

Supplementary figure 1: (A) characterization by Surface marker analysis using flow cytometry demonstrated that WJ–MSCs were positive for CD 73, CD 90, CD 105 and negative for CD 34. Representative histograms are displayed. Effect of medium washout

(MWO) on population doubling time and population doublings. WJ-MSCs were plated at a high seeding density of 8000 cells/cm<sup>2</sup> under 40°C and subjected to medium change every 12 h. They showed a rescue leading to (**B**) an increase in the number of population doublings and (**C**) decrease in population doubling time as compared to the MSCs seeded at 8000 cells/cm<sup>2</sup> but without any medium change (n = 2). (**D**) A pre-gating performed for FSC-H/SSC-H, encompassing major population while excluding the debris, is demonstrated. Then gating was applied with the only annexin-V and only PI treated control samples independently to discriminate viable and apoptotic population. (**E**) mRNA expression levels of  $\beta$ -actin as detected by qRT-PCR in NC siRNA or *VTN* esiRNA transfected WJ-MSCs under 40°C. Each bar represents mean ± SEM; n = 3 independent biological samples (one-way ANOVA with Bonferroni post-test).

Effect of ERK or PI3K pathway inhibition on p53 protein expression in WJ-MSCs exposed to 40°C. (**F**) p53 protein expression was detected in WJ-MSCs exposed to 40°C for 48 h in the absence or presence of ERK pathway inhibitor, FR180204 or PI3K pathway inhibitor, LY294002. Representative Western blotting images from three independent biological samples (n = 3) are displayed. Band densities were quantified and plotted relative to GAPDH expression used as loading control. Each bar represents mean  $\pm$  SEM. \* represent *p* < 0.05.



**Supplementary figure 2:** Exploring involvement of autophagy pathway by detecting expression level of p62. (**A**) WJ-MSCs were subjected to 40°C in the absence or presence of small molecule inhibitors for PI3K and NF- $\kappa\beta$  pathways, individually, for 48 h. p62 protein expression was detected and representative Western blotting images from four independent biological samples are displayed. Band densities were quantified and plotted relative to GAPDH expression, used as loading control. (**B**) WJ-MSCs were transfected with *VTN* 

esiRNA, or NC siRNA and were exposed to 40°C for 48 h. p62 protein expression was detected and representative Western blotting images from three independent biological samples are displayed. Band densities were quantified and plotted relative to GAPDH expression, used as loading control. (C) For autophagy inhibition study, WJ-MSCs were treated with chloroquine (CQ) at a concentration of 25  $\mu$ M, and p62 protein expression was assessed. Representative Western blotting images from three independent biological samples are displayed. Band densities were quantified and plotted relative to GAPDH expression, used as loading control. (D) Representative phase-contrast morphology images of control and 40°C treated WJ-MSCs, in the absence or presence of chloroquine, under 10X magnification (n = 3). Each bar represents mean ± standard error mean. \* represent *p* < 0.05, \*\* represent *p* < 0.01, \*\*\* represents *p* < 0.001. Data shown are representative of at least three independent biological samples (n ≥ 3).