

## Supplemental material 1 – Large domestic ruminants

Table describing isolation and characterization of iPSC from large domestic ruminants.

Author, year	Animal	Cell type	Reprogramming System	Supplementation	Days until colony	Differentiation	Reprogramming efficiency	Immunocytochemistry	Gene expression (endogenous)	Gene expression (exogenous)
Sumer, 2011	Bovine	Adult ear fibroblast	Retrovirus, hOSKM+ NANOG	LIF+ bovine bFGF	7-14 days	EB+ teratomas	0.000118%	OCT4, SSEA1	ALP1, REX1, OCT4, SOX2, NANOG, c-MYC, KLF4	OCT4, SOX2, NANOG, KLF4, C-MYC
Han, 2011	Bovine	Embryonic fibroblast	Retrovirus PMXs - bovine OCT4, SOX2, KLF4, MYC, LIN28, NANOG	LIF+ bFGF or bFGF (optimal)	+21 days	EB+ teratomas	0 - approx. 0.006%	SSEA1, NANOG, SOX2, weak for SSEA4, negative for TRA-1-60, TRA-1-81.	OCT4, SOX2, not NANOG	OCT4, SOX2, KLF4, MYC, LIN28, NANOG
Cao, 2012	Bovine	Fetal fibroblast (2.5-4m)	Lentivirus, hOCT4, pig Sox2, c-Myc, Klf4+GFP	LIF+bFGF	-	EB+teratoma+ induced differentiation into female germ cells	0.0002-0.0007%	OCT4, NANOG, SSEA1. NEGATIVE FOR SSEA3, SSEA4, TRA-1-60, TRA-1-81.	OCT4, KLF4, NANOG	OCT4, KLF4
Deng, 2012	Buffalo	Fetal fibroblasts	Retrovirus pMX, buffalo OSKM+NANOG+LIN28	bFGF+LIF	11-14 days	EB+Teratoma	-	AP, Oct4, Sox2, Nanog, SSEA-1, SSEA-4, TRA-1-81, and E-Cadherin	Oct4, Sox2, Nanog, STAT3, GP130, FOXD3, E-Cadherin, bFGF2, p53	Silenced in some cell lines
Wang, 2013	Bovine	Calf testicular cells	Electroporation of OCT4	LIF+BMP4	17 days	Induced differentiation and teratoma	0.3%	OCT4, NANOG, SOX2, SSEA-1, SSEA-4	OCT4, SOX2, MYC, KLF-4, MEF2a, SUZ12, STAT3, DNMT1	-
Kawaguchi, 2015	Bovine	Amniotic cells from a 50d gestation	PiggyBac Dox inducible transposon OSKM	Bovine LIF+FGF2 or bLIF, Mek/Erk inhibitor, GSK3 inhibitor and forskolin	8 days (primary colonies), 14 days (flattened colonies)	EB EB+ chimera	0.01%	OCT4, NANOG	OCT4, SOX2, NANOG, CDH1, REX1, ESRRB, STELLA, LIFR, SOCS3. FGF5 AND OTX2 ONLY IN PRIMED IPSCS.	OCT4-KLF, c-MYC
Talluri, 2015	Bovine	Fetal fibroblast	PiggyBac transposon - human OSKMNL	LIF+bFGF	14-17 days	EB+ teratoma		OCT4, SSEA1, SSEA3, WEAK FOR SSEA4	OCT4, SOX2, c-MYC, KLF4, NANOG, REX1, ALP, CDH1, STAT3. SALL, DPPA, SOCS.negative for Brachyuri, FGF5	-
Cravero, 2015	Bovine	Mamary epithelial cells and dermal fibroblasts	Retrovirus pMX, murine leukemia virus, mOSKM	LIF + bFGF	12 and 15 days	Teratoma, Partial differentiation into mammary cells	0.11 and 0,09%	OCT4, LIN28	OCT4, SOX2, NANOG, LIN28, REX1, C-MYC, KLF4	-
Bai, 2016	Bovine	Retinal neural stem cells	Lentivirus, bovine miR302/367	Valproic acid, with or without melatonin	4 days	Teratoma	Control: 19,24% Melatonin group: 41,25%	OCT4, NANOG	OCT4, SOX2, NANOG, miR-302a, miR302b, miR302c, miR302d miR-367	-
Zhao, 2017	Bovine	Fetal fibroblast	PiggyBac transposon bovine OSKM	LIF+bFGF	8 days	EB+ teratoma	-	OCT4, SOX2, SSEA3, SSEA4, CDH-1	OCT4 (weak), NANOG, SOX2, C-MYC, KLF4	-
Canizo 2018	Bovine	Embryonic fibroblast	Lentivirus	SB43 medium	16 days	Non-assessed	Non-assessed	Non-assessed	Non-assessed	-

iPSC: induced pluripotent stem cells; hOSKM: human Oct4, Sox2, KLF4, c-Myc; LIF: leukemia inhibitor factor; bFGF: basic fibroblast growth factor; EB: embryoid body; OCT4: octamer-binding transcription factor 4; SSEA-1: stage-specific embryonic antigen-1; AP: alkaline phosphatase; REX-1: ZFP-42; SOX2: Sex determining region Y-box 2; KLF4: Kruppel-like factor 4; c-MYC: MYC Proto-Oncogene; PMX: Moloney murine leukemia virus (MMLV); LIN28: Lin-28 Homolog A; NANOG: Nanog Homeobox; SSEA-4: stage-specific embryonic antigen-4; TRA-1-60: T cell receptor alpha locus; TRA-1-81: PODXL; GFP: green fluorescent protein; BMP4: Bone Morphogenetic Protein 4; MEF2a: Myocyte Enhancer Factor A; SUZ12: Polycomb Repressive Complex 2 Subunit; STAT3: Signal Transducer And Activator Of Transcription 3; DNMT1: DNA Methyltransferase 1; CDH1: Cadherin 1; ESRRB: Steroid hormone receptor ERR2; STELLA: Dppa3 or PGC7; LIFR: Leukemia Inhibitory Factor Receptor Alpha; SOCS3: Suppressor of cytokine

signaling 3; FGF5: Fibroblast Growth Factor 5; miR: microRNA; GP130: Interleukin 6  
Signal Transducer; FOXD3: Forkhead Box D3; P53: Tumor Protein P53.

## Supplemental material 2 – Small domestic ruminants

Table describing isolation and characterization of iPSC from small domestic ruminants.

Author, year	Animal	Cell type	Reprogramming System	Supplementation	Days until colony	Differentiation	Reprogramming efficiency	Immunocytochemistry	Gene expression (endogenous)	Gene expression (exogenous)
Bao, 2011	Ovine	Ear fibroblast (4w)	Lentiviral, Dox-inducible hOSKMNL +SV40 large t + hTERT	-	20 days	EB+teratoma	0,00041	OCT4, SOX2, NANOG, SSEA1, TRA-1-60, TRA-1-81, REX1, CDH1. Negative for SSEA3, SSEA4.	OCT4, SOX2, NANOG, TDGF1, ERAS, DNMT3B, DAX1, DPPA4, GDF3	Dox dependent
Ren, 2011	Goat	Ear fibroblast	Lentiviral, OSKM+ LIN28+ NANOG+ SV40 large t + hTERT	LIF+bFGF+eFGF	7 days	EB+teratoma	-	SSEA1, TRA-1-60, TRA-1-81, REX1, CDH1. Negative for SSEA3 E SSEA4.	OCT4, SOX2, NANOG, TDGF, REX1, DNMT3b, DAX1, CDH1	Dox dependent
Li, 2011	Ovine	Fetal fibroblast (40d)	Lentivirus Tet-on-inducible, mOSKM	hFGF2	+~14 days	EB+teratoma	-	OCT4, SOX2, NANOG, SSEA4. Negative for SSEA1, SSEA3, TRA-1-60, TRA-1-81	SOX2, NANOG	OCT4, SOX2, C-MYC, KLF4
Sartori, 2012	Ovine	Embryonic fibroblasts (30d)	Retrovirus, pMXs -mOSKM	bFGF	8 days	EB+ teratoma+ chimera	-	NANOG. Negative for SSEA1 AND SSEA4.		Silencing of SOX2, c-MYC and/or KLF4 at most lines at passage 7, but residual expression of OCT4
Liu, 2012	Ovine	Fetal fibroblasts (33,5d)	Retrovirus, pMX human OSKM	bFGF + LIF	<15 days	EB+teratoma + contribution to blastocysts	0,001875%	OCT4, NANOG	OCT4, SOX2	Silenced at p17
Song, 2013	Goat	Fetal ear fibroblasts	Lentivirus, hOSKM	bFGF	6-7 days	EB+ teratoma	-	OCT4, NANOG	OCT4, SOX2, C-MYC, low NANOG and KLF4.	Silenced at passage 15
Chu, 2015	Goat	Embryonic fibroblasts (60d)	Lentivirus, hOSKM OR PRMT5+OSKM	bFGF+LIF+ N2+B27+ascorbic acid+ PD99023+ CHIR99021	7 days	EB+ spontaneous differentiation	-	SSEA1, SSEA4, C-MYC, OCT4		
Tai, 2015	Goat	Fetal fibroblast (40d)	Tet-on-inducible lentivirus, mOSKM	LIF, LIF+VC, LIF+VPA+LIFL, LIF+VC+VPA+LIFL	7 days	EB+teratoma	0,00009-0,00045%	OCT4, SOX2, NANOG, SSEA1, TRA-1-60, TRA-1-81. Negative for SSEA3, SSEA4	OCT4, SOX2, NANOG, KLF4, LIN28, REX1, PODXL, DNMT3B	Dox-inducible
German, 2015	Ovine	Fetal fibroblasts	Retrovirus, pMXs, mOSKM	bFGF		EB+cloned blastocysts	-	OCT4, FGFR2. Negative for NANOG, GATA3, CDX2	SOX2, OCT4, COL1A1.	OCT4, SOX2, C-MYC, KLF4
Sandmaier, 2015 <sup>[1]</sup>	Goat	Fetal fibroblasts	Pseudovirus, bovine OKSMNL + MIR302/367	LIF+2i or bFGF or bFGF in SNL feeders		spontaneous differentiation (extra-embryonic and neuronal lineages) +teratoma	-	OCT4, SOX2, NANOG	OCT4, SOX2, KLF4	NANOG was silenced, OCT4 was expressed in most lineages
Song, 2016	Goat	Transgenic - lactoferrin and normal ear fibroblast	Lentivirus, hOSKM	bFGF	6-7 days	EB+teratoma + cloned cleaved embryos	0,000276 (tg) and 0,000988% (non tg)	OCT4, NANOG, AKP	NANOG, OCT4, SOX2, MYC	
Chen, 2017	Goat	Embryonic fibroblasts	Exogenous mRNA OSKM	FGF2	15 days	EB+ spontaneous differentiation	-	OCT4, SOX2, KLF4, C-MYC, NANOG, REX1, SSEA-1, TRA-1-60, TRA-1-81.	OCT4, SOX2, NANOG, DAX1, GDF3	Non applicable

iPSC: induced pluripotent stem cells; hOSKMNL: human Oct4, Sox2, KLF4, c-Myc, Nanog, Lin28; SV40: Simian virus 40; hTERT: Telomerase Reverse Transcriptase; EB: embryoid body; OCT4: octamer-binding transcription factor 4; SSEA-1: stage-specific embryonic antigen-1; AP: alkaline phosphatase; REX-1: ZFP-42 (Zinc Finger Protein 42 Homolog); SOX2: Sex determining region Y-box 2; KLF4: Kruppel-like factor 4; c-MYC: MYC Proto-Oncogene; SSEA-1: stage-specific embryonic antigen-1; TRA-1-60: T cell receptor alpha locus; TRA-1-81: PODXL; CDH1: Cadherin 1; SSEA-3: stage-specific embryonic antigen-3; SSEA-4: stage-specific embryonic antigen-4; TGDF1: Teratocarcinoma-Derived Growth Factor 1; ERAS: GTPase ERas; DNMT3B: DNA

Methyltransferase 3 Beta; DAX1: dosage-sensitive sex reversal, adrenal hypoplasia critical region, on chromosome X, gene 1; DPPA4: Developmental Pluripotency Associated 4; GDF3: Growth Differentiation Factor 3; OSKM: Oct4, Sox2, KLF4, c-Myc; LIF: leukemia inhibitor factor; bFGF: basic fibroblast growth factor; eFGF: epidermal growth factor; m OSKM: mouse Oct4, Sox2, KLF4, c-Myc; LIN28: Lin-28 Homolog A; NANOG: Nanog Homeobox; PMX: Moloney murine leukemia virus (MMLV); PMRT5: Protein Arginine Methyltransferase 5; B-27: neuronal cell culture supplement; N2: chemically-defined, serum-free supplement based on Bottenstein's N-1 formulation; PD99023: Piperonyl butoxide; VC: vitamin C; LiCl: Lithium chloride; CHIR99021: GSK3 inhibitor; VPA: Valproic acid; GATA3: GATA Binding Protein 3; SNL: feeder cells from the STO cell line, transformed with neomycin resistance and LIF genes; FGF2: Fibroblast Growth Factor 2; COL1A1: Collagen Type I Alpha 1 Chain; CDX2: Caudal Type Homeobox 2; 2i: PD 0325901 (MEK inhibitor) and CHIR 99021 (GSK3 inhibitor); GDF3: Growth Differentiation Factor 3; miRNA: microRNA.

## Supplemental material 3 – Swine

Table describing isolation and characterization of iPSC from swine.

Author, year	Animal	Cell type	Reprogramming System	Supplementation	Days until colony	Differentiation	Reprogramming efficiency	Immunocytochemistry	Gene expression (endogenous)	Gene expression (exogenous)
Esteban, 2009	Pig	Embryonic fibroblast	Retrovirus pMX, mOSKM or hOSKM	bFGF	8-10 days	Teratoma	-	AP, SSEA4 (weak), NANOG, REX1	endoSOX2, NANOG, Lin28	Present
Ezashi, 2009	Pig	Fetal fibroblast	Lentivirus, hOSKM	bFGF, 5-AZA	22 days	EB+teratoma	-	AP, SSEA1, OCT4, NANOG, SOX2	OCT4, NANOG, SOX2, TDGF1, TERT	Present
Wu, 2009	Pig	Primary ear fibroblast Primary bone marrow cells	Lentivirus, human OCT4, SOX2, KLF4, MYC + LIN28, NANOG (or not) + rTA		7 days	EB+teratoma	-	AP, SSEA3, SSEA4, TRA-1-60 TRA-81, CDH1, NANOG, REX	OCT4, SOX2, NANOG, DNMT3b, LIN28, CDH1	Not applicable
West, 2010	Pig	Bone marrow MSCs	Lentivirus, hOSKM + Lin28 + Nanog	bFGF	7 days	EB+ chimeric embryos and piglets, contribution to embryo and placenta	-	AP, OCT4, SOX2	OCT4	Not silenced - expression of human OCT4
Telugu, 2010	Pig	Fetal fibroblast	episomal Human OSKM+Nanog + Lin-28 + mouse c-Myc	LIF-based 2i medium 1uM VPA 2d of 5-aza after reprogramming	First passage at day 30	teratoma	-	AP, OCT4, SSEA1, SSEA4, pSTAT3	OCT4, SOX2, NANOG	Evidence of integration or persistence of episomal vectors
Ruan, 2011 <sup>[2]</sup>	Pig	Embryonic fibroblast	Retrovirus pMX, hOSKM	bFGF	10-14 days	EB+ teratoma	-	OCT4, SOX2, SSEA3, SSEA4, TRA-1-60	LIN28, SOX2, NANOG	Present
Montserrat, 2011	Pig	Adult fibroblast (ear)	Retrovirus, pMX hOSKM + GFP or pCAG-OSKM-GFP	bFGF+LIF	9 days (retrovirus ) 7 days	EB, in vitro induced differentiation (cardiomyocyte like) + Teratoma	-	AP, NANOG, TRA-1-60, SSEA4	-	Plasmid integration was confirmed. Not silence
Montserrat, 2012 <sup>[3]</sup>	Pig	Adult fibroblast (ear)	Retrovirus, pMX mSKM + orange or OSKM+GFP	bFGF+LIF	8 days	EB, in vitro induced differentiation + Teratoma	-	AP, SSEA4, TRA-1-60, TRA-1-81, NANOG for SKM; SSEA3, NANOG for OKSM	OCT4, SOX2	Present
Thomson, 2012	Pig	Embryonic fibroblasts	retrovirus - mouse pMXs-OSKM	LIF or bFGF	-	teratoma	-	LIF or bFGF: AP LIF: OCT4, NANOG, SSEA1, SSEA4.	OCT4, NANOG, SOX2, KLF4, KLF5	Present
Rodriguez, 2012	Pig	Fetal fibroblasts	FUW-tETO hOSKM	LIF then LIF+2i or LIF+3i	6-7 days	EB	-	AP, OCT4, NANOG, Some colonies SSEA1	OCT4, NANOG, SOX2, KLF4, NODAL, FGF5, SOME COLONIES: STELLA, REX1	Present
Hall, 2012 <sup>[4]</sup>	Mini pig	Primary embryonic fibroblast	Tet-on hOSKM + nanogP8	bFGF	7 days	EB	-	OCT4, NANOG, SOX2 (early passages), KLF4 (mosaic), c-MYC (one line). SSEA3, SSEA4 varied	varied between lines	Silenced at p10 (2 cell lines) Silenced at >p20
Cheng, 2012	Pig	Embryonic fibroblasts	Retrovirus - pbxs mouse OSKM	bFGF, LIF + bFGF or LIF + bFGF+VPA	6-8 days	EB +teratoma+ chimeric blastocyst	bFGF 0,12% bFGF+LIF 0,77% bFGF+LIF+VPA 2,7%	AP, NANOG, SSEA1, -4, TRA_1-60, TRA-1-81	OCT4, SOX2, NANOG, TERT	Downregulated after p30 but not silenced
Liu, 2012 <sup>[5]</sup>	Pig	Embryonic mesenchymal stem cell	Retrovirus - pMX porcine KLF4 and OCT4	LIF, 5i	16-20 days	EB	-	OCT4, SSEA1, Nanog Weak or negative SSEA4, TRA-1-81	-	Silenced
Park, 2013 <sup>[6]</sup>	Pig	Embryonic fibroblast	mouse pCX-OKS-2A, pCX-cMyc (episomes)	bFGF + SCF	2-3 weeks	EB	-	AP, Oct4, Sox2, Nanog, SSEA4, TRA-1-60, TRA-1-81	OCT4, SOX2, NANOG, TDGF1, REX1, bFGF, FGFR1, FGFR2, AA, Nodal	Silenced, integration detected
Fujishiro, 2013	Pig	Embryonic fibroblast	retrovirus, hOSKM	pLIF + forskolin	2 weeks	Teratoma + chimera (Contribution to ICM and TE in embryos and contribution in fetuses)	-	AP, STAT3, OCT4, NANOG, SSEA1, 3, CDH-1, ERAS, Low levels or negative for SSEA4, TRA-1-60 and -81		Not silenced
Kues, 2013	Pig	OCT4-GFP fetal fibroblasts	Electroporation Sleeping beauty transposon - mOSKM	bFGF	10-14 days	Teratoma + In vitro differentiation into neural lineage	-	OCT4, NANOG. Heterogenous SSEA1 and TRA-1-60	OCT4, SOX2, UTF1, SALL4, ESSRB, REX1, DPPA5, TERT. TEM	Silenced

Ji, 2013	Pig	Newborn ear fibroblasts, bone marrow cells, embryonic fibroblasts, adult fibroblasts	Retrovirus human OSKM, mouse OSKM, porcine OSKM, monkey OSKM or porcine OSKM				Teratomas differed between lines	-	AP, OCT4 expression and NANOG expression. SSEA1, SSEA23/4, TRA-1-60 and TRA1-1-81 showed different results between lines	Nanog, Sox2, KLF4	fetal fibroblast, LIF) showed silencing and then re-activation of exogenous factors. Cell lines (68 and 102) (monkey OSKM, bFGF+LIF+2i) showed silencing
Kwon, 2013	Mini pig	Ear fibroblasts	Lentivirus human OSKMNL	LIF + bFGF			EB+ teratoma	-	AP, OCT4, NANOG, SSEA1		Silenced
Choi, 2016 <sup>[7]</sup>	Pig	Fetal fibroblasts	Lentiviral Tet-On human OSKM	LIF, and after establishment: LIF, LIF+2i or bFGF	2 weeks		EB	-	AP, OCT4, SOX2, SSEA1 and SSEA4 varied regarding supplementation	OCT4, SOX2, KLF4, NANOG, REX1, CDH1, EpCAM, OCLN	Not applicable
Petkov, 2016	Pig	OCT4-GFP fetal fibroblasts	Sleeping beauty transposon - porcine OSKM+porcine NANOG+human LIN28	SAHA, VPA, NaB, AA or LIF and AA	12 days		Contribution to embryo development, immature teratoma	-	AP, SSEA1	OCT4, SOX2, NANOG, TERT, ZFP42, UTF1, CHD1, c-Myc, KLF4, KLF5, EpCAM, ESRRB, CDH1, TDH.	Silenced in one line; Downregulated but not silenced.
Chakritbudsabong, 2017	Pig	Embryonic fibroblasts	Retrovirus pMX hOSKM + lin28	LIF+bFGF	5 dias		EB+ spontaneous cardiac differentiation +teratoma	-	AP, OCT4, SOX2, SSEA1	SOX2, NANOG	Continuous expression of SOX2 and LIN28
Secher, 2017	Pig	Venus-expressin neonatal fibroblasts	Lentivirus TetO-pOSKM	LIF +2i or bFGF+2i	1 <sup>st</sup> passage as 17 days		EB+ chimera+ teratoma (only + for LIF+2i)	-	NANOG, SSEA3. LIF iPSCs presented SSEA4	OCT4, KLF4, c-MYC, NANOG, LIN28, NROB1	
Li, 2018	Pig	Fetal fibroblasts	Electroporation - episomes pCXLE-hOCT3/4-shp53, pCXLE-hSK; pCXLE-hUL	bFGF+2i	13 days		EB+ c Contribution to ICM and TE 48h after injection into parthenotes	-	NANOG, OCT4, SOX, SSEA1	OCT4, SOX2, NANOG,	Presence of pCXLE-sSK and pCXLE-hUL at 20p. After sub cloning at 20p, several lines were transgene free
Zhang, 2018	Pig	Embryonic fibroblasts	Retrovirus pMX pOSKM	LIF+2i with or without Albumax	First passage at 30d		EB + teratoma + contribution to parthenotes	Albumax 24.96% Control: 12.85%	AP, OCT4, SOX2, SSEA-1, NANOG		
Canizo, 2018	Pig	Embryonic fibroblasts	Lentivirus, hOSKM	SB medium, bFGF	5 days		-	-	AP, NANOG, SOX2, SSEA1, SSEA4, TRA-1-81	OCT4, KLF4, NANOG, NODAL	Present

iPSC: induced pluripotent stem cells; PMX: Moloney murine leukemia virus (MMLV); hOSKM: human Oct4, Sox2, KLF4, c-Myc; mOSKM: mouse Oct4, Sox2, KLF4, c-Myc; bFGF: basic fibroblast growth factor; EB: embryoid body; SSEA-1: stage-specific embryonic antigen-1; AP: alkaline phosphatase; NANOG: Nanog Homeobox; REX-1: ZFP-42; endo SOX2: endogenous Sex determining region Y-box 2; LIN28: Lin-28 Homolog A; TDF1: Teratocarcinoma-Derived Growth Factor 1; TERT: Telomerase Reverse Transcriptase; DNMT3B: DNA Methyltransferase 3 Beta; TRA-1-60: T cell receptor alpha locus; TRA-1-81: PODXL; CDH1: Cadherin 1; MSCs: mesenchymal stem cells; c-MYC: MYC Proto-Oncogene; VPA: Valproic acid; SSEA-4: stage-specific embryonic antigen-4; STAT3: Signal Transducer And Activator Of Transcription 3; LIF: leukemia inhibitor factor; mSKM: mouse Sox2, KLF4, c-Myc; OSKM: Oct4, Sox2, KLF4, c-Myc; 2i: PD 0325901 (MEK inhibitor) and CHIR 99021 (GSK3 inhibitor); 3i: PD 0325901 (MEK inhibitor), CHIR 99021 (GSK3 inhibitor) and SU 5402 (FGFR inhibitor); FGF5: Fibroblast Growth Factor 5; STELLA: Dppa3 or PGC7; REX-1: ZFP-42; 5i: small molecules (PD 0325901 (MEK inhibitor), CHIR 99021 (GSK3 inhibitor), forskolin, SB43152 (Activin/BMP/TGF- $\beta$  pathway inhibitor), and sodium butyrate); pCX-OKS-2A: vector

encoding three transcription factors (Oct3/4, Sox2 and Klf4) connected with 2A self-cleaving peptide (2A); pCX-c-Myc: vector encoding c-Myc; ICM: inner cell mass; TE: trophectoderm; SCF: Stem Cell Factor; FGFR1: Fibroblast growth factor receptor 1; FGFR2: Fibroblast growth factor receptor 2; ERAS: ES Cell Expressed Ras; UTF1: Undifferentiated embryonic cell transcription factor 1; SALL4: Sal-like protein 4; ESRRB: Steroid hormone receptor ERR2; DPPA5: Developmental Pluripotency Associated 5; OSKM: Oct4, Sox2, KLF4, c-Myc; OSKMN: Oct4, Sox2, KLF4, c-Myc, Nanog; EpCAM: Epithelial Cell Adhesion Molecule; OCLN: Occludin; AA: Activin A, SAHA: Epigenetic modifier; NaB: sodium butyrate (histone deacetylase inhibitor); ZFP-42: Zinc Finger Protein 42 Homolog; KLF5: Kruppel-like factor 5.

## Supplemental material 4 – Horses

Table describing isolation and characterization of iPSC from horses.

Author, year	Cell type	Reprogramming System	Supplementation	Days until colony	Differentiation	Reprogramming efficiency	Immunocytochemistry	Gene expression (endogenous)	Gene expression (exogenous)
Nagy, 2011	Fetal fibroblast	PiggyBac transposon, mOSKM	LIF+bFGF +2i+A8301+ Thiazovivin+SB431542	17-18 days	EB+teratoma	0.028%	AP, NANOG, SSEA1, SSEA4, TRA-60, TRA1-81	Oct4, Nanog, Klf4	
Khodadadi, 2012	Adult fibroblast	PMX hOSK	LIF+ bFGF+ eFGF	8-10 days	EB+teratoma	-	AP, OCT4, NANOG, SSEA1, SSEA4	OCT4, SOX2, NANOG, STAT3	OCT4, SOX2, KLF4, C-MYC
Breton, 2013	Foal fibroblast	PMX, mOSKM	LIF+bFGF	9 days	EB+teratoma	-	AP, OCT4, SOX2, NANOG, REX1, TRA1-60, SSEA1, SSEA4, LIN28	OCT4, SOX2, LIN28, NANOG, DNMT3B, REX1	OCT4, C-MYC
Whitworth, 2014	Adult fibroblast	Lentivirus, hOSKM	LIF	-	EB+ in vitro teratoma assay	-	AP, NANOG, REX1, SSEA4, TRA1-60, TRA1-81	NANOG, OCT4, TERT	OCT4, SOX2
Sharma, 2014	Foal keratinocytes	PMX, mOSKM	LIF	5 days	EB+teratoma + neuronal differentiation	0.18%	AP, OCT4, SOX2, LIN28, SSEA1	OCT4, SOX2, LIN28, NANOG, DNMT3B, REX1	OCT4, SOX2, KLF4, C-MYC
Quattrocchi, 2016	Myogenic angioblast and peripheral mesenchymal stem cells	Retroviral pMX, hOSKM	bFGF	-	Teratoma + in vitro spontaneous differentiation	0.0001%	AP, OCT4, SOX2, NANOG, LIN28	OCT4, SOX2, NANOG, LIN28	Silenced
Lee, 2016	Adult eAdMSC	Lentivirus TetO, mOSKM	LIF	15-16 days	EB+teratoma+ myogenic differentiation (in vivo- mice)	0.003%	AP, OCT4, SOX2, NANOG, SSEA1,	OCT4, SOX2, NANOG, LIN28, REX	-
Moro, 2018	Adult fibroblast	Lentivirus, hOSKM	LIF + bFGF	10-12 days	EB+ spontaneous differentiation in vitro	-	AP, OCT4, SOX2, C-MYC	OCT4, REX1, NANOG	-
Pessôa, 2019	Adult fibroblast and adipose tissue mesenchymal cells, umbilical cord tissue	Lentivirus, hOSKM	bFGF	11-15 days	EB+ spontaneous differentiation in vitro	-	AP, OCT4	OCT4, NANOG	Present

iPSC: induced pluripotent stem cells; 2i: PD 0325901 (MEK inhibitor) and CHIR 99021(GSK3 inhibitor); A8301: Activin/NODAL/TGF- $\beta$  pathway inhibitor; SB31542: Activin/BMP/TGF- $\beta$  pathway inhibitor; EB: embryoid body; AP: alkaline phosphatase; NANOG: Nanog Homeobox; SSEA-1: stage-specific embryonic antigen-1; TRA-1-60: T cell receptor alpha locus; TRA-1-81: PODXL; OCT4: octamer-binding transcription factor 4; KLF4: Kruppel-like factor 4; PMX: Moloney murine leukemia virus (MMLV); hOSK: human Oct4, Sox2, KLF4; LIF: leukemia inhibitor factor; bFGF: basic fibroblast growth factor; eFGF: epidermal growth factor; REX-1: ZFP-42 (Zinc Finger Protein 42 Homolog); SOX2: Sex determining region Y-box 2; LIN28: Lin-28 Homolog A; SSEA-4: stage-specific embryonic antigen-4; DNMT3B: DNA Methyltransferase 3 Beta; TERT: Telomerase Reverse Transcriptase; hOSKM: human Oct4, Sox2, KLF4, c-Myc; mOSKM: mouse Oct4, Sox2, KLF4, c-Myc.



## Supplemental material 5 – Dogs

Table describing isolation and characterization of iPSC from dogs.

Author, year	Cell type	Reprogramming System	Supplementation	Days until colony	Differentiation	Reprogramming efficiency	Immunocytochemistry	Gene expression (endogenous)	Gene expression (exogenous)
Shimada, 2010	embryonic fibroblast	Retrovirus, predicted canine OSKM	LIF+bFGF+2i+ valproic acid+ A8301	7 days	Direct differentiation	-	AP, Oct3/4	-	-
Luo, 2011	Adult testicular fibroblast	Lentivirus, hOSKM	LIF+bFGF	6-8 days	EB	-	OCT4, SOX2, NANOG, LIN28, TRA-1-60, SSEA4	SOX2, c-MYC, LIN-28, SOCS3, STAT3, GBX2	Expressed in different levels
Lee, 2011	Adult fibroblast	lentivirus, hOSKM	LIF+bFGF	12-15 days	EB/Teratoma	Fibro: +- 0.84% cAdMSC: +- 1.74%	AP, Oct-4, Sox2, Nanog, TRA-1-60, SSEA-4	Oct-4, Sox2, Nanog	-
Whitworth, 2012	Adult dermal fibroblast	Lentivirus, hOSKMLN	LIF	12 days	EB/teratoma	0.0007%	AP, Oct4, SSEA1, SSEA4, TRA1-60, TRA1-81, Rex1	Oct4, Nanog, Telomerase	"barely detectable or absent"
Koh, 2013	Adult skin fibroblast	Retrovirus, mOSKM	LIF+bFGF	7-9 days	EB direct differentiation /Teratoma	-	AP, SSEA1	OCT4, SOX2, NANOG, LIN28, PODXL, FGF5, REX1, LAMP1, TERT, partial DPPA5	"Not fully silenced"
Baird, 2015	Adult aneuploidy cAdMSC	Retrovirus, hOSKM +GFP	LIF+bFGF	+ 3 days	EB	-	AP, Oct - 4, TRA - 1 - 60, TRA - 1 - 81, SSEA - 4	-	Silenced (absent GFP expression)
Nishimura, 2017	embryonic fibroblast	Lentivirus, mOSKM	Feeder free, bFGF	5 days	EB/ no teratoma	0.048%	OCT4, NANOG, SSEA4	OCT3/4, C-MYC, KLF4, SOX2, GBX2, NANOG	Expressed
Gonçalves, 2017	Fetal fibroblast	Lentivirus, mOSKM, hOSKM, mOSKM+hOSKM	bFGF	11 days	EB/teratoma	-	AP, OCT4, SOX2	OCT4, SOX2	Silenced on hOSKM ciPS, present on mOSKM ciPS
Chow, 2017	Adult skin fibroblasts	Sendai virus, OSKM	Lif	-	EB/Teratoma induction into mesenchymal lineage	-	OCT3/4, NANOG, CD105		Non- integrative
Tsakamoto, 2018	Embryonic fibroblasts	Sendai virus SeVdp, hOSKM	LIF+bFGF	7 days	EB/ Teratoma	0.02%	AP, NANOG, SSEA1, TRA-1-60 (partially)	OCT4, SOX2, NANOG	Non-integrative

iPSC: induced pluripotent stem cells; OSKM: Oct4, Sox2, KLF4, c-Myc; LIF: leukemia inhibitor factor; bFGF: basic fibroblast growth factor; 2i: PD 0325901 (MEK inhibitor) and CHIR 99021(GSK3 inhibitor); A8301: Activin/NODAL/TGF- $\beta$  pathway inhibitor; AP: alkaline phosphatase; OCT3/4: octamer-binding transcription factor 3/4; hOSKM: human Oct4, Sox2, KLF4, c-Myc; EB: embryoid body; OCT4: octamer-binding transcription factor 4; SOX2: Sex determining region Y-box 2; NANOG: Nanog Homeobox; LIN28: Lin-28 Homolog A; TRA-1-60: T cell receptor alpha locus; SSEA-4: stage-specific embryonic antigen-4; REX-1: ZFP-42 (Zinc Finger Protein 42 Homolog); SOCS3: Suppressor of cytokine signaling 3; STAT3: Signal Transducer And Activator Of Transcription 3; TRA-1-81: PODXL; GBX2: Gastrulation Brain Homeobox 2; cAdMSC: canine adipose derived mesenchymal cells; TERT: Telomerase Reverse Transcriptase; DPPA5: Developmental Pluripotency Associated 5; SSEA-1: stage-specific embryonic antigen-1; FGF5: Fibroblast Growth Factor 5; LAMP1: Lysosomal Associated Membrane Protein 1.

## Supplemental material 6 – Rabbits

Table describing isolation and characterization of iPSC from rabbits.

Author, year	Cell type	Reprogramming System	Supplementation	Days until colony	Differentiation	Reprogramming efficiency	Immunocytochemistry	Gene expression (endogenous)	Gene expression (exogenous)
Honda, 2010	Adult liver and stomach cells	Lentiviral, hOSKM	bFGF+ mLif	8-15 days	EB+ induced differentiation+ teratoma	0.55% 0.25%	AP, SSEA1, SSEA4, OCT3/4, NANOG	OCT4, SOX2, KLF4, c-MYC	silenced
Osteil, 2013	Adult fibroblast	Retroviral, hOSKM	bFGF	-	EB+ teratoma	-	AP, OCT4	OCT4, NANOG	silenced
Phakdeedindan, 2018	Embryonic fibroblast	Retroviral, hOSKM	LIF+bFGF	4 days	EB+ Teratoma + Cardiac differentiation	0.191%	AP, OCT-3/4, SSEA-4	OCT3/4, NANOG, SOX2, KLF4	silenced

iPSC: induced pluripotent stem cells; bFGF: basic fibroblast growth factor; mLIF: mouse leukemia inhibitor factor; AP: alkaline phosphatase; OCT3/4: octamer-binding transcription factor 3/4; SSEA-1: stage-specific embryonic antigen-1; SSEA-4: stage-specific embryonic antigen-4; EB: embryoid body; NANOG: Nanog Homeobox; KLF4: Kruppel-like factor 4; c-MYC: MYC Proto-Oncogene; LIF: leukemia inhibitor factor.

## Supplemental material 7 – Avian

Table describing isolation and characterization of iPSC from avian species.

Author, year	Animal	Cell type	Reprogramming System	Supplementation	Days until colony	Differentiation	Reprogramming efficiency	Immunocytochemistry	Gene expression (endogenous)	Gene expression (exogenous)
Lu, 2012	Quail	Embryonic fibroblast	Lentivirus, hOSKMNL	bFGF	17 days	EB+neural differentiation+ chimera	-	AP, POU5F1, SOX2	-	OCT4, SOX2, c-MYC, LIN28, NANOG
Rosselló, 2013	Zebra finch, chicken and quail	Embryonic fibroblast	Lentivirus, mOSKM (Stemcca)	LIF+ bFGF+ 3i	5 days	EB + teratoma + chimera	-	AP, SSEA1	Oct4, Sox2, c-Myc, Nanog, Vasa	Silenced: Chicken, Present: quail, zebra finch
Yu, 2014	Chicken	Embryonic fibroblast	Mini circle DNA, hOSLN	bFGF	2 weeks	EB + chimera	-	AP, POU5F1, SOX2, NANOG	Pou5f1, Sox2, Nanog, Rex-1, Slc2a3, Dnmt3b, Terf1	-
Choi, 2016	Chicken	Embryonic fibroblast	Retroviral, hOSKM, +Nanog	bFGF+Lif	8 days	-	-	AP, SSEA1	Nanog, Sox2	-
Fuet, 2017	Chicken	Embryonic fibroblast	Piggybac transposon, cOSKM + NANOG	LIF	7-8 days	EB	-	AP, SSEA1, EMA1	ALPL, OCT4, SOX2, NANOG, CLDN3, SALL4, TRIM71	-
Kim, 2017	Chicken	Adult feather follicle cells	pMX mOSKM + NANOG	LIF+bFGF	3-4 days	EB + chimera	-	SSEA1	NANOG, POUV, LIN28	Present
Katayama, 2018	Chicken	Fibroblast	Lentivirus, mOSKM+ Lin28	bFGF		EB + teratoma	-	AP, SSEA1, SSEA3, SSEA4	PouV, Sox2, Nanog, Tbx3, Esrrb, Rex1	Present

iPSC: induced pluripotent stem cells; hOSKMNL: human Oct4, Sox2, KLF4, c-Myc, Nanog, Lin28; bFGF: basic fibroblast growth factor; EB: embryoid body; AP: alkaline phosphatase; POU5F1: POU class 5 homeobox 1 (OCT4); SOX2: Sex determining region Y-box 2; c-MYC: MYC Proto-Oncogene; LIN28: Lin-28 Homolog A; NANOG: Nanog Homeobox; mOSKM: mouse Oct4, Sox2, KLF4, c-Myc; LIF: leukemia inhibitor factor; 3i: PD 0325901 (MEK inhibitor), CHIR 99021(GSK3 inhibitor) and SU 5402 (FGFR inhibitor); SSEA-1: stage-specific embryonic antigen-1; hOSNL: human Oct4, Sox2, Nanog, Lin28; REX-1: ZFP-42 (Zinc Finger Protein 42 Homolog); SLC2A3: Solute Carrier Family 2 Member 3; DMNT3B: DNA Methyltransferase 3 Beta; cOSKM: chicken Oct4, Sox2, KLF4, c-Myc; TERF1: Telomeric repeat-binding factor 1; EMA1: Erythrocyte merozoite antigen 1; CLDN3: Claudin 3; TRIM71: Tripartite Motif Containing 71; PMX: Moloney murine leukemia virus (MMLV); TBX3: Tbox 3; ESRRB: Steroid hormone receptor ERR2.

## Supplemental material 8 – Wild

Table describing isolation and characterization of iPSC from wild species.

Author, year	Animal	Cell type	Reprogramming System	Supplementation	Days until colony	Differentiation	Reprogramm ing efficiency	Immunocytoche mistry	Gene expression (endogenous)	Gene expression (exogenous)
Ben-Nun, 2011	Drill primatenort hen white rhinoceros;	Fibroblast	Drill: Retrovirus, hOSKM Rhino: VSV.G	bFGF	30 days(Drill) 27 days (Rhino)	EB+ teratoma (Drill)	Drill: 0.0003 to 0.001% Rhino: 0.0006%	Drill: Sox2, Nanog, Oct4 and AP Rhino: Sox2, Nanog, OCT4	Drill: Oct4, Sox2, Nanog	Silenced
Rosselló, 2013	Mouse, Chicken, Quail, Zebra finch, zebrafish, Drosophila	Fibroblast	Lentivirus, mOSKM (Stemcca)	LIF (mouse) LIF+ bFGF+ 3i (avian) LIF+ 3i (zebrafish) 3i (drosophila)	5-7 days	EB (avian, fish, drosophila) + teratoma (quali, chicken) + Chimera (chicken and fish)	-	AP, SSEA1 (exception of Dosophila)	Oct4, Sox2, c-Myc, Vasa, Nanog (except fish) Drosophila: Vasa, VVL, dMyc, SoxN, Dichaete, Escargot, Snail,	Silenced- Chicken,zebra fish present- quali, zebra finch, Drosophila
Menzorov, 2015	Mink	Embryonic fibroblast	Lentivirus LeGo, hOSKM		2 weeks	Teratoma	-	-	Oct4, Sox2, Nanog, Rex1, Otx2, Gata6	c-Myc and KLF4: silenced; Oct4 and Sox2: not analyzed
Weeratunga, 2018	Tasmania devil	Adult fibroblasts	Lentivirus, hOSKMNL	LIF+bFGF	12-14 days	EB+ in vitro teratomas	0.0005%–0.00075%	AP, OCT4, SOX2, NANOG	OCT4/POU5F1, POU5F3, NANOG, SOX2, DAX1, ESRRB	Silenced
Whitworth, 2018	Platypus	Adult fibroblasts	Lentivirus, hOSKMNL	LIF+bFGF+3i+SB4315 42		EB+ in vitro teratomas	-	AP, SSEA1, SSEA4, TRA1–60	OCT4, SOX2, and NANOG	Sox2: silenced; rest: present
Verma, 2012	Snow leopard	Adult ear fibroblast	Retrovirus pMX, hOSKMNL	LIF	3 days	Teratoma	-	AP, NANOG, OCT4, SSEA4	OCT4, NANOG	OCT4, SOX2, NANOG: silenced KLF4, c-MYC: present
Verma, 2013	Bengal tiger, leopard, Serval	Adult ear fibroblast	Retrovirus pMX, hOSKM+NANOG	LIF	3 days	EB+Teratoma	-	AP, NANOG, OCT4, SSEA4	OCT4, NANOG	OCT4, SOX2, NANOG: silenced KLF4, c-MYC: present
Mo, 2014	Bat	Embryonic fibroblasts	PiggyBac hOSKMNL+NR5A2+ bat MIR302/367	LIF+3i	14 days	EB+teratoma	-	AP, Oct4, Sox2, Nanog, TBX3, TRA-1-60	Oct4, Sox2	-
Katayama, 2016	Prairie Vole	Embryonic fibroblasts	PiggyBac mOSKMNL	bFGF+LIF+2i+ thiazovivin	12-19 days	EB+teratoma	-	AP, SSEA-1, SSEA-4, OCT4 (not sure endo or exogenous)	Tbx3, Esrrb, Sox2, Oct3/4	-
Liu, 2008	Rhesus monkey	Adult ear fibroblasts	pMX retrovirus, monkey OSKM		26-29 days	EB+direct differentiation+ teratoma	-	AP, NANOG, SSEA-4, TRA-1-60, TRA-1-81	OCT4, SOX2, NANOG, DPPA2, DPPA4, SALL4, Lin28, CRIPTO, DNMT3b, NFE2L3	Silenced
Tamioka, 2010 [8]	Marmoset	Fetal liver cells	Retrovirus, hOSKMNL	LIF	4-5 weeks	EB+teratoma	-	AP, SSEA - 3, SSEA - 4, TRA - 1 - 60, TRA - 1 - 81	Oct4, Sox2, Klf4, c - Myc, Nanog, Lin28	Silenced
Chan, 2010	Huntington transgenic rhesus monkey	Huntington fibroblasts	pMX retrovirus, monkey OSK	bFGF and Valproic acid	2 weeks	Teratoma + direct differentiation into neural cells	-	AP, OCT4, SSEA4, TRA-1-60	OCT4, SOX2, KLF4	OCT4, SOX2, KLF4
Shimozawa, 2013	Cynomolgus monkey	Newborn skin cells and fetal fibroblasts	pMX retrovirus, monkey OSKM	LIF+bFGF	4 weeks	EB+teratoma	-	Oct-3, SSEA4, TRA-2-54, TRA-1-60, TRA-1-81, Nanog	POU5F1, SOX2, c-MYC, KLF4, Nanog, REX1	Silenced
Fang, 2014	Rhesus monkey	Adult ear fibroblasts	Retrovirus, Oct4 + KLF4	First bFGF Later LIF+2i + SB203580	7-10 days	Teratoma+ chimera	-	AP, OCT4, SOX2, NANOG, TRA-1-81/TBX3, TRA-1-60, and SSEA-4	OCT4, SOX2, SALL4, NANOG	-
Ramaswamy, 2015	Orangutan	Adult skin fibroblasts	pMX retrovirus, hOSKM	bFGF	2 weeks	EB + in vitro differentiation + teratoma	-	AP, TRA-1-60, TRA-1-81, SSEA4, OCT4, SOX2, NANOG	-	-
Thoma, 2016	Cynomolgus monkey	Adult kidney fibroblasts	Senday virus, hOSKM	bFGF + Y-27632	20 days	Differentiations into endothelial cells	-	OCT4, SOX2, NANOG	-	-

Zhang, 2017	Rhesus monkey	Dermal fibroblasts (ear)	Episomal vectors, hOCT4 +SOX2 +KLF4 + L-MYC + LIN28 + shp53	bFGF+ CHIR99021+ IWR-1, ACTIVNI A + hVITRONECTIN	3-4 weeks	EB+ in vitro differentiations + Teratoma	-	Oct3/4, Sox2, Nanog, tra-1-81, tra-1-60, SSEA4	OCT3/4, SOX2, NANOG	Silenced
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iPSC: induced pluripotent stem cells; hOSKM: human Oct4, Sox2, KLF4, c-Myc; VSV.G: Vesicular stomatitis virus G; bFGF: basic fibroblast growth factor; EB: embryoid body; SOX2: Sex determining region Y-box 2; NANOG: Nanog Homeobox; OCT4: octamer-binding transcription factor 4; AP: alkaline phosphatase; LIF: leukemia inhibitor factor; 3i: PD 0325901 (MEK inhibitor), CHIR 99021(GSK3 inhibitor) and SU 5402 (FGFR inhibitor); SSEA-1: stage-specific embryonic antigen-1; VVL: Ventral veins lacking; d-MYC: MYC Proto-Oncogene; OCT4: octamer-binding transcription factor 4; SOX2: Sex determining region Y-box 2; NANOG: Nanog Homeobox; REX-1: ZFP-42; OTX2: Orthodenticle Homeobox 2; GATA6: GATA Binding Protein 6; hOSKMNL: human Oct4, Sox2, KLF4, c-Myc, Nanog, Lin28; bFGF: basic fibroblast growth factor; SB43152: Activin/BMP/TGF- $\beta$  pathway inhibitor; SSEA-4: stage-specific embryonic antigen-4; TRA-1-60: T cell receptor alpha locus; DAX1: dosage-sensitive sex reversal, adrenal hypoplasia critical region, on chromosome X, gene 1; ESRRB: Steroid hormone receptor ERR2; PMX: Moloney murine leukemia virus (MMLV); hOSKMN: human Oct4, Sox2, KLF4, c-Myc, Nanog; NR5A2: Nuclear Receptor Subfamily 5 Group A Member 2; KLF4: Kruppel-like factor 4; c-MYC: MYC Proto-Oncogene; mOSKMNL: mouse Oct4, Sox2, KLF4, c-Myc, Nanog, Lin28; miR: microRNA; TBX3: Tbox 3; TRA-1-81: PODXL; DPPA2: Developmental Pluripotency Associated 2; DPPA4: Developmental Pluripotency Associated 4; SALL4: Sal-like protein 4; CRIPTO: Teratocarcinoma-derived growth factor 1; DNMT3B: DNA Methyltransferase 3 Beta; NFE2L3: Nuclear Factor, Erythroid 2 Like 3; OSK: Oct4, Sox2, KLF4; OSKM: Oct4, Sox2, KLF4, c-Myc; POU5F1: POU class 5 homeobox 1; SB203580: pyridinyl imidazole inhibitor; Y-27632: ROCK inhibitor; CHIR99021: GSK3 inhibitor; IWR-1: WNT pathway inhibitor.

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