Supplementary Information

FIG. S1. Metabolic stress leads to the stabilization of p53 protein. U2OS cells were cultured in glucose deprivated DMEM media or treated by AICAR (1 mM) for 6 h, followed by CHX (50 ug/ul) treatment. Cell lysates (30 μg) were loaded and detected by p53 (DO-1) and beta-actin antibodies. Quantitative results were analyzed with ImageJ software and plotted with Excel.

FIG. S2. AICAR treatment does not induce the formation of γ-H2AX foci in HCT116(+/+) cells, and AICAR activation of p53 is independent of ATM. (**A**) Representative pictures of γ-H2AX foci (green) and p53 (red) in HCT116(+/+) cells treated by DMSO (in the same volume as that for AICAR), 1mM AICAR or 1 mM hydroxyurea for 12 h. Red, cells were stained with mouse anti-p53 antibodies (DO-1) and goat anti-mouse antibodies conjugated with Alexa Fluor 546; Green, cells were stained with rabbit anti-γ-H2AX antibodies and goat anti-rabbit antibodies conjugated with FITC. (**B**) Graphical representation of the percentage of positive cells treated by DMSO, AICAR or hydroxyurea. γ-H2AX foci and p53 positive cells were determined from more than 500 cells for each condition. (**C**) Wild type ($AT^{+/+}$) and ATM knockout ($AT^{-/-}$) MEFs were treated with AICAR for 6h, and p53 induction was determined by WB with indicated antibodies.

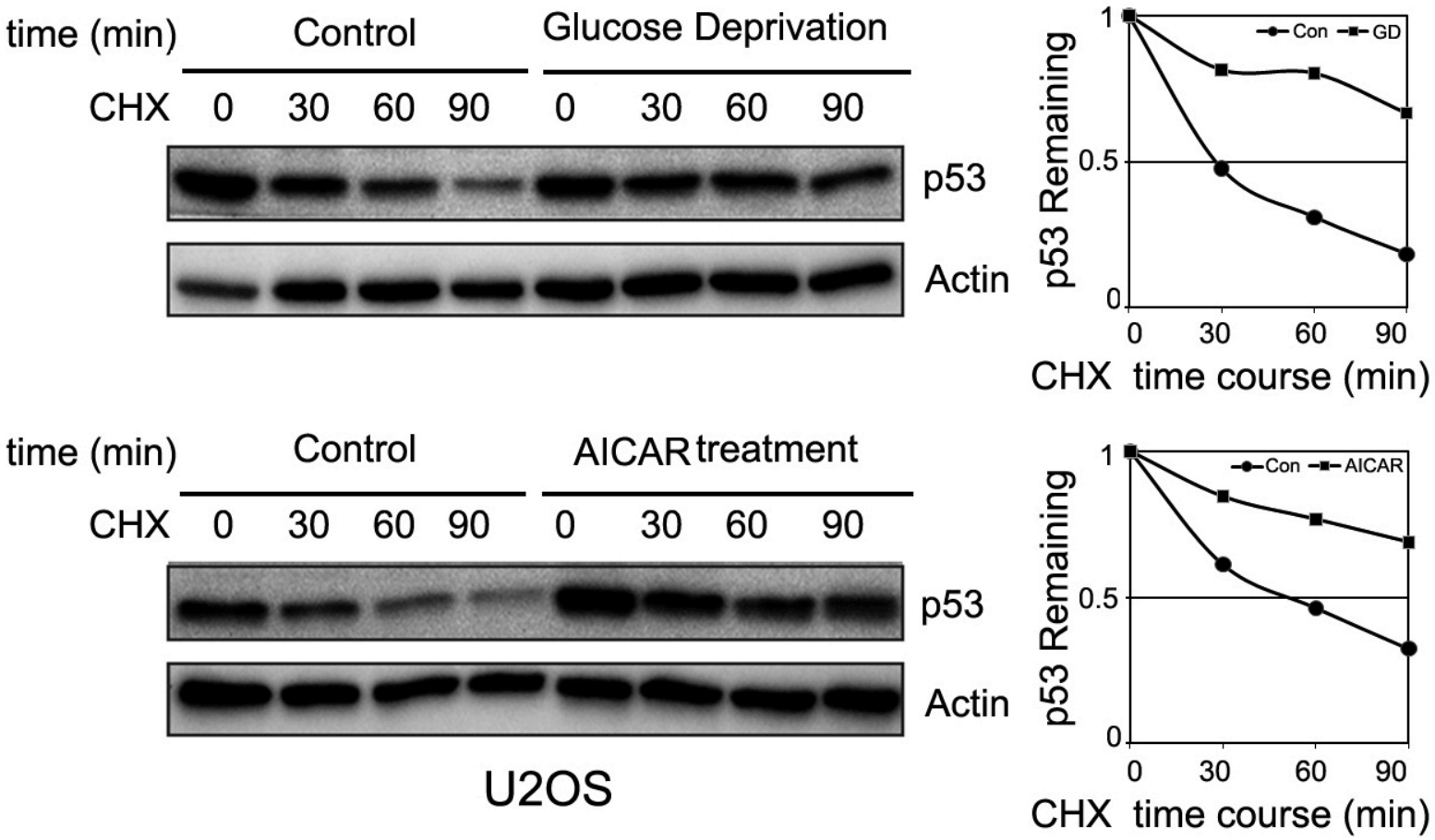
FIG. S3. AMPK enhances the interaction between MDMX and 14-3-3s. H1299 cells were transfected with HA-MDMX (2 μg) and Flag-14-3-3 (1 μg) expression plasmids as

indicated on the top. 500 μg of cell lysates were for IP with anti-Flag antibodies and probed by anti-HA antibodies. 50 μg of cell lysates were loaded for straight WB analysis.

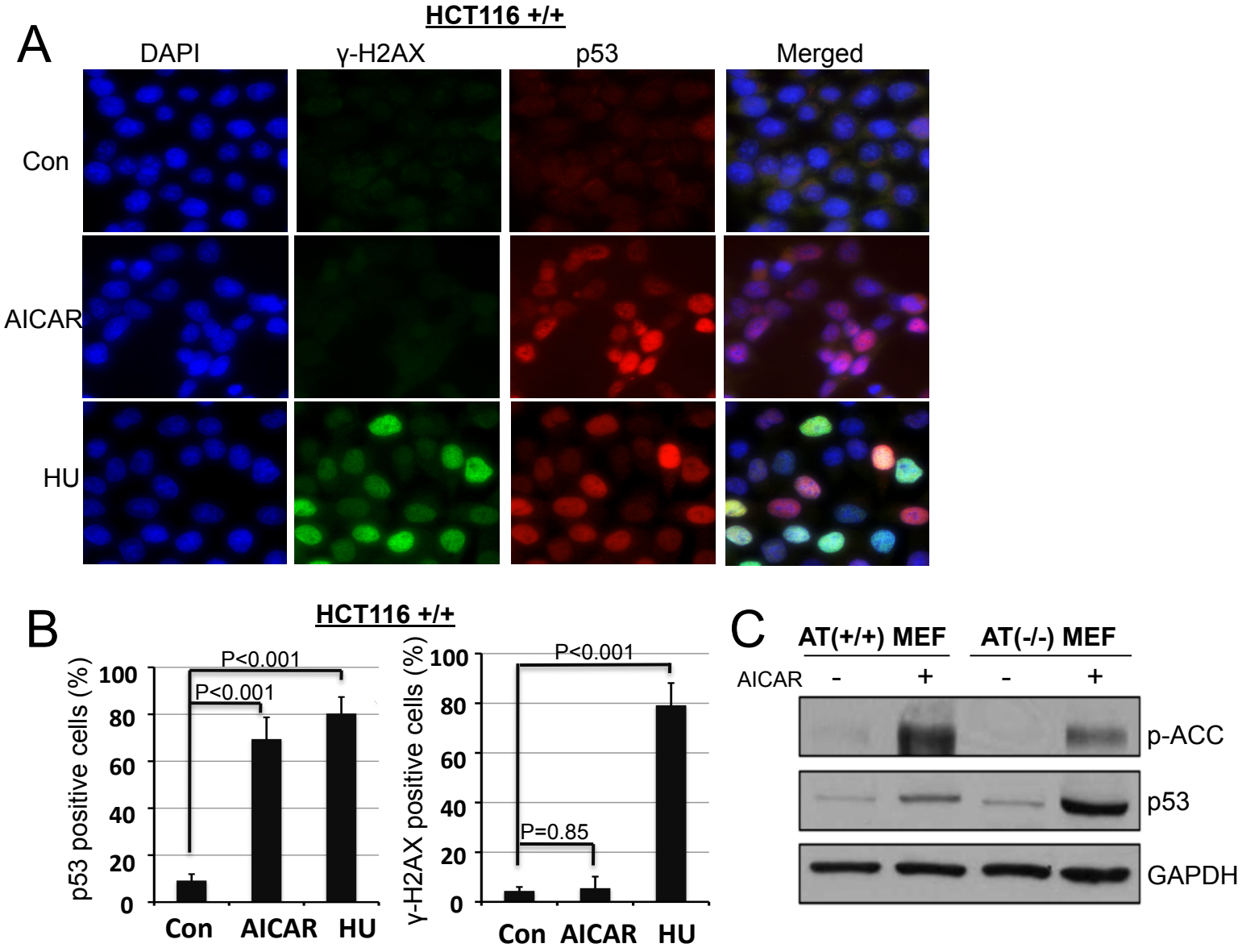
FIG. S4. AMPK is required for AICAR-induced MDMX and 14-3-3γ interaction. **(A)** and **(B)** HCT116(+/+) cells were transfected with 50 nM final concentration of AMPK siRNA (s100 and s11085), which were different from the siRNAs used for Fig. 4, or scramble siRNA by using BIONTEX siRNA transfection reagent and following manufacturer's instruction. At 48 h post-transfection, cells were treated with AICAR (1 mM) for 6 h before harvesting. The efficiency of the si-RNA was confirmed by WB (**A**), and co-IP (**B**) was performed with the anti-14-3-3γ monoclonal antibody (CG31) followed by WB with polyclonal anti-14-3-3γ (C-16) and monoclonal anti-MDMX (7A8) antibodies.

FIG. S5. AICAR can not induce G2 arrest in p53 null MEF cells. p53 knockout ($p53^{-/-}$) MEF cells were treated with AICAR (1mM), Metformin (10mM), and Salicylate (10mM), respectively, or DMSO as a negative control for 24 hours, and stained with PI for cell cycle analysis by FACS. Data were presented as means ± SEM, and *p*-values were statistically evaluated by One-way ANOVA.

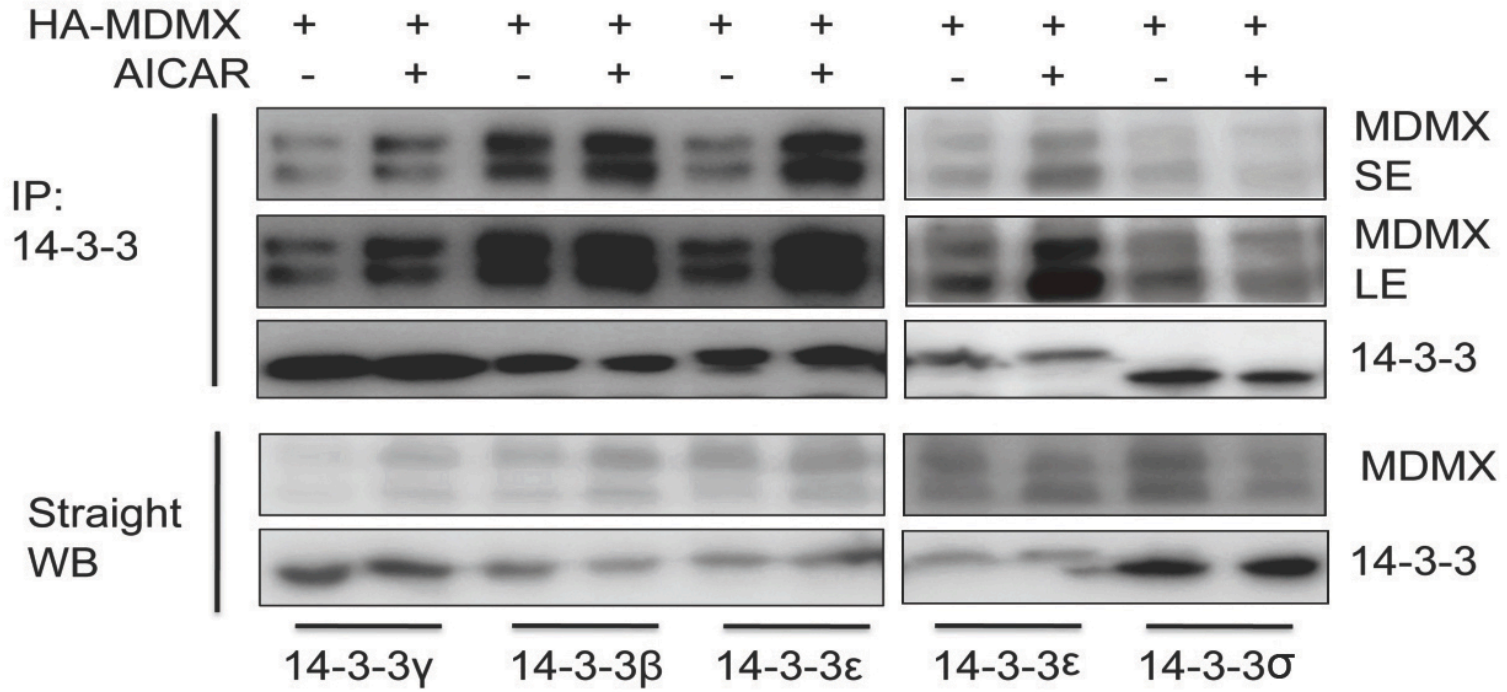
Supplemental Fig. S1



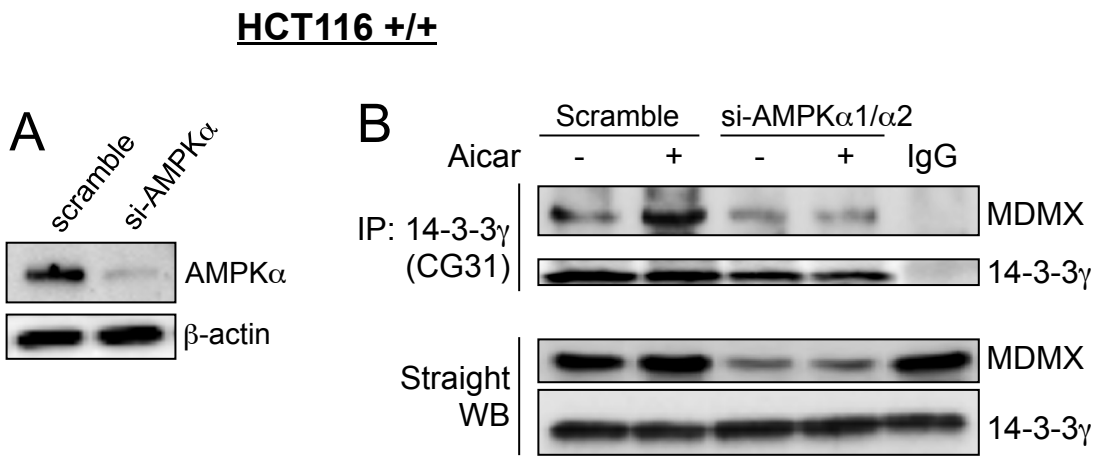
Supplemental Fig. S2



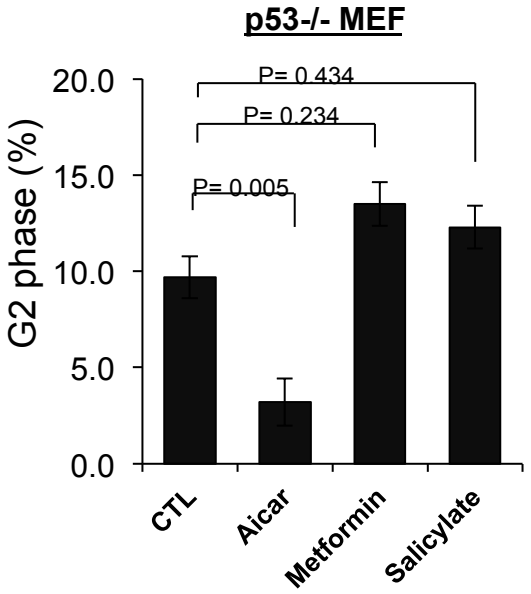
Supplemental Fig. S3



Supplemental Fig. S4



Supplemental Fig. S5



Cell cycle distribution. (n=4)

	p53-/- MEF		
	G1	**G2**	**S**
CTL	52.0 ± 2.51	9.7 ± 1.10	38.2 ± 1.42
Aicar	42.3 ± 2.05	3.2 ± 1.22	54.5 ± 0.10
Metformin	43.5 ± 3.92	13.5 ± 1.14	42.9 ± 2.84
Salicylate	39.9 ± 2.41	12.3 ± 1.12	47.8 ± 1.55