

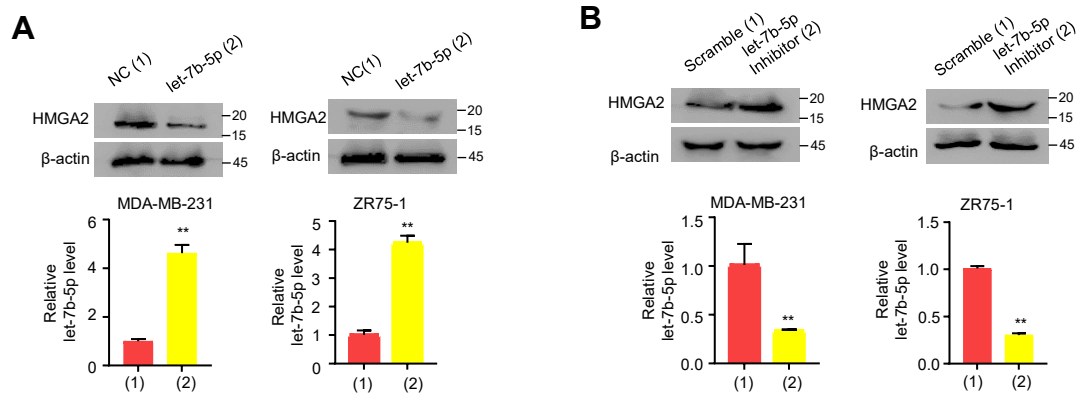


Fig. S1 Let-7b-5p targets HMGA2. **A, B** Western blot for HMGA2 protein expression in indicates BC cells after transfection with let-7b-5p mimic or NC (**A**), or let-7b-5p inhibitor or scramble (**B**) (n = 3, mean ± SD). Histograms under western blot show let-7b-5p expression by RT-qPCR (n = 3, mean ± SD). **p < 0.01 versus corresponding control.

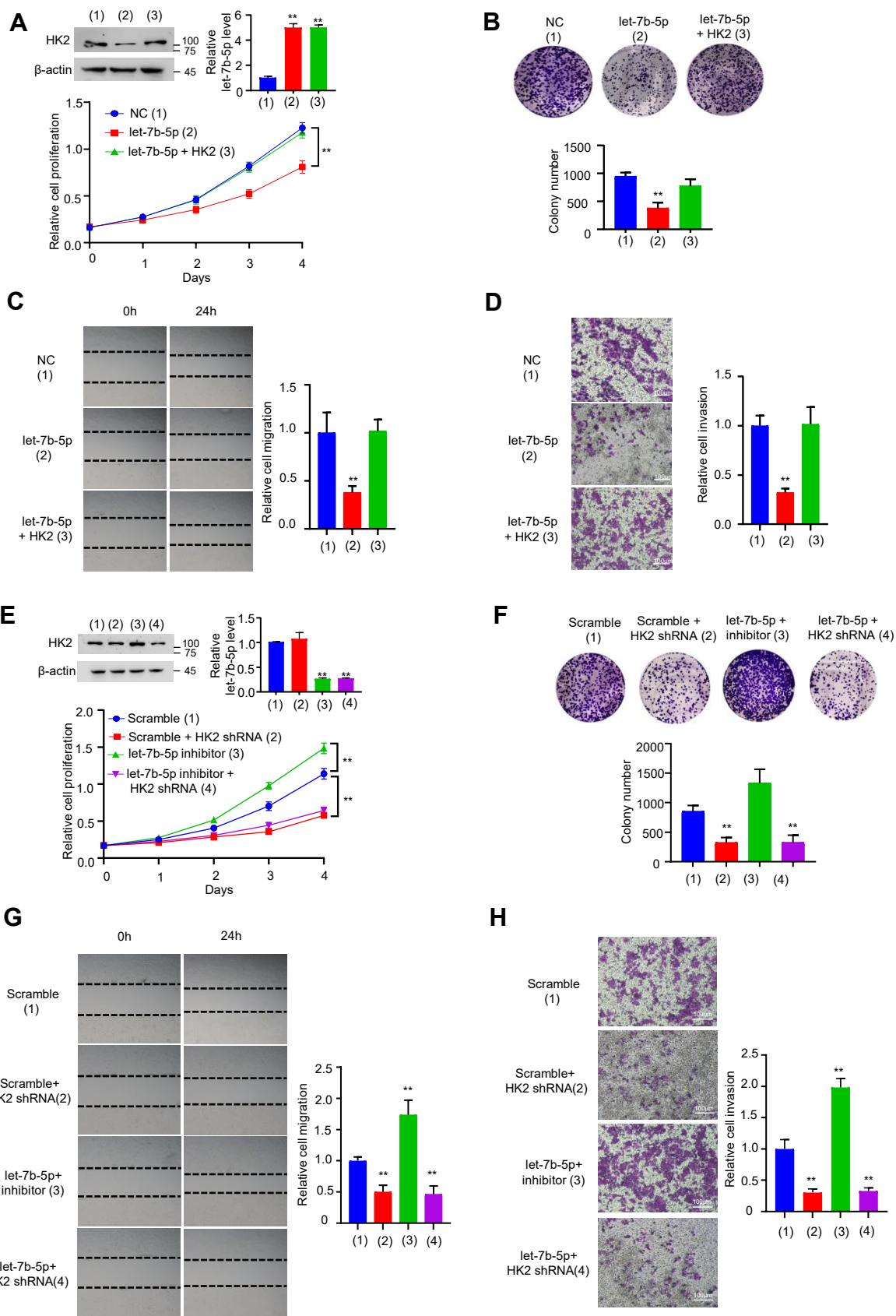


Fig. S2 Let-7b-5p suppresses proliferation, migration and invasion through inhibition of HK2 expression in ZR75-1 cells. **A** Proliferation curve was analyzed by CCK-8 Kit after ZR75-1 cells were transfected with NC, let-7b-5p mimic or let-7b-5p mimic plus HK2 plasmid ($n = 3$, mean $\pm$ SD). Western blot and RT-qPCR showed HK2 and let-7b-5p expression respectively. **B** Colony formation analysis of ZR75-1 cells after the transfection as in (A). Histograms display the colony number ($n = 3$, mean $\pm$ SD). **C**, **D** Scratch test (**C**) and transwell assay (**D**) of ZR75-1 cells after the transfection as in (A). Histograms display relative cell migration or invasion ($n = 3$, mean $\pm$ SD). **E**, **F** Control or HK2 shRNA ZR75-1 cells with the transfection of let-7b-5p inhibitor or scramble were analyzed as in (A) and (B) ($n = 3$, mean $\pm$ SD). **G**, **H** Scratch test (**G**) and transwell assay (**H**) of control or HK2 shRNA ZR75-1 cells with the transfection as in (E, F) ($n = 3$, mean $\pm$ SD). Scale bar, 100 μ m. * $p < 0.05$, ** $p < 0.01$ versus corresponding control.

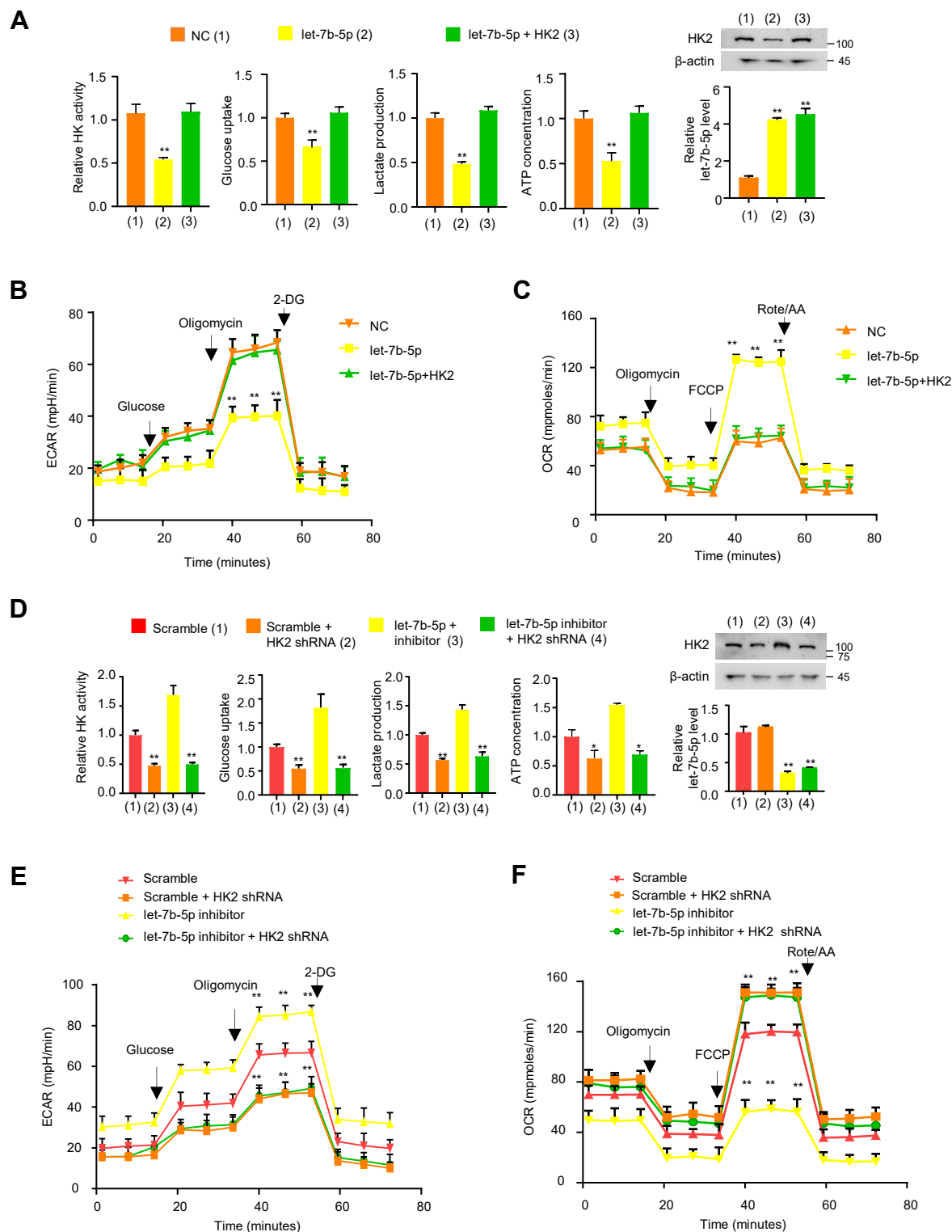


Fig. S3 Let-7b-5p dampens glycolysis via inhibition of HK2 expression in ZR75-1 cells. **A** ZR75-1 cells were transfected with NC, let-7b-5p mimics or let-7b-5p mimics plus HK2. HK activity, glucose uptake and the production of lactate and ATP were determined ($n = 3$, mean $\pm$ SD). Representative immunoblot reveals HK2 expression. qRT-PCR analysis indicates let-7b-5p expression. **B**, **C** ZR75-1 cells were transfected as in (A), and ECAR (**B**) and OCR (**C**) were then determined ($n = 4$, mean $\pm$ SD). **D** Control and HK2 shRNA ZR75-1 cells were transfected with scramble or let-7b-5p inhibitor and analyzed as in (A) ($n = 3$, mean $\pm$ SD). **E**, **F** ECAR (**E**) and OCR (**F**) assays of control and HK2 shRNA ZR75-1 cells after transfection as in (D) ($n = 4$, mean $\pm$ SD). $^{**}P < 0.01$ versus corresponding control.

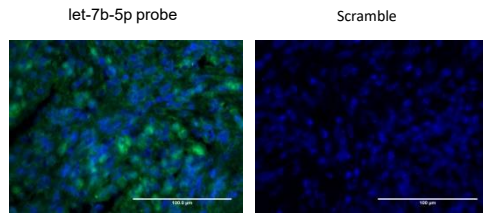
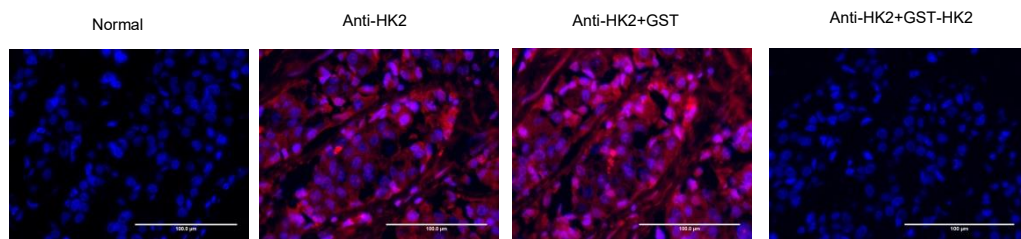
A**B**

Fig. S4 Specificity validation of let-7b-5p probe and HK2 antibody. **A** FISH of breast cancer samples with let-7b-5p probe or scramble probe. Scale bar, 100 μ m. **B** Immunohistochemical staining of breast cancer samples incubated with normal IgG or anti-HK2. To validate antibody specificity, the anti-HK2 was pre-incubated with recombinant GST-HK2 protein or GST for 1 h prior to applying to tissue. Scale bar, 100 μ m.