Derivation and characterization of LIF and FGF2 dependent Porcine Induced Pluripotent Stem Cells

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Authentic embryonic stem cells (ESC) have probably never been derived from the inner cell mass (ICM) of pig, despite over 25 years of effort. Recently, several groups, including ours, have reported derivation of induced pluripotent stem cells (iPSC) from swine by reprogramming somatic cells with a combination of four factors (OCT4, SOX2, KLF4, C-MYC) delivered by retroviral transduction. The piPSC resembled FGF2-dependent human (h) ESC and are likely to advance swine as a model in biomedical research, since grafts could potentially be matched to the animal that donated the cells for re-programming. The dependence of piPSC on FGF2 also draws parallels to murine pluripotent stem cells derived from advanced epiblast, so-called 'epiblast stem cells'. Indeed, an emerging concept is that there are two kinds of ESC, one dependent on FGF2 and not competent to contribute to germ-line chimeras, the other upon LIF and germ-line competent. The objective of our recent investigations has been to develop LIF-dependent piPSC by using the same reprogramming factors but selecting the colonies on a modified LIF- medium supplemented with two kinase inhibitors, CHIR99021, which inhibits GSK-3beta, and kenpaullone, which inhibits both GSK-3beta and CDK1. The LIF-dependent piPSC, derived here from outgrowths of umbilical cord mesenchyme, expressed markers consistent with pluripotency and bore a striking resemblance to ICM-derived murine ESC in colony morphology, culture characteristics, and short cell cycle time. Currently, the ability of LIF-piPSC to give rise to teratoma and chimeras is under investigation. Supported by Missouri Life Sciences Board Grant 00022147 and NIH grant HD21896.