

SIPA1 promotes aerobic glycolysis by EPAS1 in breast cancer

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Aerobic glycolysis or Warberg effect is a fundamental feature of cancer cells, which rely heavily on glycolytic fermentation for energy metabolism, even with ambient oxygen supply. Although the Warburg effect is now well appreciated, the mechanisms driving aerobic glycolysis are not fully revealed. Here we show that aberrant expression of SIPA1 facilitates aerobic glycolysis in three-negative breast cancer (TNBC) cells. Moreover, TNBC cells high expression of SIPA1 rely on aerobic glycolysis instead of OXPHO in mitochondria to produce ATP. Mechanically, SIPA1 can be located in the nucleus of breast cancer cells and facilitates the transcription of EPAS1, which codes the transcription factor HIF2a targeting glycolysis related genes, by interacts with its promoter. We further demonstrated that activation of EPAS1 mediated by SIPA1 reprogramed the energy metabolism by PDK1 in a hypoxia- or hypoxia-inducible factor-1 (HIF-1)-independent manner. Importantly, we illustrate a novel pathway to mediate metabolism rewrite of breast cancer, which suggests a potential rationale to target EPAS1 for cancer therapy in malignancies with aberrant expression of SIPA1.

Fig.1 The expression of SIPA1 is correlated to glycolysis in TNBC.

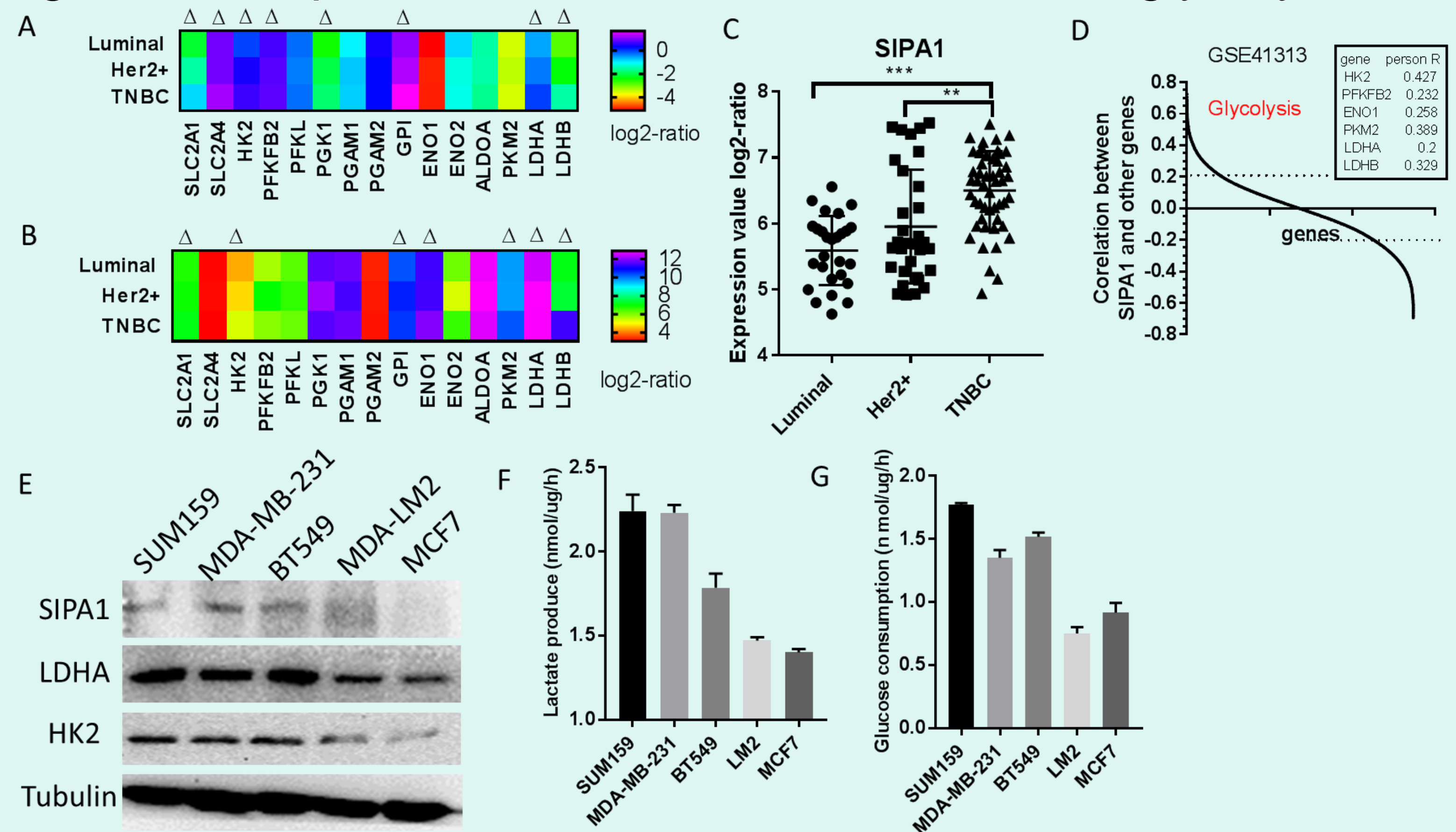


Fig.3 SIPA1 regulates aerobic glycolysis via EPAS1.

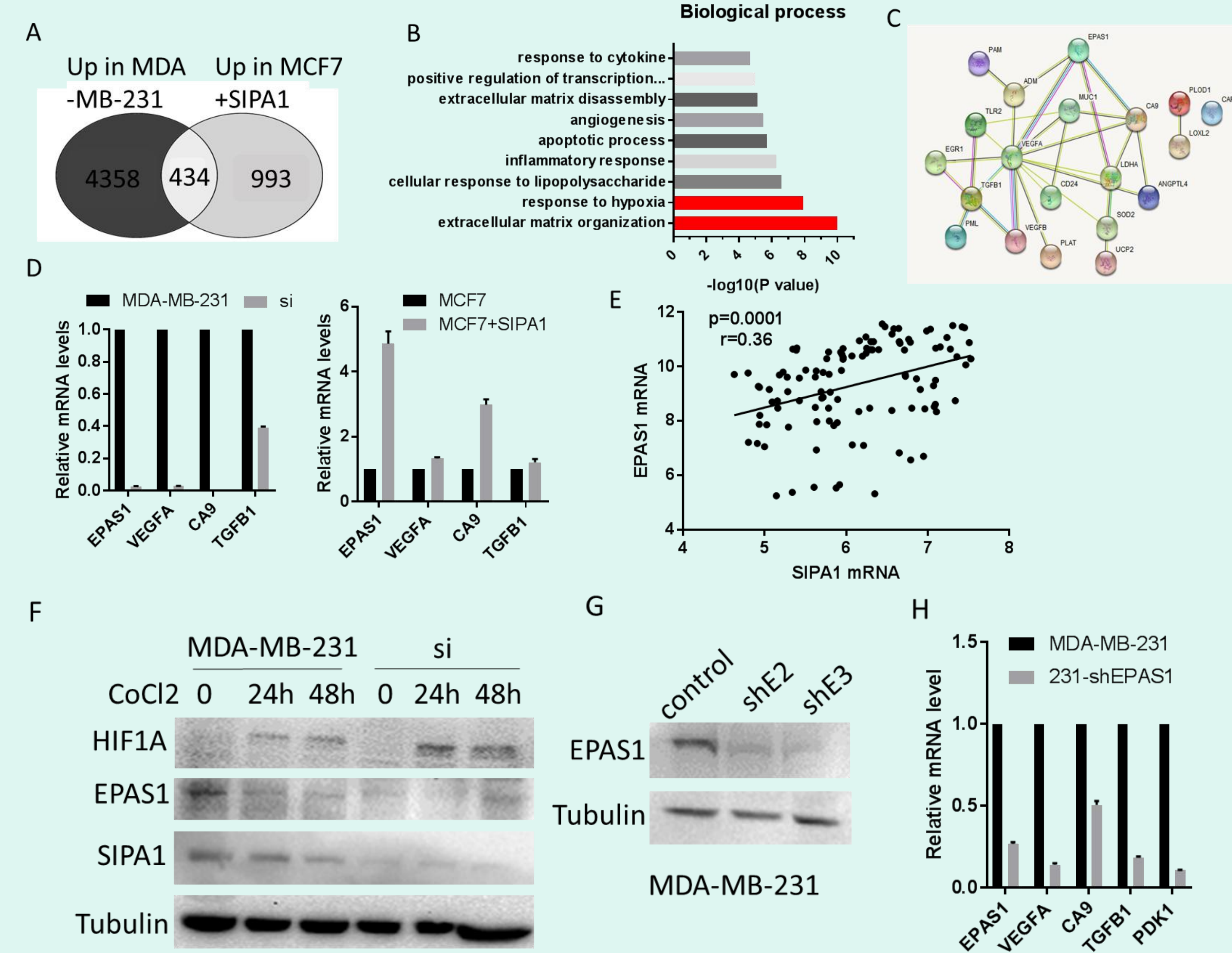


Fig.2 SIPA1 promotes Warburg effect in breast cancer cells.

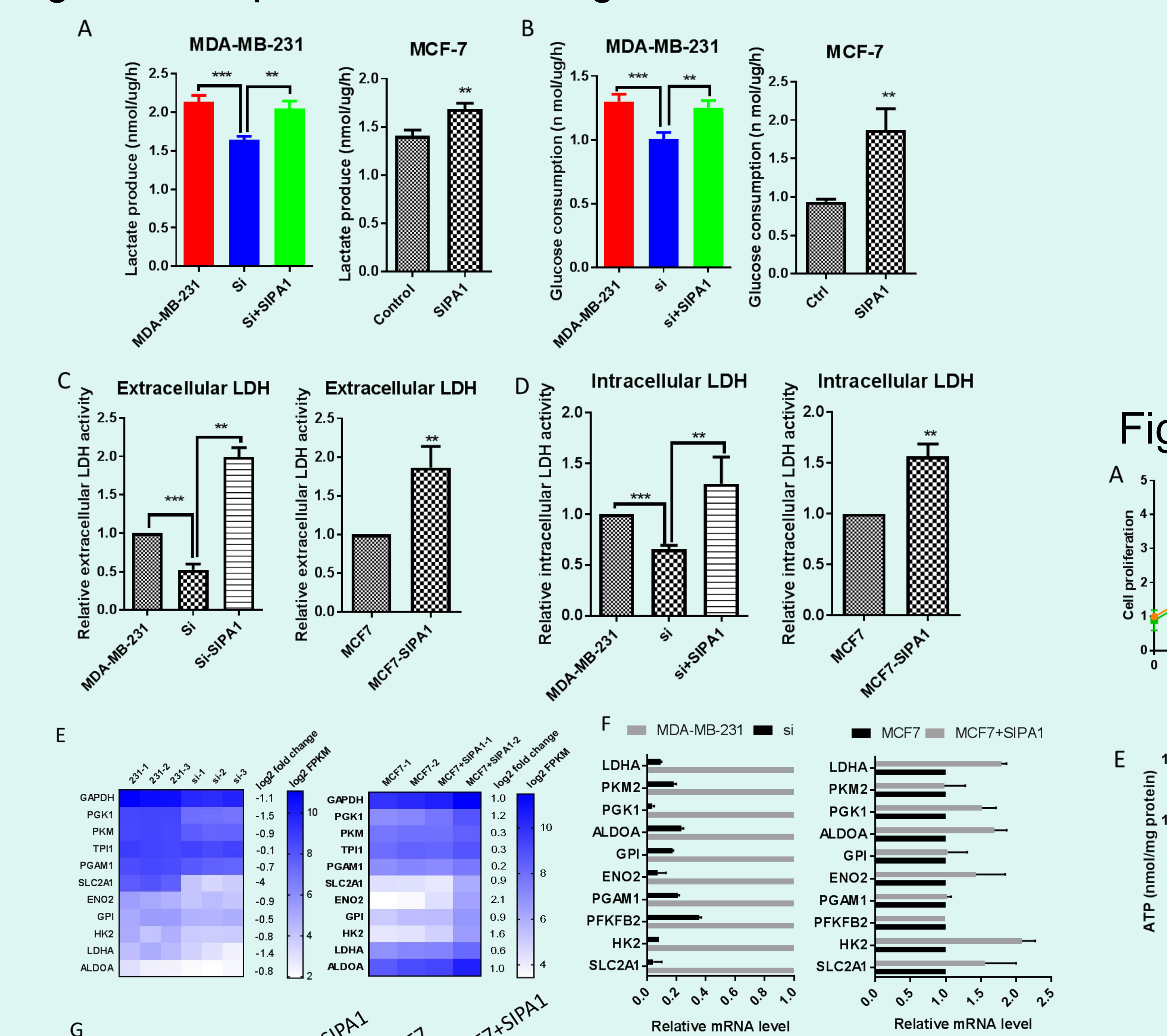


Fig.4 SIPA1 rewrites the ATP production by EPAS1/PDK1.

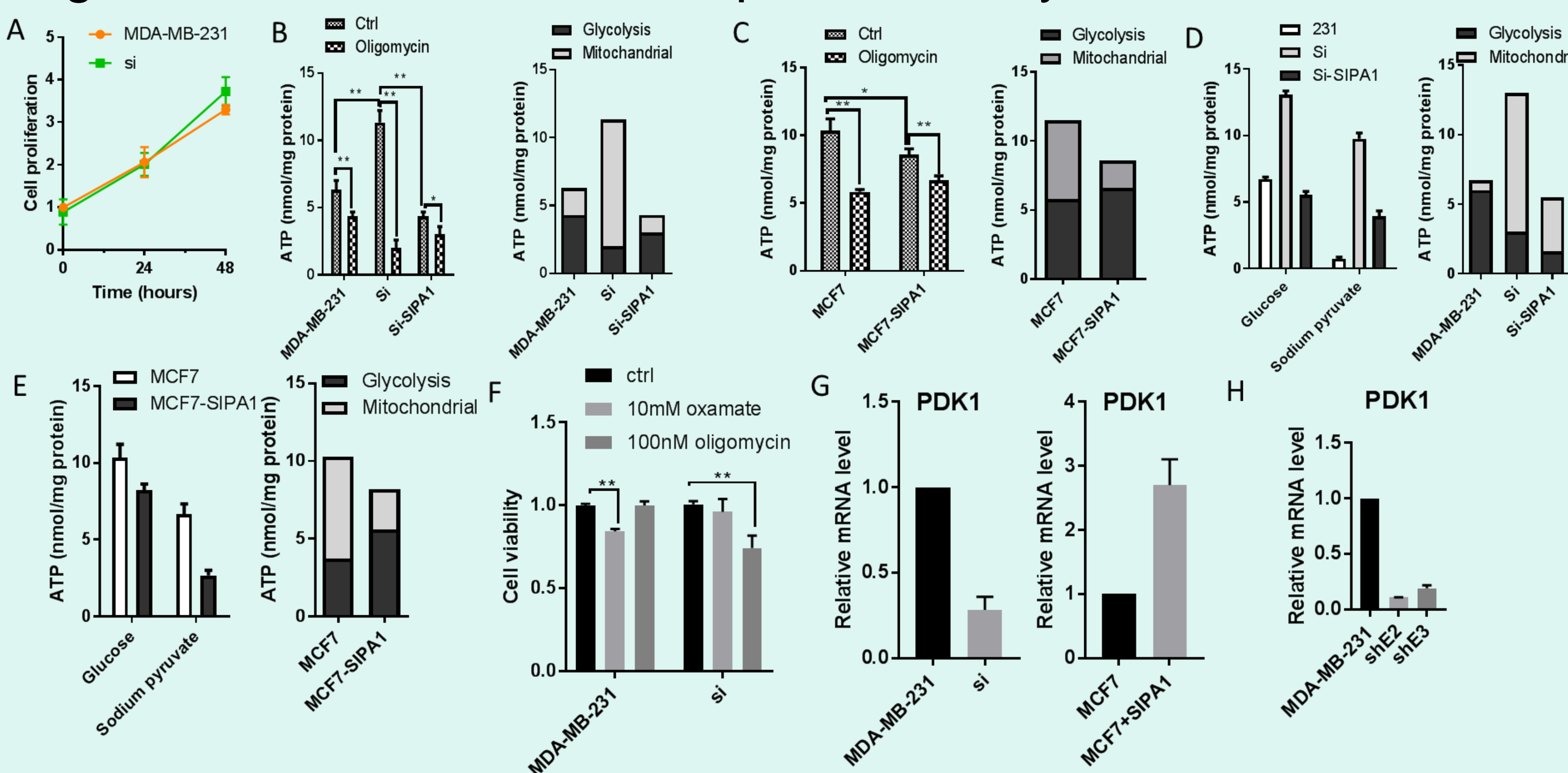


Fig.5 SIPA1 activates transcription of EPAS1 by binding to its promoter

