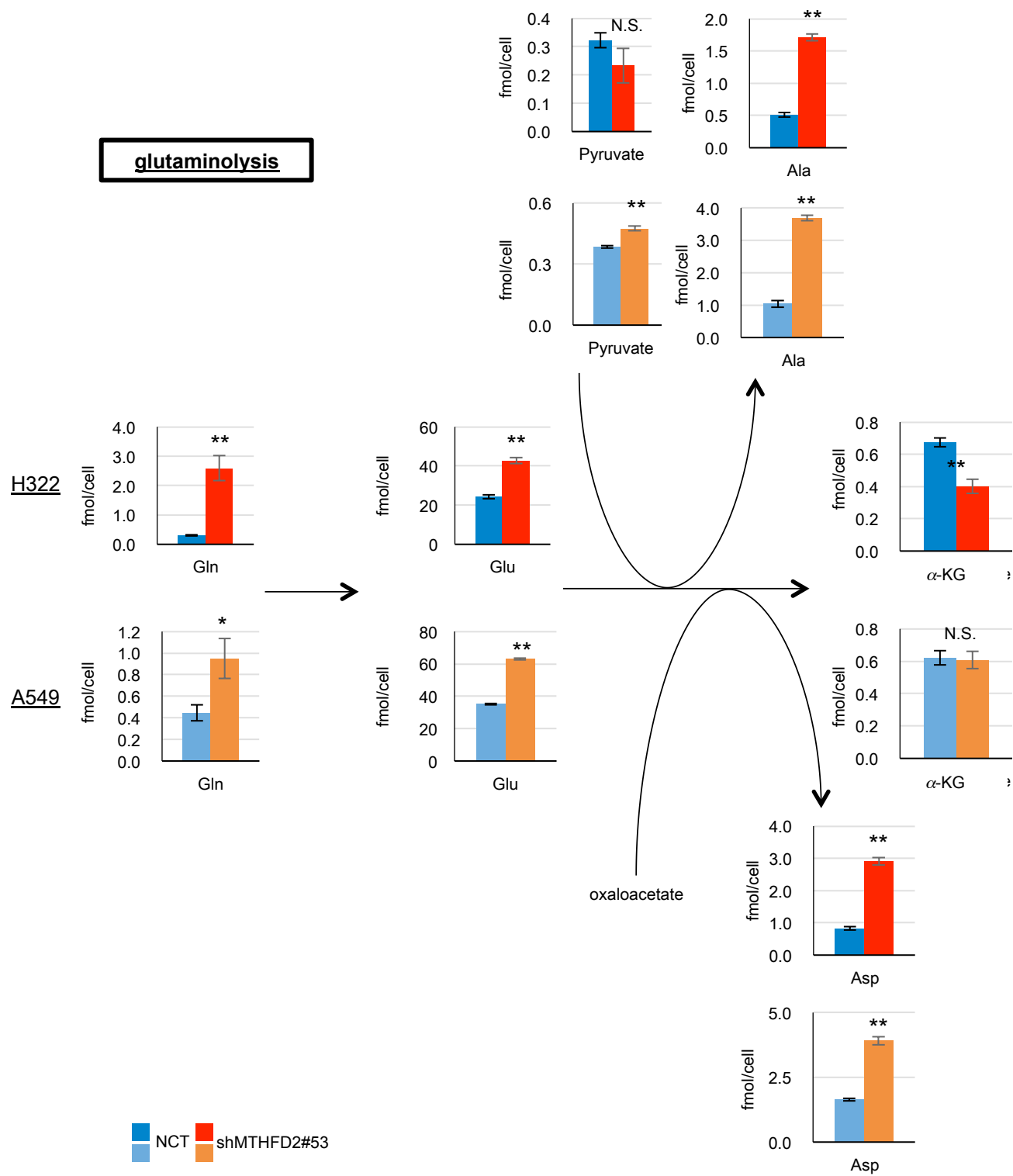
Supplementary Figure 4



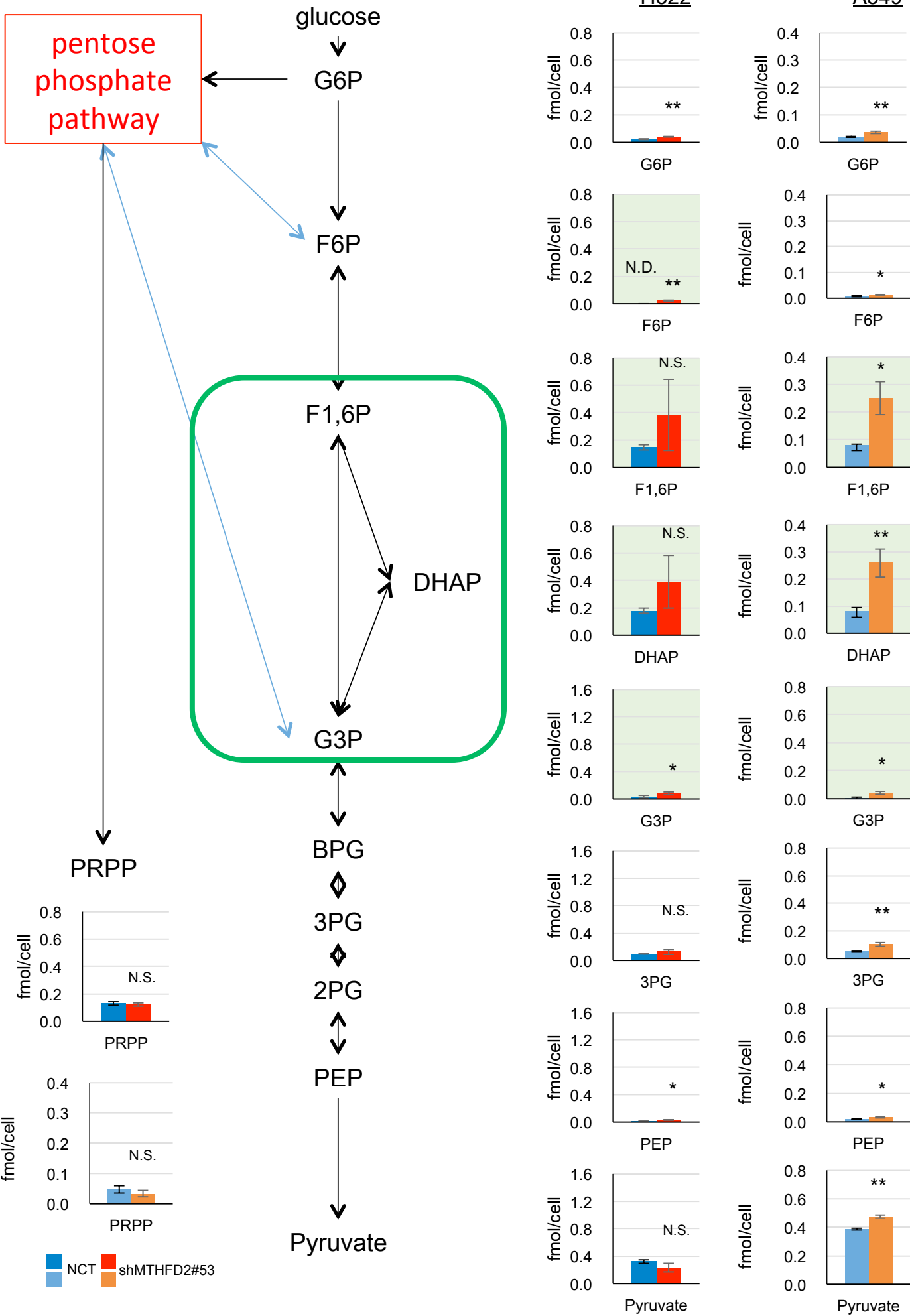
Supplementary Figure 5



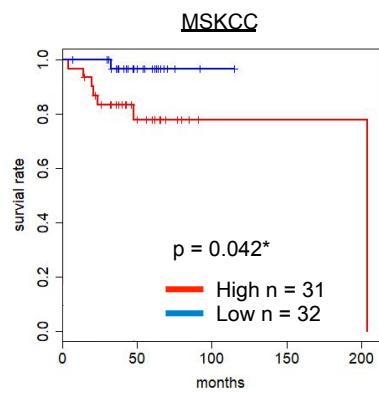
Supplementary Figure 6



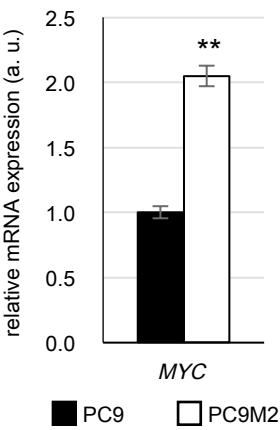
Supplementary Figure 7



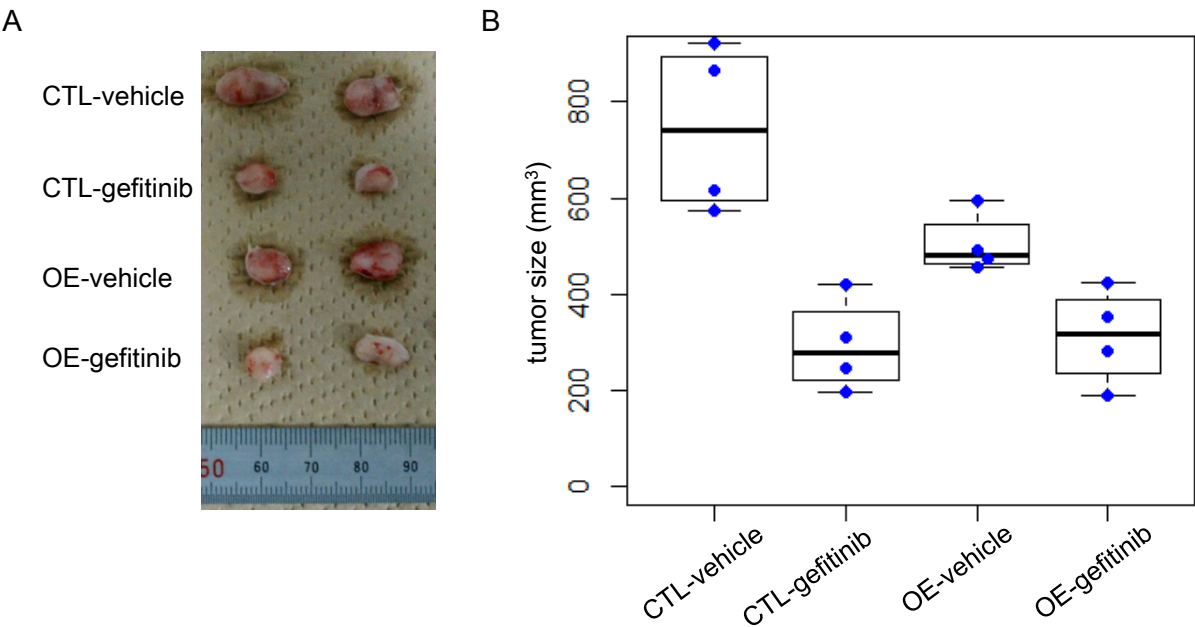
Supplementary Figure 8



Supplementary Figure 9



Supplementary Figure 10



Supplementary Table 1

Hazard ratios for overall survival (cox proportional hazard model)

Data set	Variable	Hazard ratio	95% confidence Interval	p value
NCC (n = 195)	Age	1.0	0.98-1.1	0.27
	Stage (II/I)	3.2	1.6-6.4	0.00080**
	<i>MTHFD2</i> (High/Low)	2.2	1.1-4.8	0.037*
MSKCC (n = 63)	Age	0.95	0.89-1.0	0.21
	Stage (II/I)	1.9	0.18-20	0.59
	Stage (III/I)	12	1.9-74	0.0076**
	<i>MTHFD2</i> (High/Low)	14	1.4-140	0.025**

Supplementary Table 2

Dependence on MTHFD2 for cell growth

Cell line	Mutation status of <i>EGFR</i>	Gefitinib sensitivity	MTHFD2 dependency
HCC827	Five amino acids deletion in <i>EGFR</i>	sensitive	-0.973
HCC827GR5	Five amino acids deletion in <i>EGFR</i> and <i>MET</i> amplification	resistant	-2.37
NCIH1975	Mutations L858R and T790M in <i>EGFR</i>	resistant	-2.88

Database analysis was carried out by using Project Achilles, <https://portals.broadinstitute.org/achilles>. A large negative value means cell growth activity is strongly dependent on MTHFD2. HCC827 cells harbor gefitinib-sensitive deletion of 5 amino acids, E746 to A750, in *EGFR*. HCC827GR5 cells are derived from HCC827 cells and show acquired gefitinib-resistance due to *MET* amplification. NCIH1975 cells harbor gefitinib-sensitive mutation, L858R, but show acquired gefitinib-resistance due to secondary mutation, T790M, in *EGFR*.