





**Supplementary information, Figure S10.** Smad5 shuttling could not regulate metabolism-related gene expression. (**A**) Long-term maintenance of extracellular pH through adjusting CO<sub>2</sub> levels leads to efficient accumulation of GFP-Smad5 in the nucleus (10% CO<sub>2</sub>) or the cytoplasm (0.5% CO<sub>2</sub>). Scale bar, 10 μm. (**B, C**) qRT-PCR analyses showing no obvious gene expression change after acute extracellular pH adjustment at 5%, 10% CO<sub>2</sub> and 0.5% CO<sub>2</sub> for 3, 6 or 12 hours. Data are presented as mean ±s.e.m of three independent experiments.