Supplementary Information

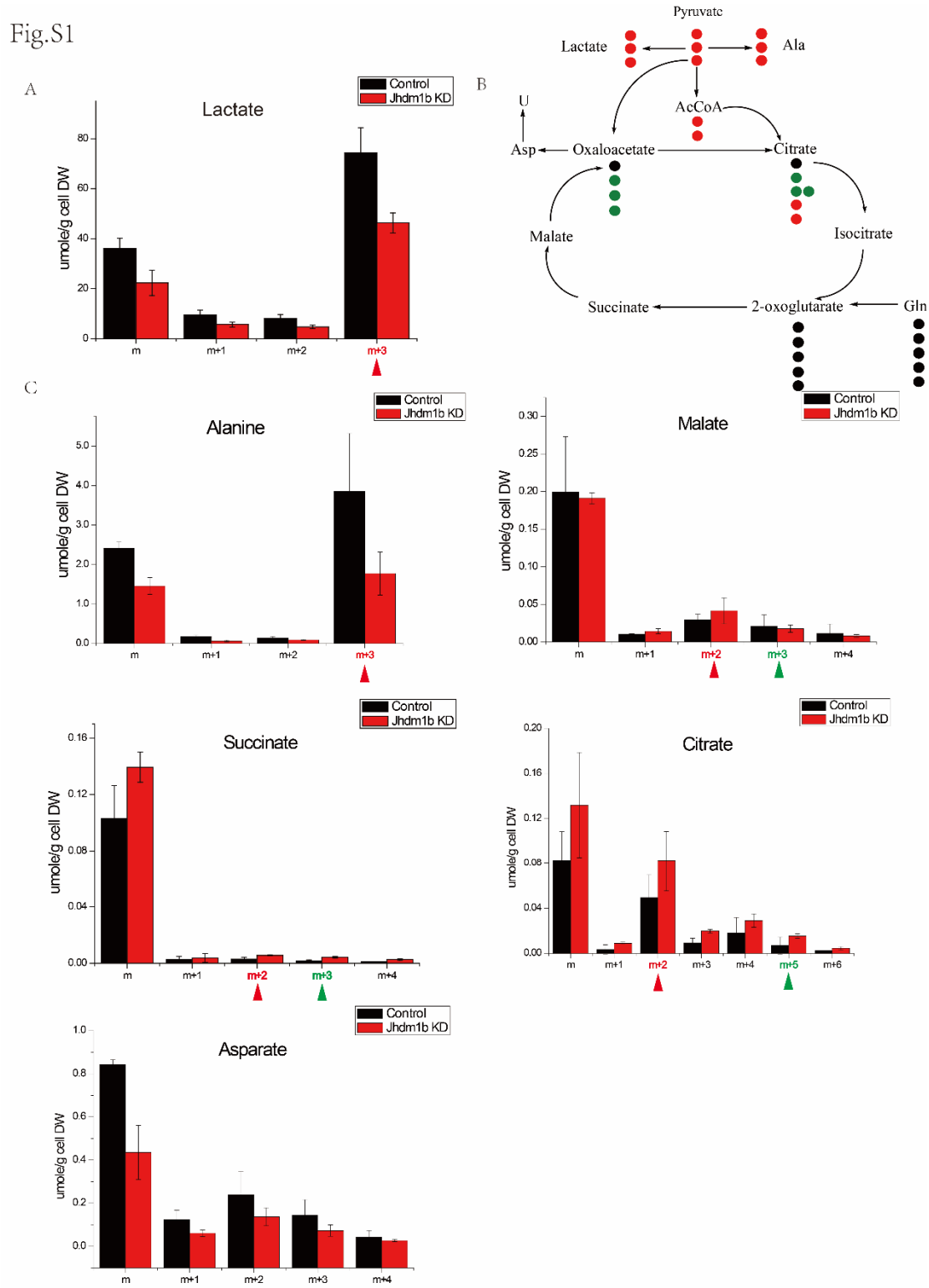

Figure S1. Glycolysis was suppressed and TCA cycle was sustained in Jhdm1b knockdown cells.

(A) GC-MS analysis of isotopologue concentrations of lactate in media from wild type and Jhdm1b knockdown HeLa cells. (B) Carbon flow from [U-^{13}C]- glucose through glycolysis, Krebs cycle, pyruvate carboxylation, and pyrimidine nucleotides.(C) GC-MS analysis of ^{13}C isotopologue distribution of intermediate metabolites of TCA cycle from wild type and Jhdm1b knockdown HeLa cells. The incorporation of ^{13}C atoms from $^{13}C_6$-Glucose into

intermediate metabolites are denoted as m+n, where n is the number of ^{13}C atoms. Red and green arrows show the ^{13}C carbon skeleton patterns derived from $^{13}C_6$-Glucose without or with pyruvate carboxylation. The error bars represent SEM. (n=3)

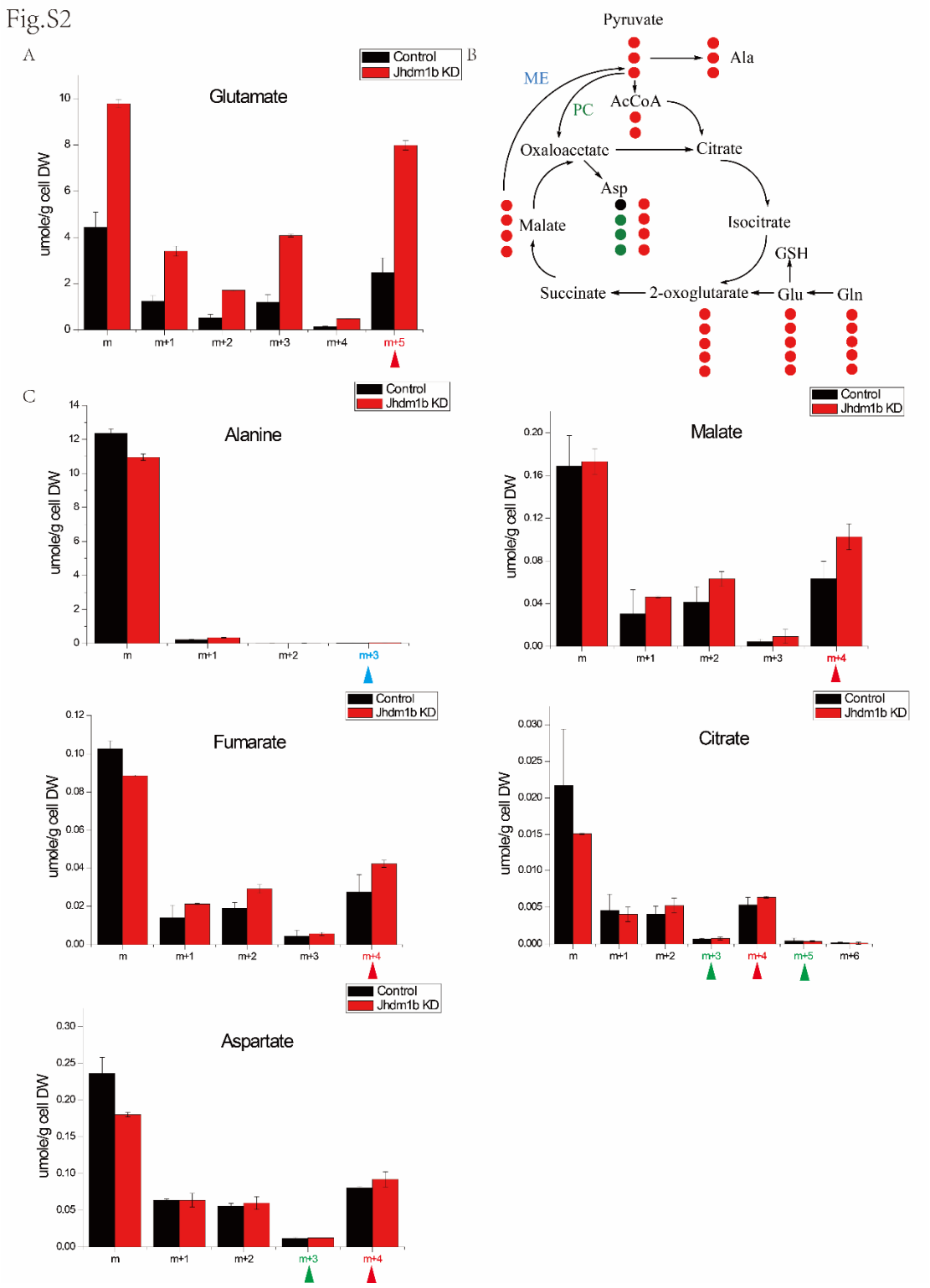

Figure S2. Glutamine entry into TCA cycle was enhanced in Jhdm1b knockdown HeLa cells

(A) GC-MS analysis of isotopologue concentrations of intracellular glutamate in cell pellet from wild type and

Jhdm1b knockdown HeLa cells. (B) Carbon flow from [U-^{13}C]- glutamine through glutaminolysis, Krebs cycle, pyruvate carboxylation, and malic enzyme (ME) reaction. (C) GC-MS analysis of ^{13}C isotopologue distribution of intermediate metabolites of TCA cycle from wild type and Jhdm1b knockdown HeLa cells. The incorporation of ^{13}C atoms from $^{13}C_5$-Glutamine into intermediate metabolites are denoted as m+n, where n is the number of ^{13}C atoms. Red and green arrows show the ^{13}C carbon skeleton patterns derived from $^{13}C_5$-Glutamine without or with pyruvate carboxylation. Blue arrow show the ^{13}C carbon skeleton patterns derived from ME reaction. The error bars represent SEM. (n=3)

Fig.S3

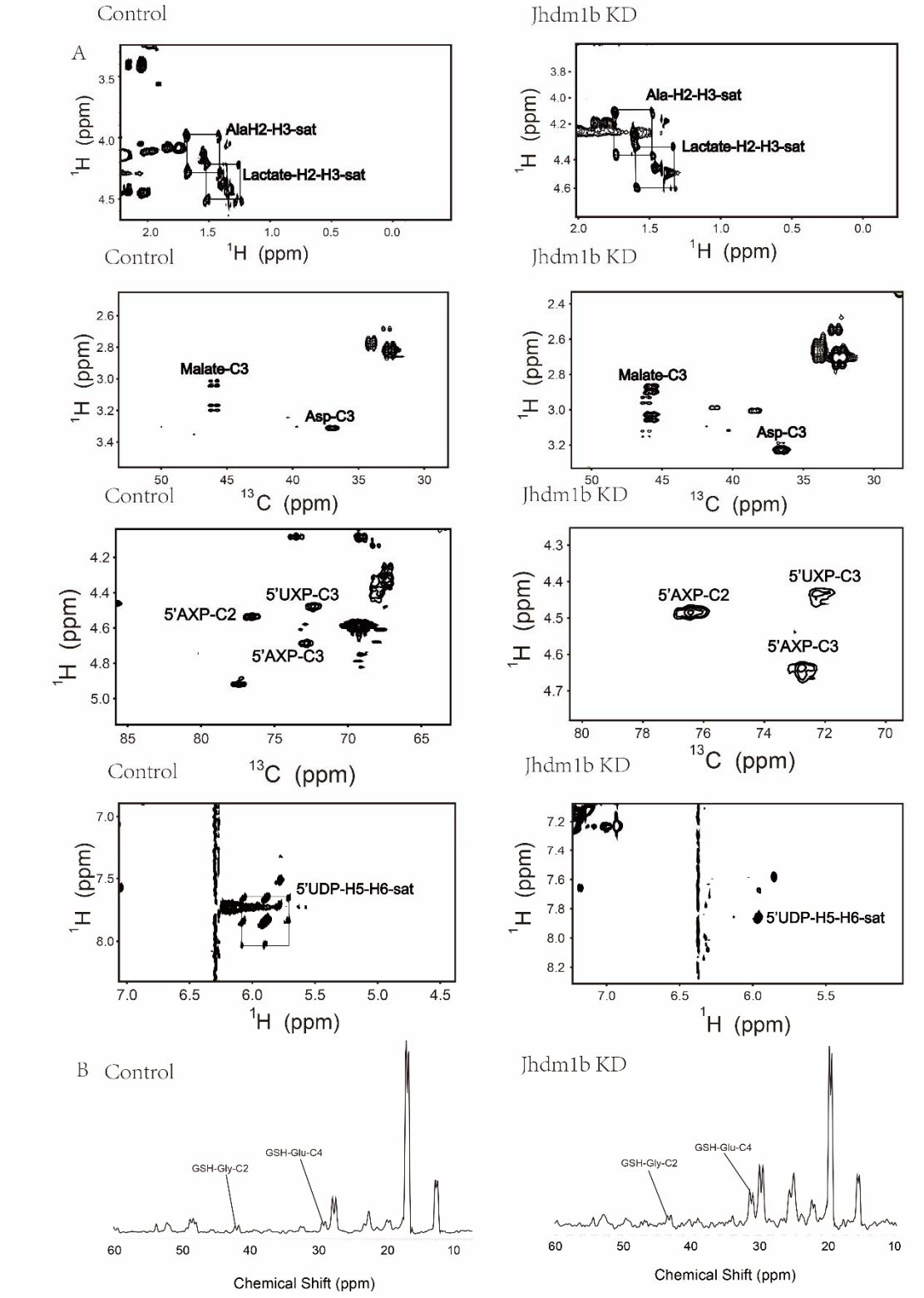

Figure S3. Comparison of several ^{13}C-labeled metabolites in NMR experiments.

(A) Several metabolites of 2D ^{1}H-^{13}C HSQC and TOCSY spectra of extracts of wild type and Jhdm1b HeLa cells.

(B) 1D ^{13}C(^{1}H) HSQC spectra of glutathione (GSH)-glycine and glutamate in wild type and Jhdm1b HeLa cells.

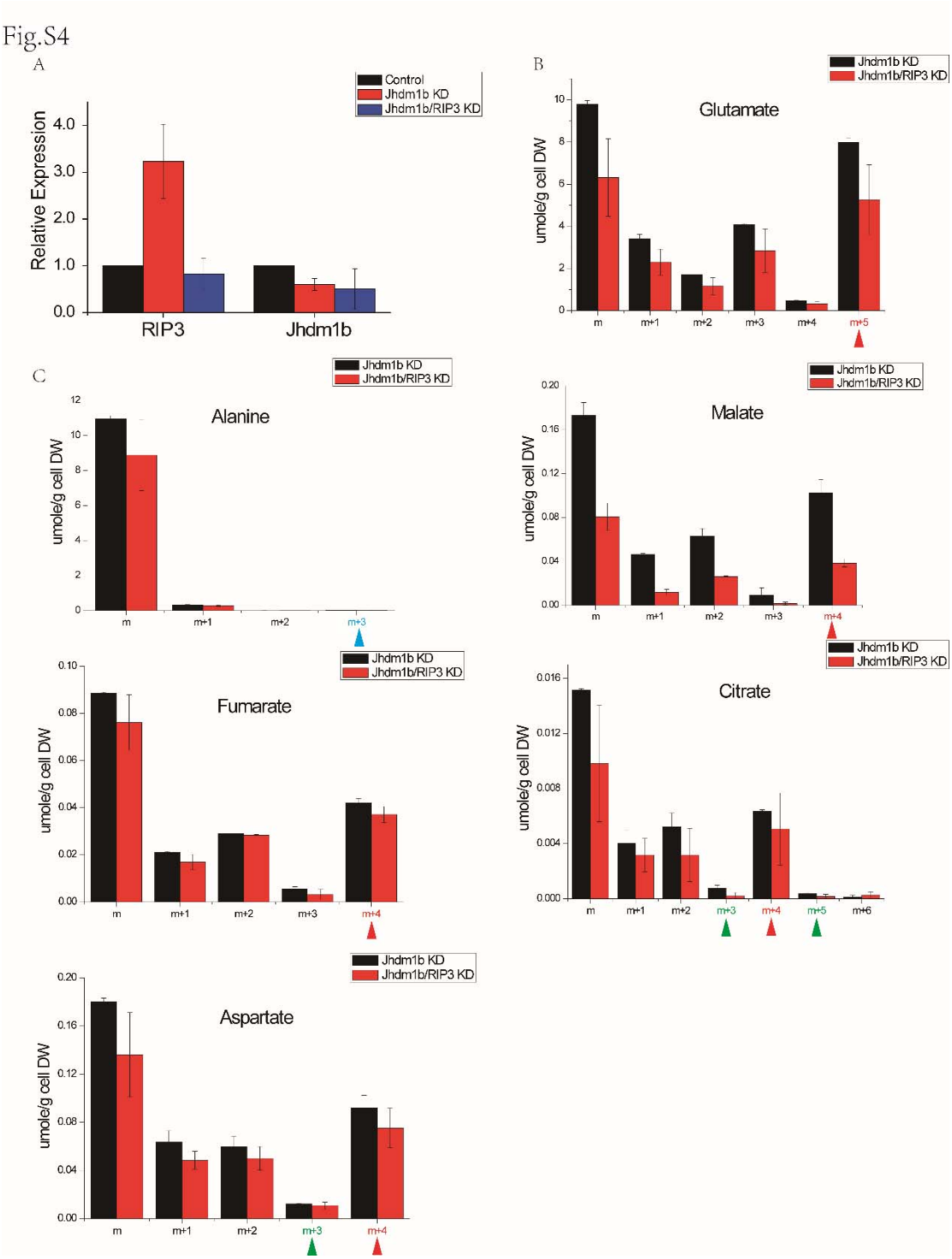

Figure S4. RIP3 knockdown reverted enhancement of TCA cycle induced by Jhdm1b knockdown.

(A) RIP3 and Jhdm1b mRNA levels by real-time PCR of HeLa cells infected with a lentivirus expressing RIP3 and Jhdm1b shRNA. (B) GC-MS analysis of isotopologue concentration of glutamate in Jhdm1b knockdown and Jhdm1b/RIP3 double knockdown cells. (C) GC-MS analysis of isotopologue concentrations of intermediates of TCA cycle produced by $^{13}C_5$-glutamine in Jhdm1b knockdown and Jhdm1b/RIP3 double knockdown cells. All ^{13}C labeling patterns products were derived with $^{13}C_5$-Gln as tracer. The error bars represent SEM. (n=3)