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A network among TGFβ1/activin/nodal, FGF and Wnt pathways cooperate to maintain pluripotency and self-renew of rabbit embryonic stem cells

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Pluripotency and self-renew of embryonic stem cells (ESCs) is one important but not so clearly issue, which may depend on species difference with variant signaling pathways. Rabbit is one of good animal models for study of human physiological disorders and our previously report showed that the rabbit ESCs (rESC) more like primate ESCs than mouse ESCs. In the present study, regulation of pluripotency and self-renew in rESCs were tested with TGFβ, FGF, and Wnt signalings. Differentiation of the rESCs was precipitated when TGFβ/activin/nodal and FGF pathway were inhabited, and also decreased proliferation of the rESC. Down-regulation of betacatenin suggested Wnt pathway affected on the self-renewal of rESCs. The more study showed that inhibition of Wnt pathway resulted in differentiation of rESCs accompanied with down-regulation of phospho-Smad2/3 and up-regulation of phospho-Smad1/5, but did not effect on the expression of bFGF. Maintenance pluripotency of rabbit ESCs could be achieved with the combination of Activin, Nodal, or TGFβ1 plus bFGF and Noggin in feeder- and serum-free culture system. These findings indicated FGF and TGFβ pathways were essential for the pluripotency and proliferation of rESCs, which was similar to human ESCs. Our findings also suggested that there was a regulatory network among FGF, Wnt, and TGFβ pathway to regulate the pluripotency and selfrenew of rabbit ESCs.

***Keywords*:** rabbit embryonic stem cells, TGFβ1/activin/nodal and FGF pathway, WNT pathway, pluripotency, proliferation

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