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Original Article

α-ketoglutarate promotes the specialization of primordial germ cell -like cells through regulating epigenetic reprogramming

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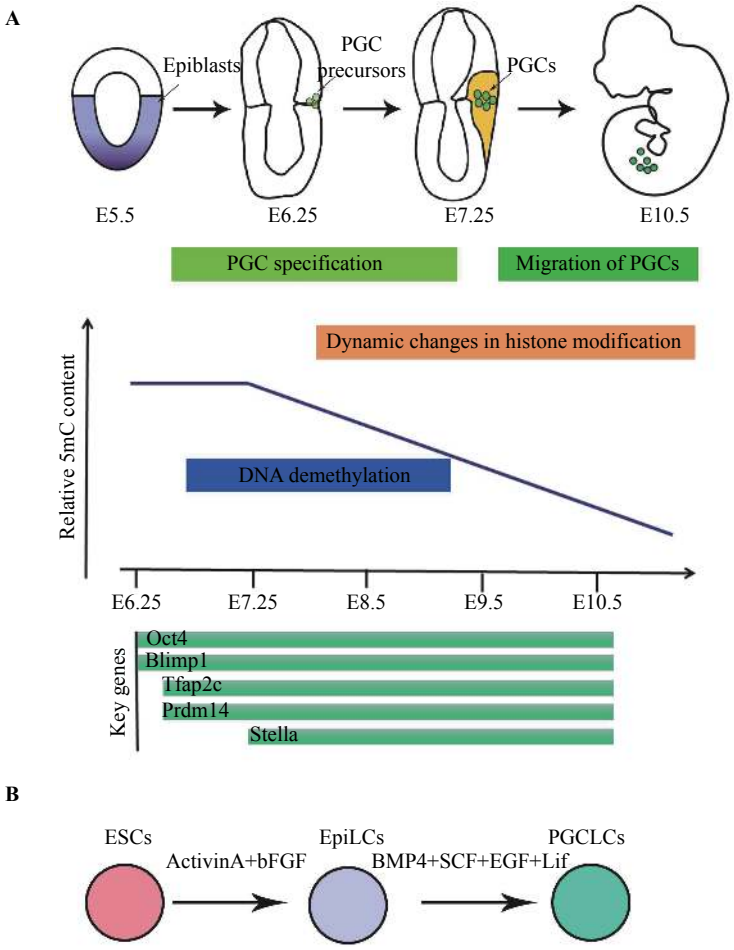

Supplementary Fig. 1 **Diagrams of the specification of mouse germ cells *in vivo* and *in vitro*.** A: A schematic diagram depicts the specification and development of the mouse germ cell lineage with the dynamic epigenetic changes and gene expression. B: A schematic diagram depicts *in vitro* PGCLC differentiation system.

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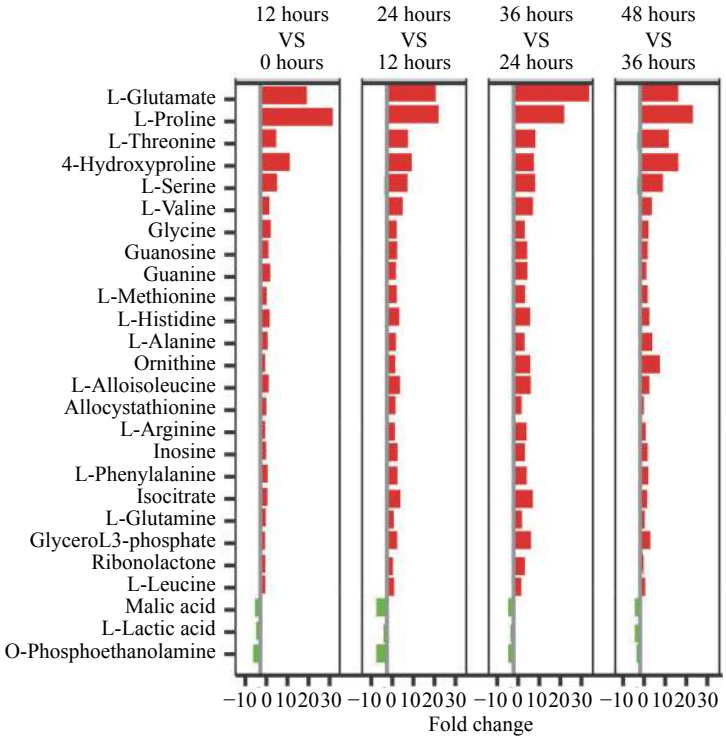
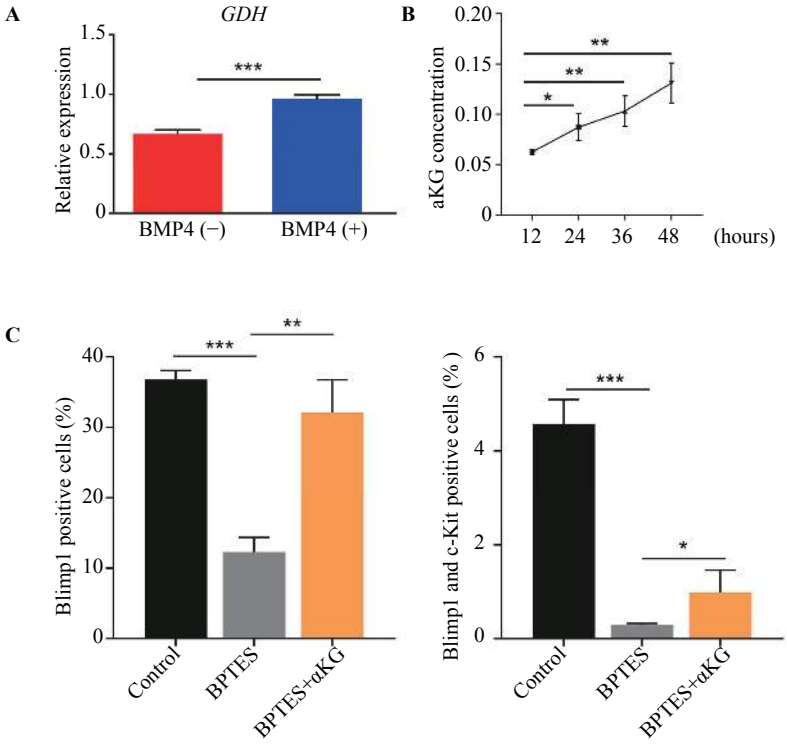
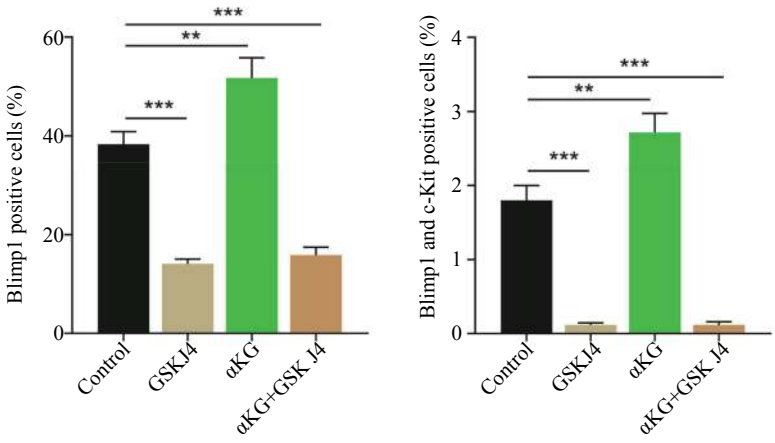


Supplementary Fig. 2 **Representative differential metabolites detected by mass spectrometry.** Representative differential metabolites showing significant changes stimulated by the signals of PGCLC differentiation from univariate statistical analysis. Red and green boxes represent fold increase and fold decrease detected in the metabonomics, respectively.



Supplementary Fig. 3 **Glutamate and αKG were required for PGCLC induction.** A: qRT-PCR analysis showed the mRNA expression level of *Glud1* in the 48-hour cell aggregates cultured in the presence or absence of BMP4. The relative expression is normalized to *Actin* and represented as mean ± SD from three biological replicates. B: Assay of αKG concentrations in the cell aggregates at the indicated time points during PGCLC differentiation. The unit of the Y-axis is nmol/μL. Data are represented as mean±SD from three biological replicates. $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$. C: Statistical analysis of the percentages of *Blimp1* positive cells or *Blimp1* and *c-Kit* double positive cells indicated in ***Fig. 2E***. Data are represented as mean ± SD from three biological replicates. $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$.



Supplementary Fig. 4 **H3K27me3 demethylation was essential for PGCLC specialization.** Statistical analysis of the percentages of *Blimp1* positive cells or *Blimp1* and *c-Kit* double positive cells indicated in *Fig. 4B*. Data are represented as mean±SD from three biological replicates. $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$.