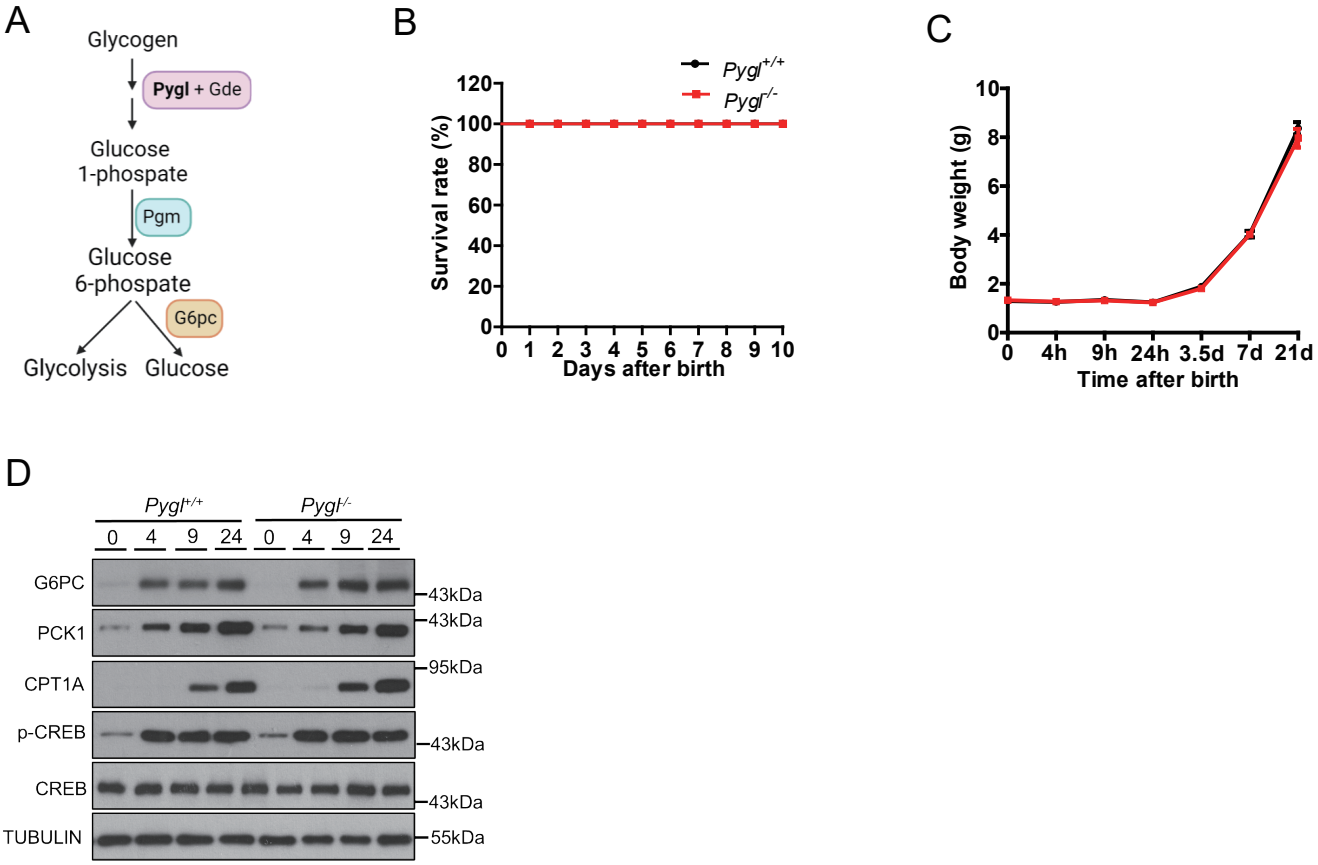Supplementary Fig. 2