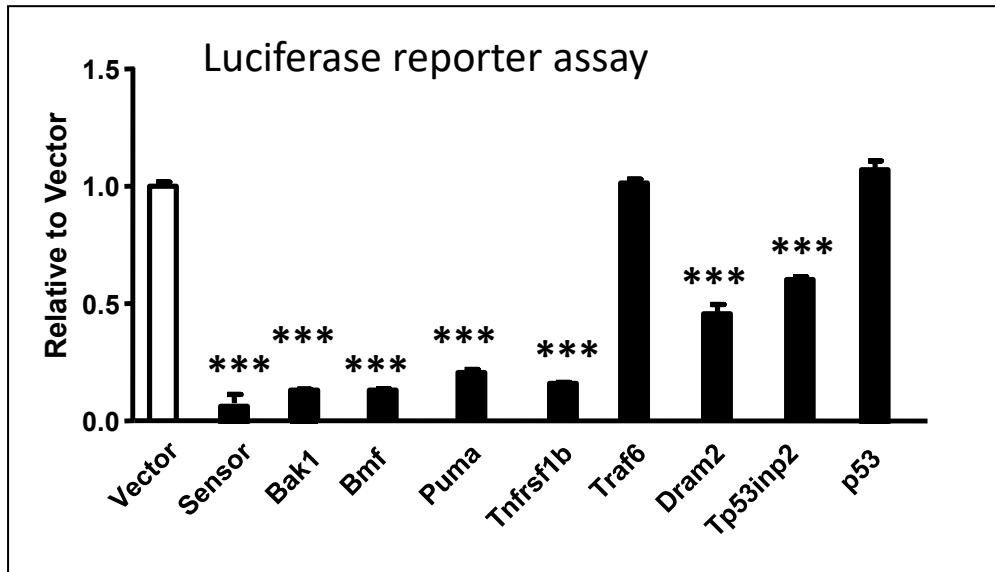
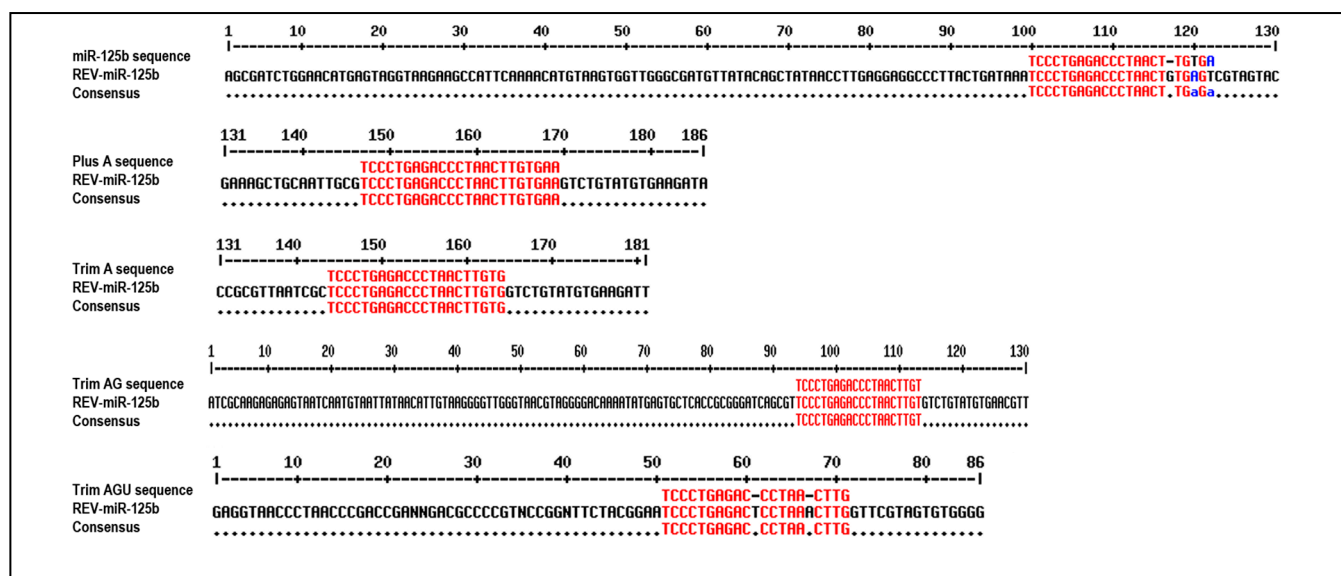


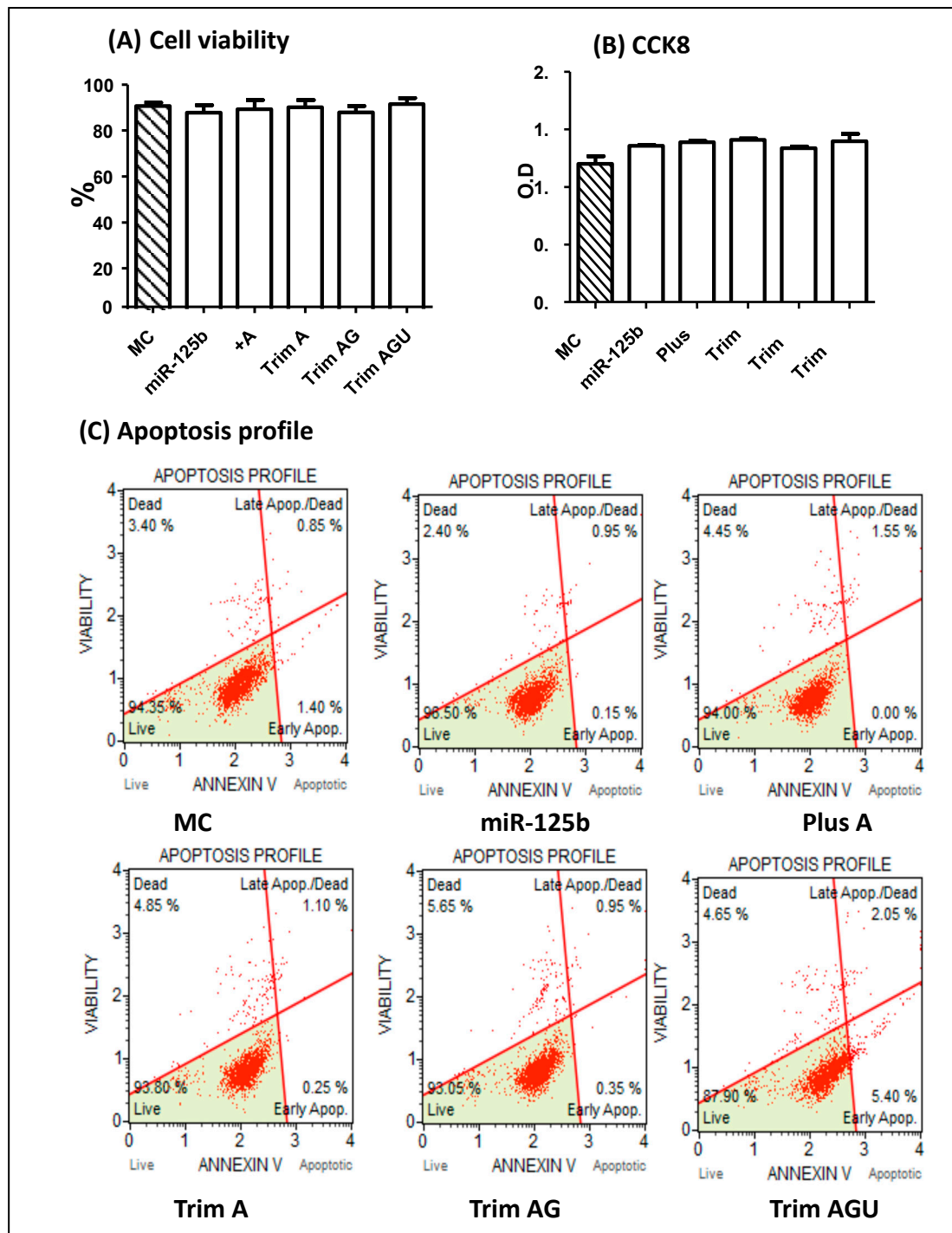
SUPPLEMENTARY DATA



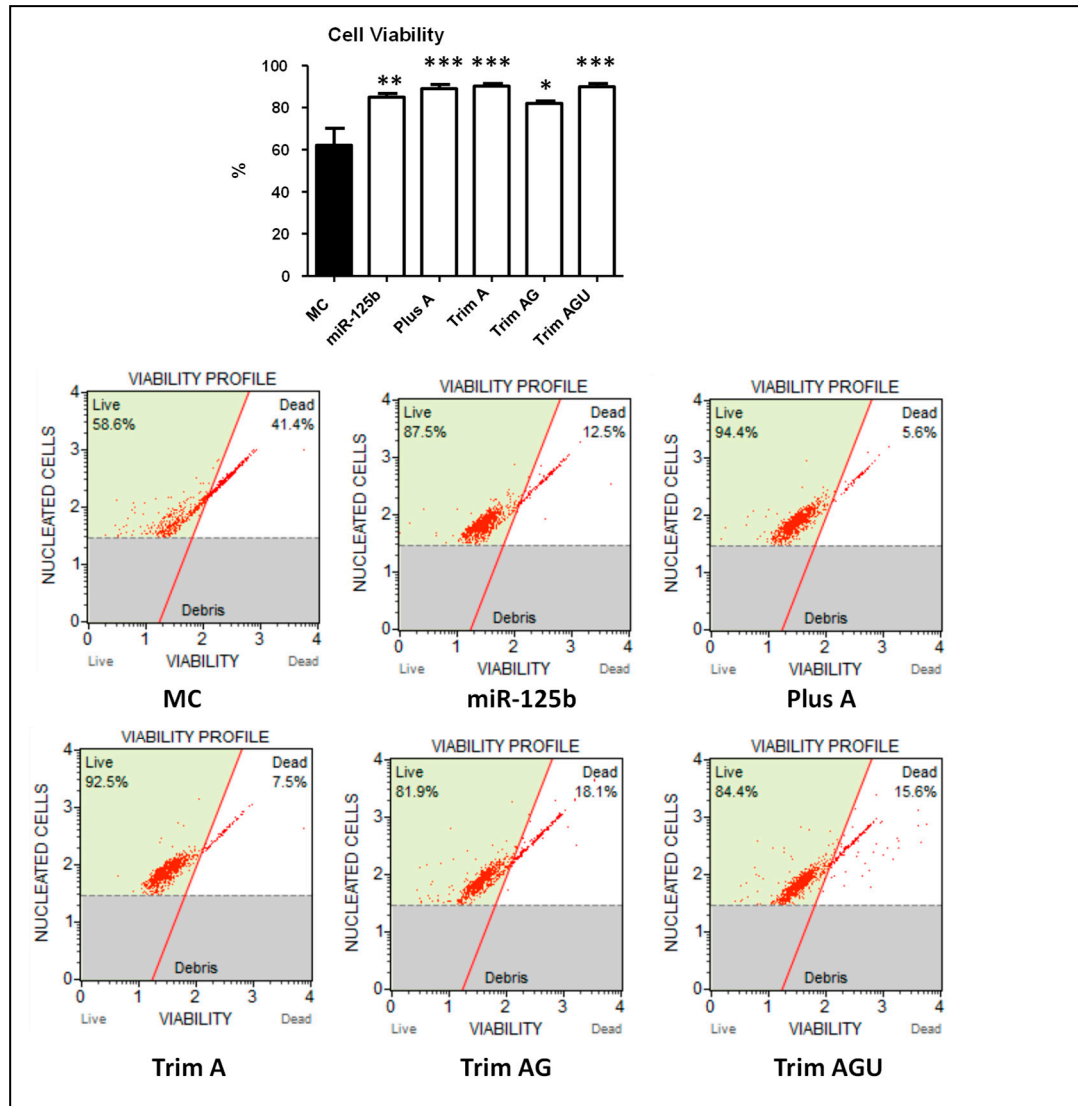
Suppl. Figure S1: Confirmation of miR-125b target genes by luciferase reporter assays. Target gene 3'-UTR cDNA sequences were cloned into psiCHECK™-2 dual luciferase reporter plasmid (Promega Corp., Singapore). MiR-125b sensor, the complementary binding sequence to miR-125b, was cloned as a positive control. The plasmids were co-transfected with miR-125b for 24 hr. Renilla and Firefly luciferase activities were measured using Dual-Glo® luciferase assay system (Promega Corp., Singapore). Luciferase activity for miR-125b targets were significantly decreased. Data are presented as Mean \pm SD, *** p < 0.001 vs. Empty vector by two-tail unpaired t-test. N=3 in triplicates.



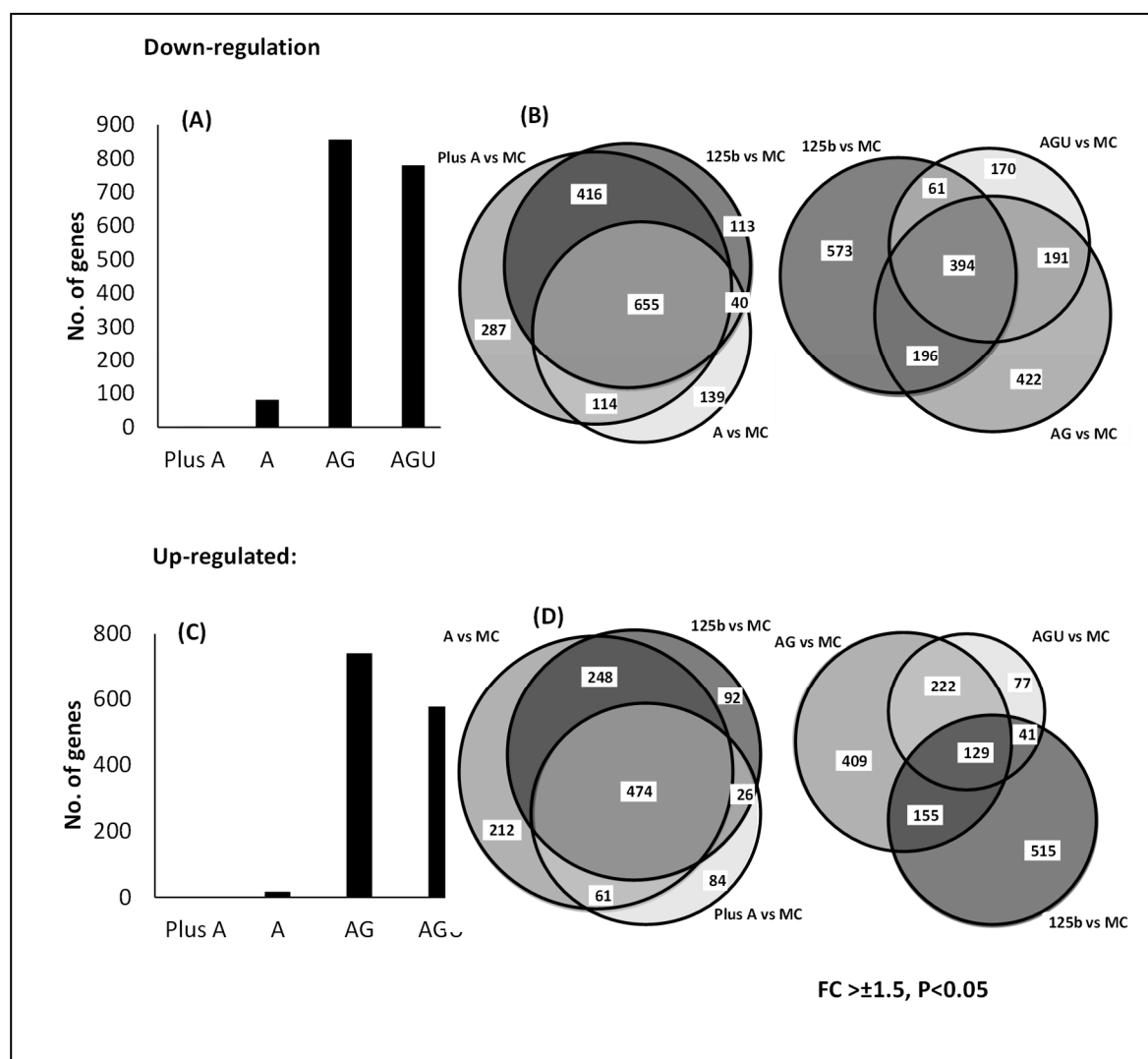
Suppl. Figure S2: Sanger sequencing alignment of miR-125b and isomiRs sequences.



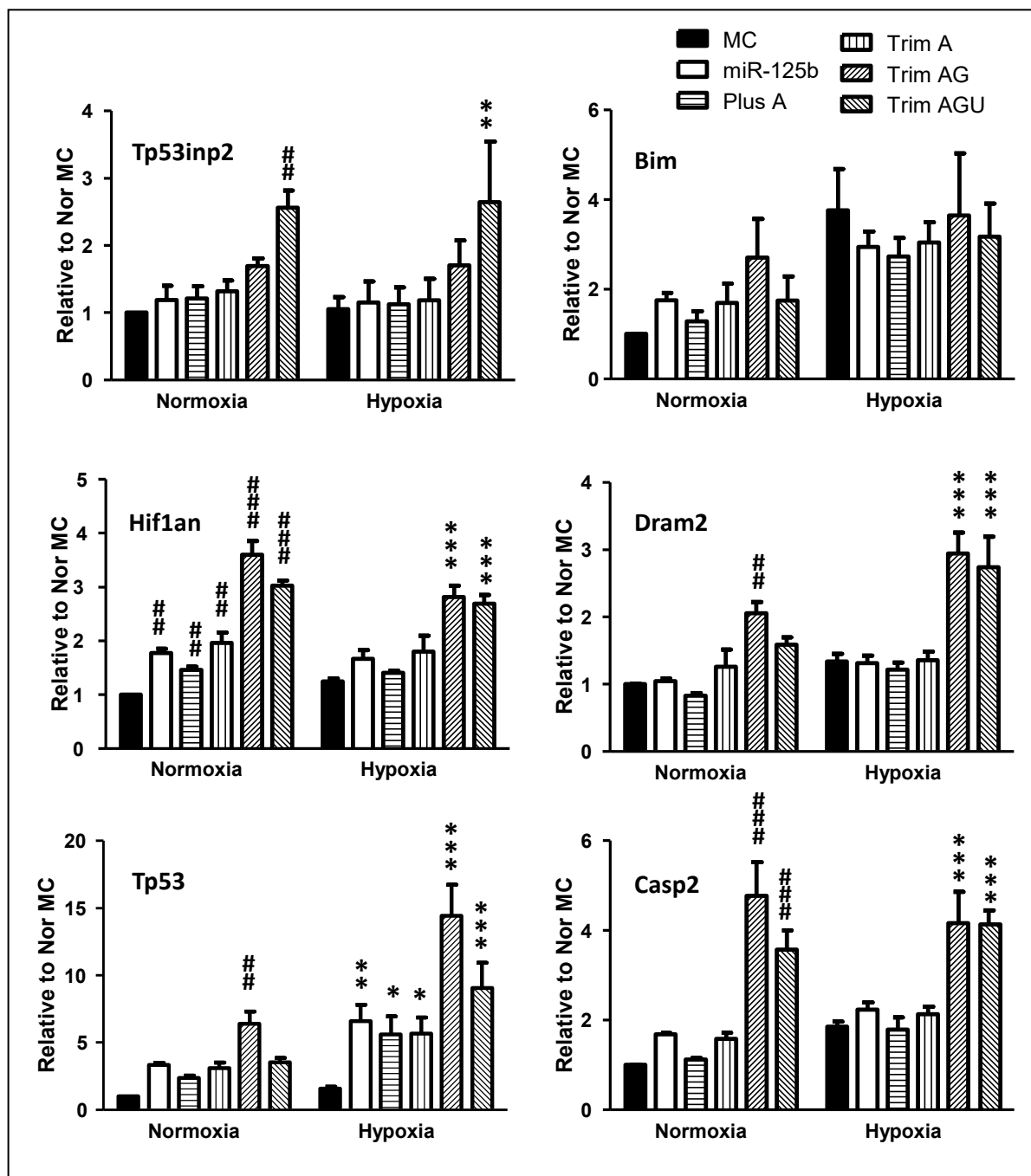
Suppl. Figure S3: Effects of miR-125b and its isomiRs under normoxia. miR-125b and its isomiRs mimics were transfected into H9c2. Under normoxia, miR-125b and its isomiRs did not affect the cell viability (A), CCK-8 activity (B) and apoptosis detected by Annexin V/7-AAD double staining (C). Data are presented as Mean \pm SD, significance was determined by two-tail unpaired t-test. N=3 in triplicates.



Suppl Figure S4: Protective effects of miR-125b and its isomiRs during hypoxia. miR-125b and its isomiRs mimics were transfected into H9c2 and subjected to hypoxia. miR-125b and its isomiRs significantly increased the cell viability as compared with MC. Data are presented as Mean \pm SD, * p <0.05, ** p <0.01, *** p < 0.001 vs. MC by two-tail unpaired t-test. N=3 in triplicates.



Suppl Figure S6: Differences of gene regulation by isomiRs in comparison between miR-125b and its isomiRs under normoxia. Genes regulated by miR-125b and isomiRs by ≥ 1.5 -fold change with $p(\text{adj}) < 0.05$ compared to MC were included for further analysis. (A) and (C) show the number of up- and down-regulated genes by direct comparison between miR-125b and isomiRs. The number of overlapping genes between miR-125b and its isomiRs are presented in the proportional venn diagram (B and D).



Suppl Figure S7: Gene regulations under normoxia and hypoxia assessed by RT-qPCR. Data are presented as Mean \pm SD with Student's t-test, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs. MC by two-tail unpaired t-test. N=3 in triplicates.