Supplementary Materials: Supplementary Results

Table S1. Proteins included in the curated genetic network.

AFP	bCAT*	BMP2	BMP2K	cAMP*	CDX2	CDX4	CEBP
CSH1	E2F4	FOXA1	FOXA2	FOXD3	FOXO1A	GATA2	GATA3
GATA4	GATA6	GDF3	hCGa*	hCGb*	KLF4	LEF1	LEF1-bCat
LMCD1	Mad	Mad-Max	MAX	MYC	Myc-Max	MYC-SP1	NANOG
NFYA	OCT4	Oct4-FOXD3	Oct4-Sox2	PBX1	PIAS1	PIASy	PRDM14
SALL4	SOX17	SOX2	SP1	SP3	SUMO1	T	TCF3
TDGF1	ZFP42*	ZIC3	ZNF206*				

*bCAT= Beta-catenin; CTNNB1; cAMP=cyclic-AMP; hCGa=CGA; hCGb=CGB; ZFP42=REX1; ZNF206=ZSCAN10;

Table S2. Edges and supporting evidence in the curated genetic network (Edge Number: 124; Activation: 85; Repression: 39)

Parent Node	Child Node	Interaction Type (1=activation; 0=repression)	References
FOXA1	AFP	1	(1, 2)
FOXA2	AFP	1	(3)
SOX2	BMP2	0	(4),(5),(6)
NANOG	BMP2	0	(7),(8)
BMP2K	BMP2	1	(9)
HNF4A	BMP2K	1	(10)
OCT4	CDX2	0	(7),(11)
NANOG	CDX2	0	(7),(12)
CDX2	CDX2	1	11, 67
SP1	CEBP	0	(13),(14)
E2F4	CEBP	0	(7),(15),(16)
PRDM14	CSH1	0	(17)
FOXD3	FOXA1	1	(18)
OCT4-FOXD3	FOXA1	0	(18),(19)
FOXA1	FOXA1	1	(18)
FOXD3	FOXA2	1	(18)
OCT4-FOXD3	FOXA2	0	(18),(19)
FOXA2	FOXA2	1	(18)
SOX17	FOXA2	1	(20),(21),(22),(23),(24),(18),(25),(3)
NANOG	FOXD3	1	(7),(26)
OCT4	FOXD3	1	(18),(27),(7)
SOX2	FOXD3	1	(7),(26)
E2F4	FOXD3	1	(7),(28),(29)
OCT4	FOXO1A	1	(7),(26)
SOX2	FOXO1A	1	(7),(26)
NANOG	FOXO1A	1	(7),(26)

SUMO1	GATA2	0	(30)
PIASy	GATA2	0	(30)
SOX2	GATA2	0	(31)
NANOG	GATA2	0	(31)
NANOG	GATA3	0	(7),(32)
OCT4	GATA4	0	(7),(11),(33)
SUMO1	GATA4	1	(34)
PIAS1	GATA4	1	(34)
NANOG	GATA4	0	(7),(11),(33)
PRDM14	GATA6	0	(17)
NANOG	GATA6	0	(7),(35),(12),(36)
OCT4	GATA6	0	(7),(27)
GATA4	GATA6	0	(37)
LMCD1	GATA6	0	(38)
GATA6	GATA6	1	(39-42)
NANOG	GDF3	1	(7),(43)
OCT4	hCGa	0	(32),(44),(33),(45),(46)
GATA2	hCGa	1	(47)
GATA3	hCGa	1	(47)
cAMP	hCGa	1	(48),(49),(50)
OCT4	hCGb	0	(32),(44),(33),(45),(46)
SP1	hCGb	1	(51)
cAMP	hCGb	1	(48),(49),(50)
SP3	hCGb	1	(52),(53)
GATA6	HNF4A	1	(54, 55)
bCAT	HNF4A	1	(56)
OCT4	KLF4	1	(7),(57)
SOX2	KLF4	1	(7),(57)
NANOG	KLF4	1	(7),(57)
NANOG	LEF1	0	(7),(58)
OCT4	LEF1	0	(7),(57)
LEF1	LEF1-bCat	1	(59)
bCAT	LEF1-bCat	1	(59)
NANOG	LMCD1	1	(7),(58)
cAMP	LMCD1	0	(60)
MAX	Mad-Max	1	(61, 62)
Mad	Mad-Max	1	(61, 62)
PRDM14	MYC	1	(63)
E2F4	MYC	1	(7),(15),(16)
LEF1-bCat	MYC	1	(64)
TCF3	MYC	0	(65, 66)
MYC	Myc-Max	1	(67)
MAX	Myc-Max	1	(67)

MYC	MYC-SP1	1	(68)
SP1	MYC-SP1	1	(68)
ZIC3	NANOG	1	(69)
NANOG	NANOG	1	(7)
Oct4-Sox2	NANOG	1	(7)
PBX1	NANOG	1	(70)
KLF4	NANOG	1	(70)
GATA6	NANOG	0	(39-42)
SOX2	NFYA	1	(7),(71)
E2F4	NFYA	1	(7),(15),(16)
NANOG	OCT4	1	(7)
Oct4-Sox2	OCT4	1	(7)
CDX2	OCT4	0	(11, 72)
OCT4	OCT4-FOXD3	1	(18)
FOXD3	OCT4-FOXD3	1	(18)
OCT4	Oct4-Sox2	1	(7)
SOX2	Oct4-Sox2	1	(7)
NANOG	PBX1	1	(7),(70)
PIAS1	PIAS1	1	(73)
E2F4	PIAS1	1	(7),(74)
PIAS1	PIASy	1	(73)
OCT4	PRDM14	1	(7, 75),(57)
SOX2	PRDM14	1	(7, 75),(57)
NANOG	PRDM14	1	(7, 75),(57)
LEF1	SALL4	1	(76)
NANOG	SALL4	1	(77),(26)
SOX2	SALL4	1	(77),(26)
ZIC3	SOX17	0	(69)
OCT4	SOX17	0	4,(78, 79)
NANOG	SOX2	1	4
Oct4-Sox2	SOX2	1	4
E2F4	SP1	1	4,(80)
SP1	SP1	1	(80)
SP3	SP1	0	(80)
CEBP	SP1	1	(80)
NFYA	SP1	1	(80)
MYC-SP1	SP1	0	(68)
SUMO1	SP3	0	(81, 82)
PIAS1	SP3	0	(81, 82)
NANOG	SUMO1	1	4
E2F4	SUMO1	1	4,(83),(28)

NANOG	T	0	4,(12, 84)
PRDM14	T	0	(17)
E2F4	T	0	4,(74)
OCT4	T	0	4,(11)
E2F4	TCF3	1	4
OCT4	TDGF1	1	(11)
NANOG	TDGF1	1	4,(17)
SOX2	TDGF1	1	4,(57)
NANOG	ZFP42	1	(7, 85)
OCT4	ZFP42	1	(7, 11)
SOX2	ZIC3	1	4,(26)
NANOG	ZIC3	1	(7, 69)
NANOG	ZNF206	1	4,(57)

Table S3. 22 Marker genes for hESCs and differentiated cells.

Pluripotency Markers	**OCT4, SOX2,NANOG,Oct4-Sox2,KLF4,FOXD3,ZIC3,ZFP42,GDF3, TDGF1,PBX1**
Differentiation Markers	FOXA2, AFP, SOX17, GATA4, GATA6, T, GATA2, GATA3, hCGa*, hCGb*, CDX2

*hCGa=CGA; hCGb=CGB

Figure S1a-f. Pearson correlation coefficient (r) and p-value (p) between predicted and experimental gene expression changes (in log2). (a)-(c): Day 3, 5 and 7 after knocking down OCT4 by Won et al.(77); (d)-(e) Day 2 and 3 after knocking down OCT4 by Kunarso et al.(86); (f) Day 4 after knocking down NANOG by Hyslop et al.(12).

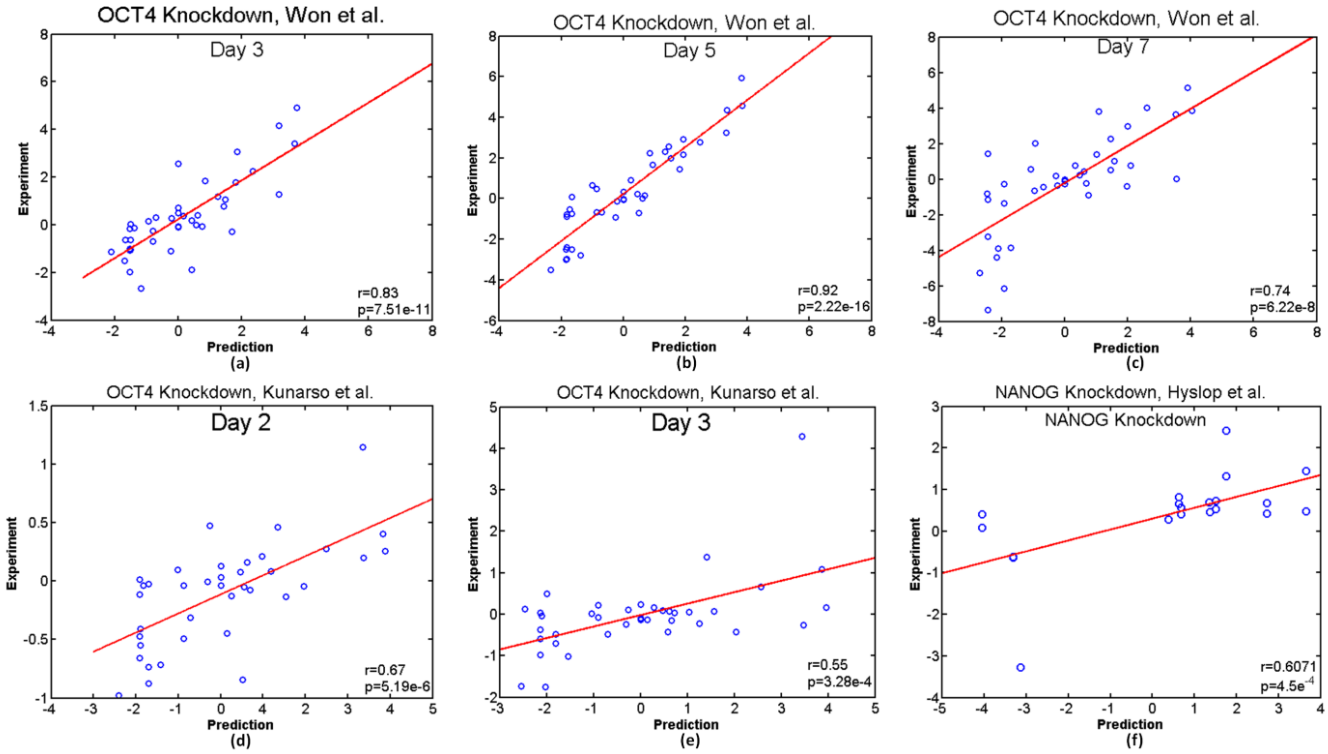


Figure S2. Reprogramming efficiency and gene expression similarity. The gene expression similarity is represented by RMSD, Pearson correlation, and Spearman rank correlation.

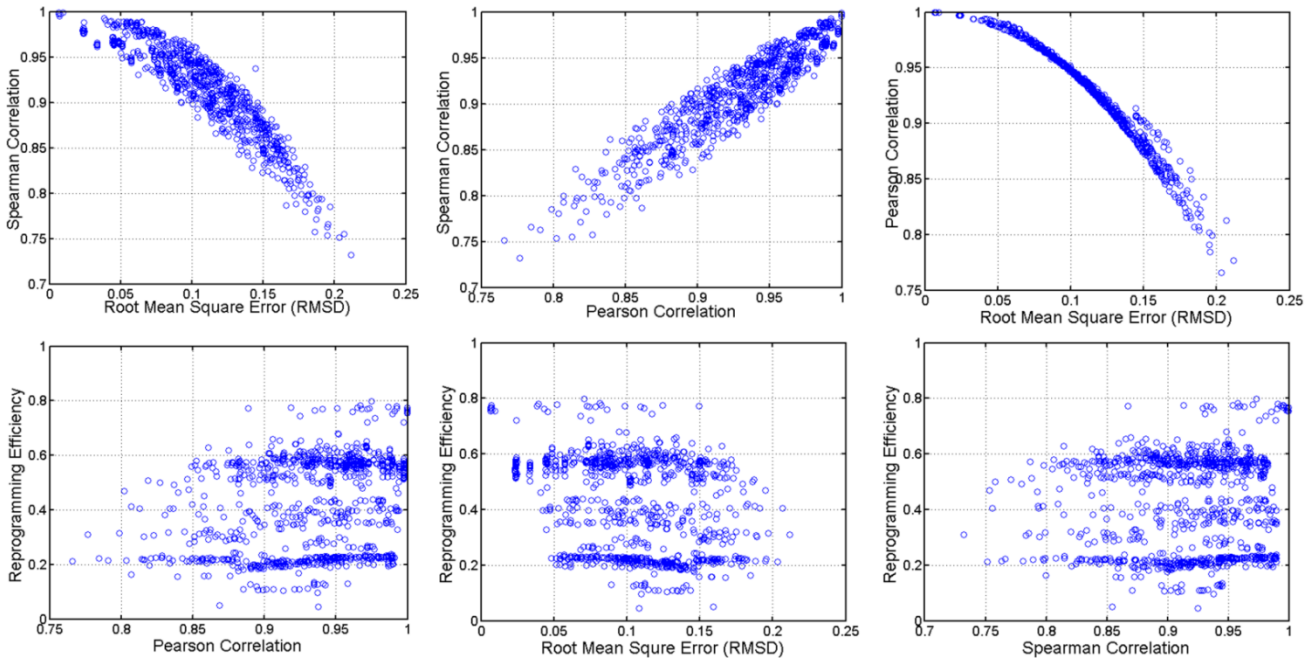


Figure S3. Distribution of Reprogramming Recipe's RMSD, Pearson and Spearman correlation.

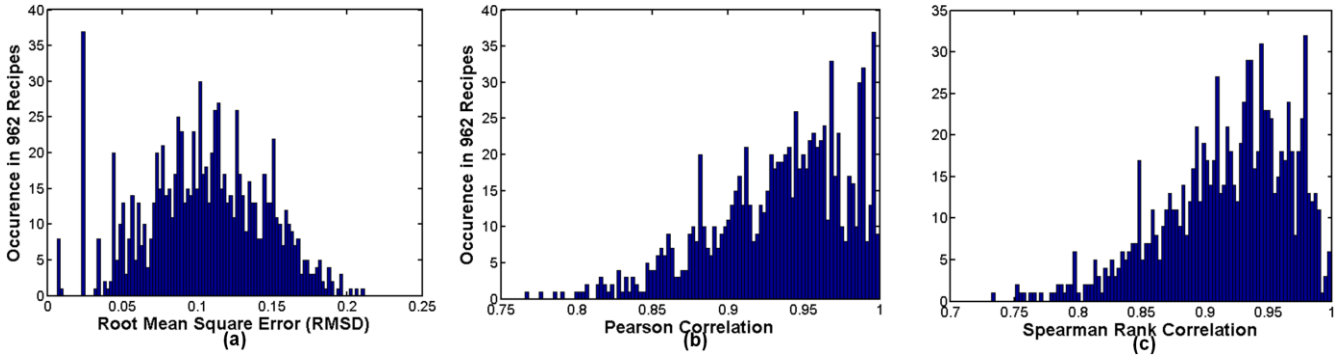
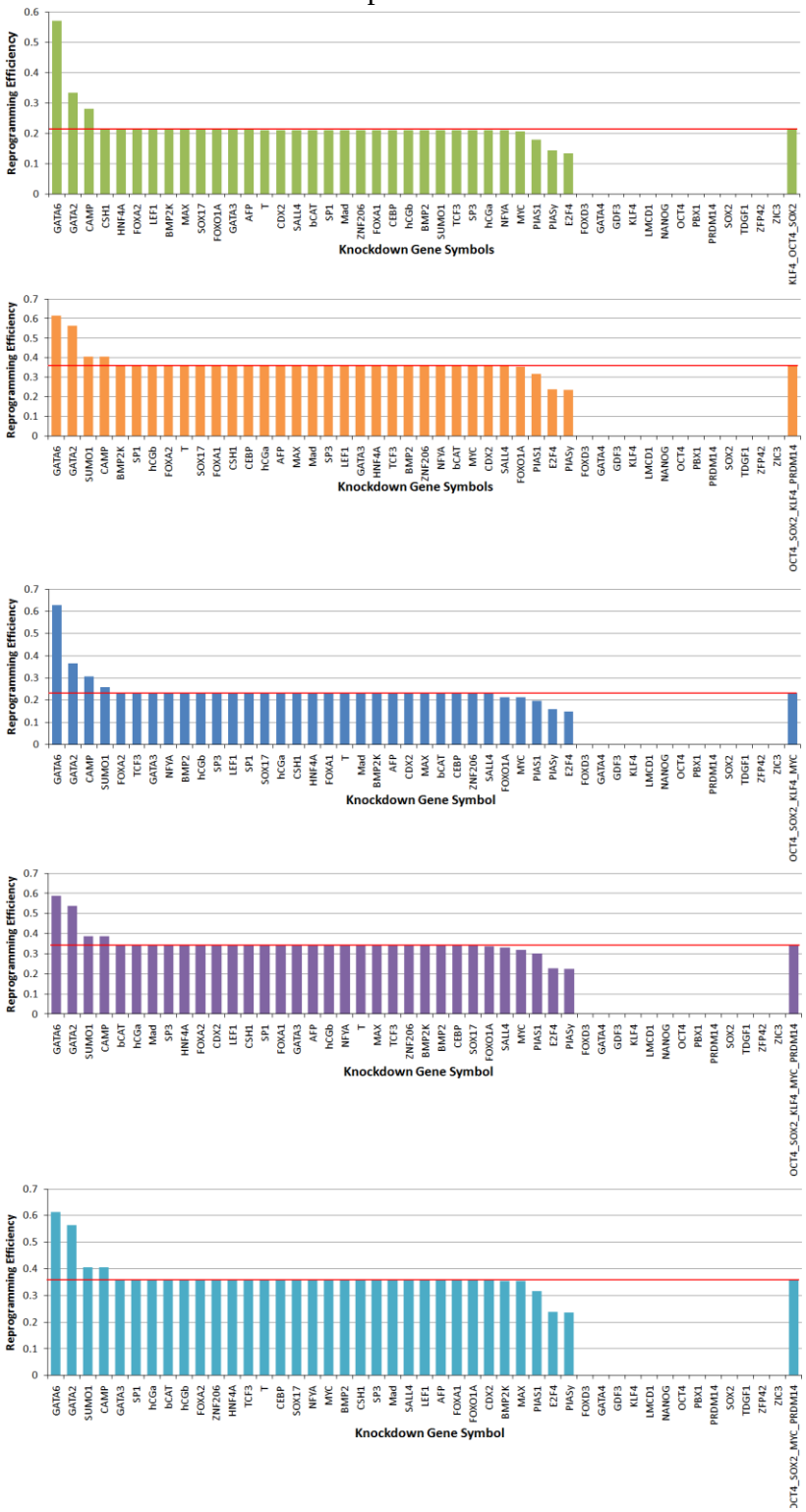


Figure S4. Reprogramming efficiencies of experimental recipes plus single gene knockdown. The experimental recipes are shown at the right end. The additional knockdown genes are shown in the order of reprogramming efficiency. If a component of a recipe is also knocked down, knockdown overwrites overexpression in the simulation.



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