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The Order of Differentiation Capacity in Rabbit Pluripotent Stem Cell is maintained even after Naïve-like Conversion

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Pluripotent stem (PS) cells are classified as 'naïve' when established from mouse or rat, or as 'primed' when established from non-rodent mammalian species. The greatest difference between these states is that naïve PS cells can differentiate into a germline lineage and create a chimeric individual when injected into preimplantation embryos, whereas primed PS cells cannot. Previously, we showed that the neural differentiation capacity of rabbit induced (i)PS cells *in vitro* was inferior to that of embryonic stem (ES) cells; however, naïve-like iPS cells differentiated more than did primed ES cells. Here we analyzed whether the differentiation capacity of rabbit ES cells could be improved by naïve-like conversion. To convert rabbit ES cells into the naïve-like state, they were transfected with a transgene driving h*OCT3/4* expression under the control of the EF1α promoter. These naïve-like rabbit ES cells produced domed colonies and could be maintained/passaged without the need for supplementation with fibroblast growth factor 2. We confirmed that they exhibited several features indicating pluripotency, including teratoma formation. Next, we assessed their capacity for differentiating *in vitro* into neural (oligodendrocyte) cells. The neural differentiation capacity of these naïve-like ES cells was much superior to naïve-like iPS cells. However, although they contributed efficiently to forming the inner cell mass of blastocysts, no chimeric pups were obtained. Thus, whereas naïve-like conversion in this system effectively improved the neural differentiation capacity of rabbit PS cells to be equivalent to that of the primed state, it could not improve their potential to form a true naïve state.