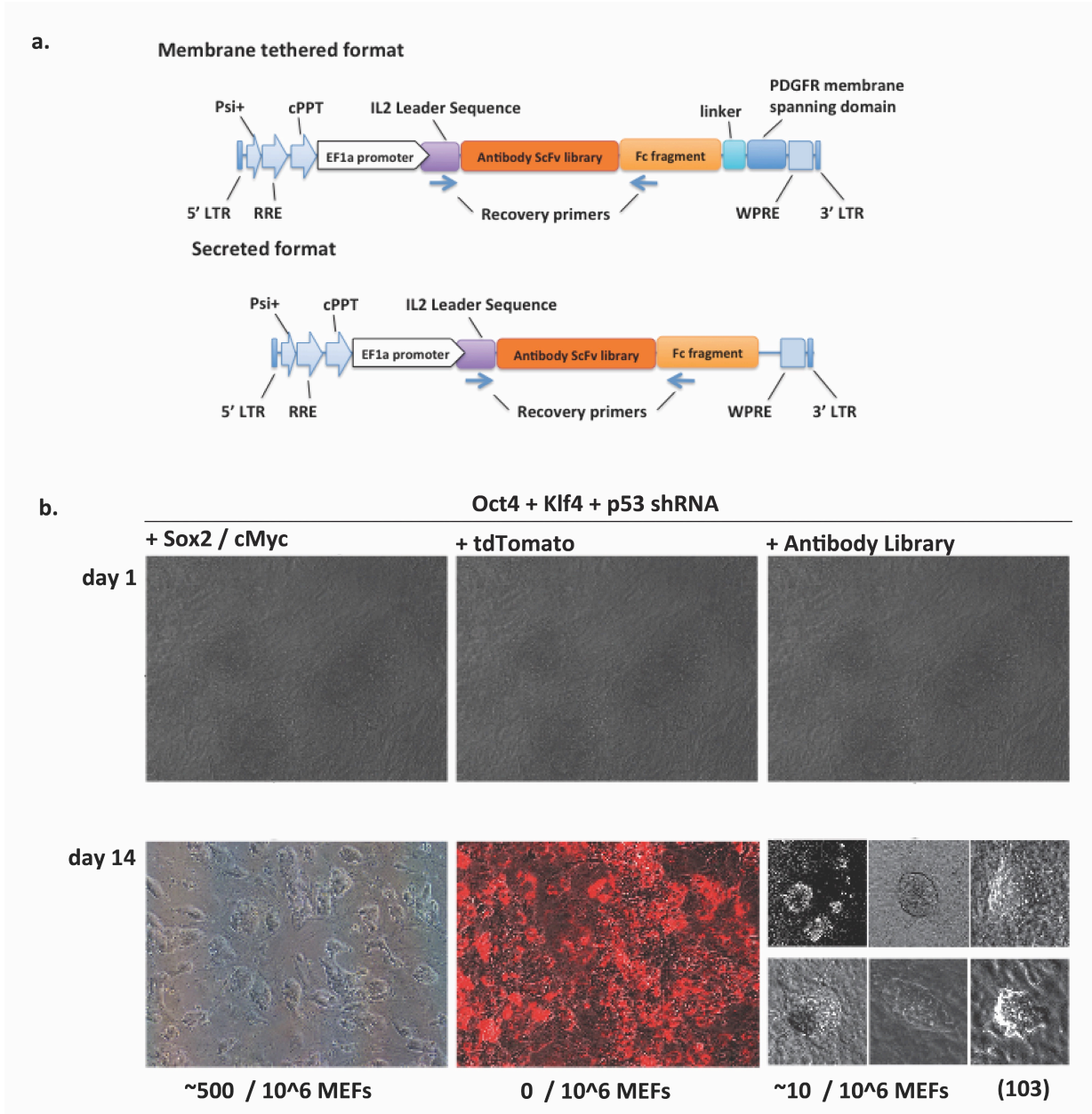Figure S1

Fig. S1. a) Schematic of lentiviral constructs for expressing antibody libraries in either membrane or secreted forms. **b)** Results from the Sox2 replacement screen showing colony production in the positive control condition using Oct4/Klf4/p53shRNa + Sox2/cMyc, but not in wells lacking Sox2/c-Myc except when the antibody library was added (far right wells, rare colonies are shown prior to picking and expansion).

Figure S2.
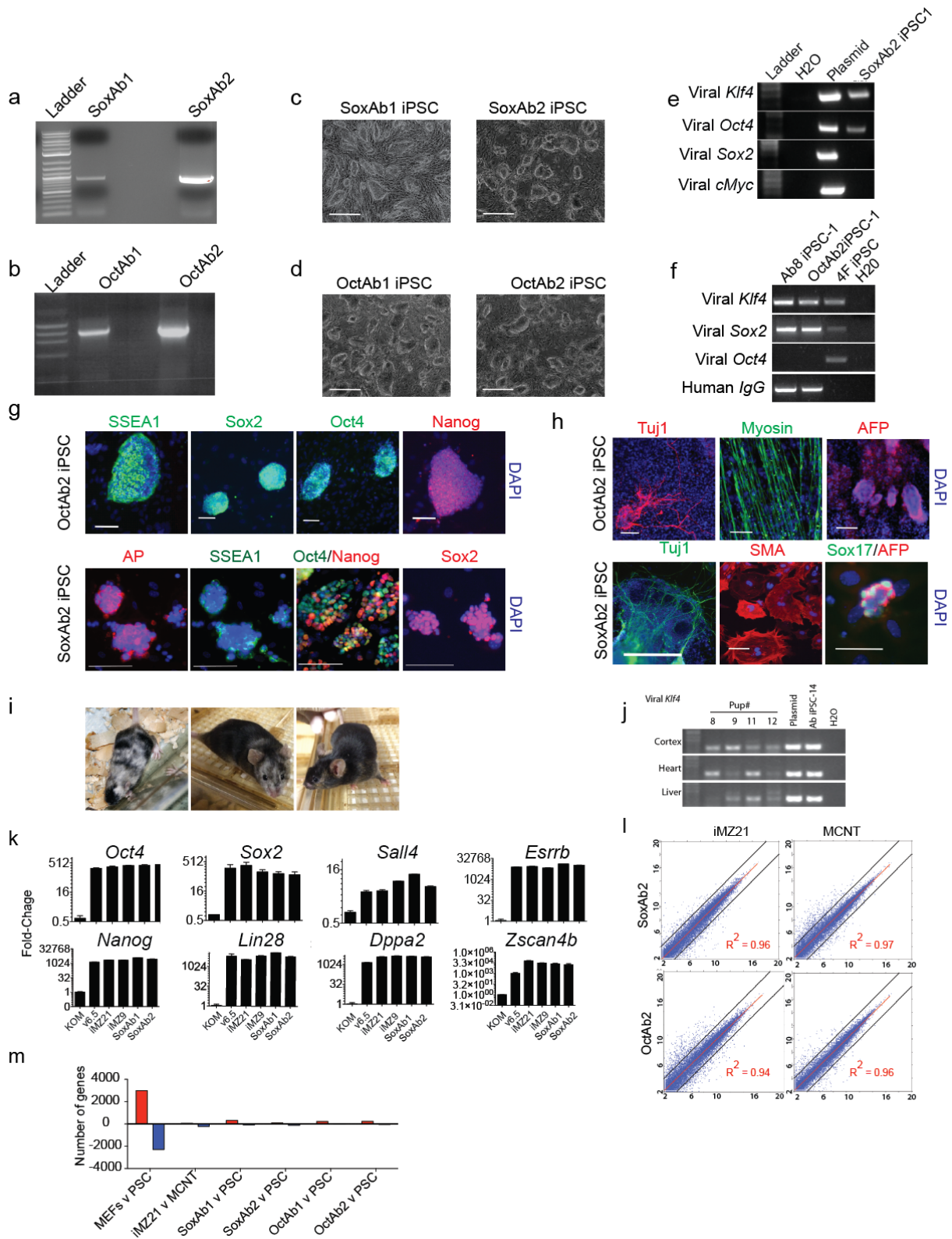
Fig. S2. a and b) Antibody genotypes were recovered by PCR performed on genomic DNA from established iPSC lines. Primer binding sites are depicted in Fig. S1b as "Recovery primers". The amplicons were purified by gel extraction and sub-cloned into expression vectors. **c)** Primary colonies induced by Sox2 antibodies can be expanded into cell lines and cultured under standard mES conditions for at least ten passages. **d)** Primary colonies induced by Oct4 antibodies can be expanded into cell lines and cultured under standard mouse ES cell conditions for at least ten passages. **e)** iPSC lines generated with SoxAb2 do not harbor transgenic *Sox2* or *cMyc*. **f)** iPSC lines generated with OctAb1 and 2 do not harbor transgenic *Oct4*, but do harbor transgenic human IgG. **g)** iPSC lines generated with SoxAb2 and OctAb1 express pluripotency markers SSEA1, Sox2, Oct3/4, and Nanog. Scale bars = 100 µm. **h)** iPS cell lines generated with OctAb2 and SoxAb2 differentiate *in vitro* to the three embryonic germ layers. Scale bars = 100 µm. **i)** iPSC lines generated with SoxAb1 differentiate *in vivo* and contribute to chimeric offspring. Eight-week old chimeric mice formed by injection of KO + SoxAb1 cells (CD1 genetic background) into a C57BL6 blastocyst. **j)** Chimeric pups display contribution of antibody iPSCs across three embryonic germ layers. **k)** Quantitative RT-PCR confirmation of the expression of pluripotency genes in the SoxAb1 and SoxAb2 iPSC lines, fully pluripotent iPSCs (iMZ-9,iMZ-21) and mESCs (V6.5) compared to control fibroblasts expressing OKM for twelve days under identical culture conditions used to derive the iPSCs. Bars represent the mean of two biological replicates. Error bars = SEM. **l)** RNAseq scatter plots show that global gene expression of antibody-derived iPSC lines is highly similar to TEC competent iPSC (iMZ21) and mESC (MCNT) lines but different from somatic MEFs. **m)** Summary of DESeq2 analysis showing the number of genes significantly upregulated (red) and downregulated (blue), that exhibit a greater than 2-fold change in expression in MEFs, and antibody-iPSC lines compared to TEC-competent iPSCs and ESCs.

Figure S3
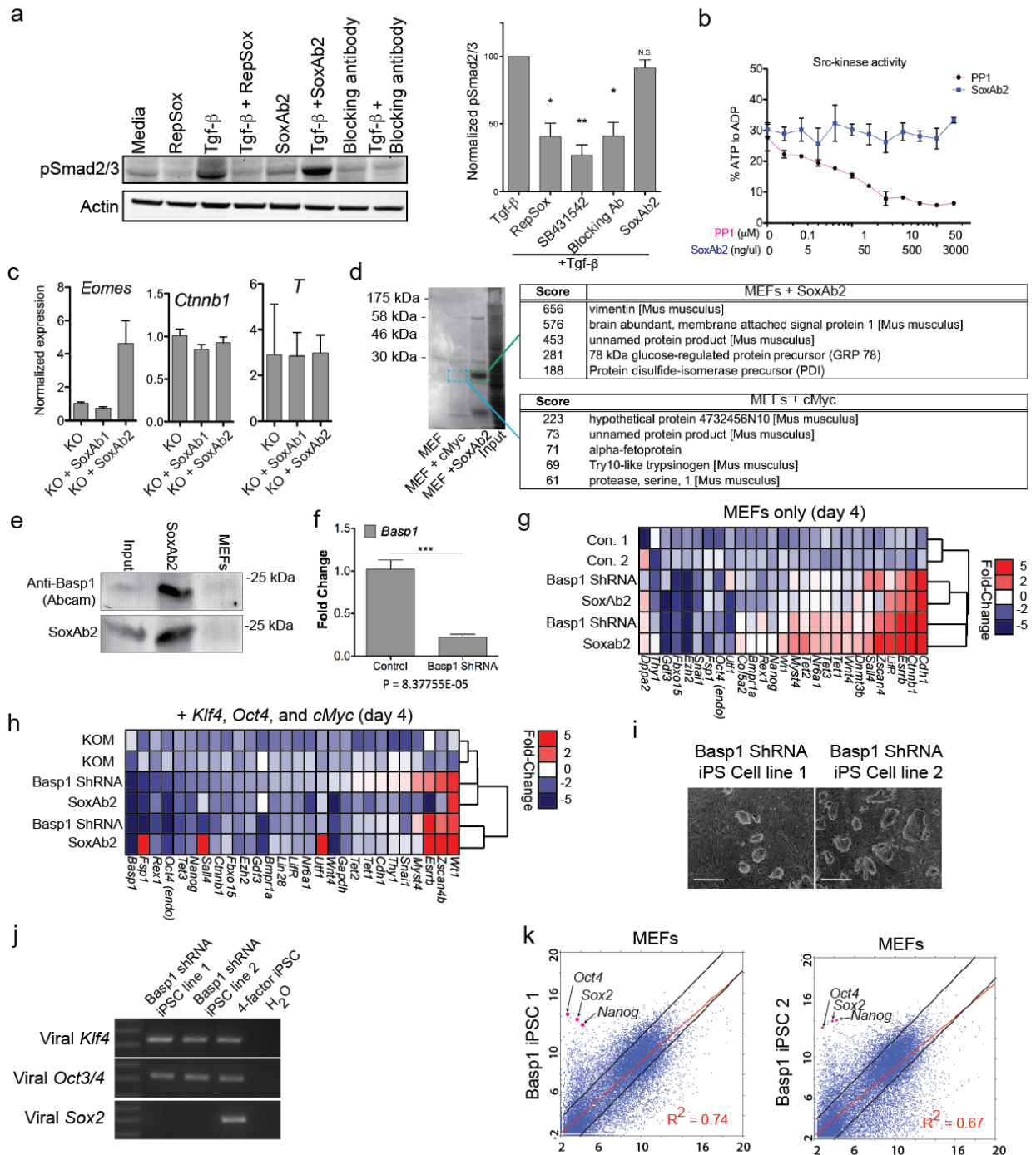
Fig. S3. a) SoxAb2 does not inhibit Tgf-β induced phosphorylation of Smad2/3 whereas small molecule inhibitors RepSox and Tgf-β neutralizing antibodies previously reported to promote Sox2-independent reprogramming inhibit Tgf-β induced phosphorylation of Smad2/3. For each treatment (SoxAb2,RepSox, SB431542, and Tgf-β neutralizing antibodies) ability to inhibit Smad2/3 phosphorylation was quantified from three independent western blots. The graph depicts the mean from the three blots. Error bars

represent SEM. Significance was determined by ANOVA followed by Newman-Keuls post-hoc analysis, *p<0.05, ** p<0.01. **b)** SoxAb2 does not directly inhibit Src-kinase activity. SoxAb2 ability to inhibit Src-kinase activity was compared to the small molecule PP1 a known Src-kinase inhibitor able to promote Sox2-independent reprogramming. **c)** SoxAb2 does not antagonize the induction of mesoderm genes. Mesoderm genes *Eomes*, *T*, and *Ctnnb1* were quantified in three biological replicates of MEFs expressing Klf4 and Oct4 by RT-PCR following 96 hours expression of SoxAb2. Significance was assessed by ANOVA, no significant differences were observed. **d)** Proteins were immunoprecipitated with SoxAb2 separated by SDS-PAGE and stained with Coomassie brilliant blue. A ~25 KDa based was excised from control (blue) and SoxAb2-expressing (green) lanes and analyzed by trypsin digestion and mass spectrometry which identified candidate proteins enriched in each sample. **e)** SoxAb2 immunoprecipitates endogenous Basp1. MEFs were transduced with Basp1 (lanes 1,2) or not transduced (lane3). Lysates were immunoprecipitated with SoxAb2 (lanes 2 and 3) and Western blots were performed with either Anti-Basp1 (top) or the SoxAb2 (bottom). Basp1 protein was present and detected by both antibodies in the whole lysate from MEFs overexpressing *Basp1* and enriched in pull-downs with the SoxAb2, demonstrating that the SoxAb2 recognized Basp1 protein. **f)** Quantitative RT-PCR confirming Basp1 shRNA significantly reduces Basp1 expression in MEFs. **g)** The changes in gene expression in MEFs directed by SoxAb2 or knockdown of *Basp1* are strongly correlated. Heatmap and hierarchical clustering of control MEFs compared to MEFs expressing SoxAb2 or Basp1 shRNA. Clustering represents single linkage Euclidian distance. **h)** Heatmap and hierarchical clustering in MEFs expressing Klf4, Oct4, and cMyc (KOM) compared to KOM MEFs expressing SoxAb2 or Basp1 shRNA. Clustering represents single linkage Euclidian distance. **i)** Primary colonies induced by *Basp1* knockdown + KOM can be expanded into cell lines and cultured under standard mES conditions for at least ten passage. **j)** *Basp1* knockdown iPSC lines do not harbor transgenic *Sox2*. **k)** RNAseq scatter plots showing global gene expression of Basp1 knockdown iPSC lines is highly divergent from somatic MEFs relative to iPSC and mESC (Figure 3g).

Figure S4

a

	Input	Protein G	IgG (rb)	α-Basp1 (rb)	Blot:
55 KDa					α Wt1 (ms)

b

KOM + Wt1 iPS cell line 1

KOM + Wt1 iPS cell line 2

c

KOM + Wt1 iPS cell line 1

SSEA1
Sox2

KOM + Wt1 iPS cell line 2

Sox2
Oct4
SSEA1
Nanog

d

KOM + Wt1 iPSC Line 2

MEFs — Oct4, Sox2, Nanog — $R^2 = 0.67$

iMZ21 (4N comp. iPSC) — Oct4, Sox2, Nanog — $R^2 = 0.97$

MCNT (4N comp. mESC) — Oct4, Sox2, Nanog — $R^2 = 0.96$

e

KOM + Wt1 iPSC 1

MEFs — Oct4, Sox2, Nanog — $R^2 = 0.68$

f

Wt1 iPSC 2

alpha actinin
Tuj1
Troma-1

g

Day 4

KOM + Wt1 + Basp1 ShRNA Expression

Not signifigant: Cdh1, Lin28, Utf1, Dppa2

KOM Expression

Day 12

KOM + Basp1KD + Wt1 Expression

Esrrb, Lin28, Cdh1, Col5a2

KOM Expression

h

SSEA1 Sox2 Oct4 Nanog

Klf4, Oct4, cMyc + Esrrb

Klf4, Oct4, cMyc + Esrrb and Lin28

i

iMZ9 iPSC

Fold Change

** — Wt1
* — Lin28B
Esrrb
* — cMyc

Control | Wt1 ShRNA

v6.5 mESC

Fold Change

** — Wt1
* — Lin28B
* — Esrrb
* — cMyc

Control | Wt1 shRNA

6

Fig. S4. a) Wt1 was co-immunoprecipitated with Basp1 in somatic MEFs. **b)** Primary colonies induced by *Wt1* overexpression + KOM can be expanded into cell lines and cultured under standard mES conditions for at least ten passage. **c)** *Wt1* overexpression + KOM iPSC lines appropriately express pluripotency marker SSEA1, Sox2, Oct4, and Nanog. **d and e)** RNAseq scatter plots showing global gene expression of KOM + Wt1 iPSC lines are highly similar to TEC competent iPSC (iMZ21) and mESC (MCNT) lines but very different from somatic MEFs. **f)** *Wt1* overexpression + KOM iPS Cell lines differentiate to the three embryonic germ layers *in vitro*. **g)** Scatter plots depicting mean changes in gene expression induced by Wt1 overexpression and Basp1 knockdown on day four and twelve of reprogramming. Expression is normalized to KOM only samples. Error bars = SEM. **h)** iPSC lines generated with Lin28/Esrrb + Klf4 and Oct4 express pluripotency markers SSEA1, Sox2, Oct4, and Nanog. **i)** Quantitative RT-PCR showing shRNA-mediated knockdown of Wt1 in iPSC line iMZ9 iPSC and v6.5 mESC reduces expression of *Esrrb*, *Lin28,* and the downstream target *cMyc*. Bars represent means from three biological replicates. Error bars = SEM. Significance was tested by Students t-test for each comparison, * $p < 0.05$, **$p < 0.01$.

Figure S5
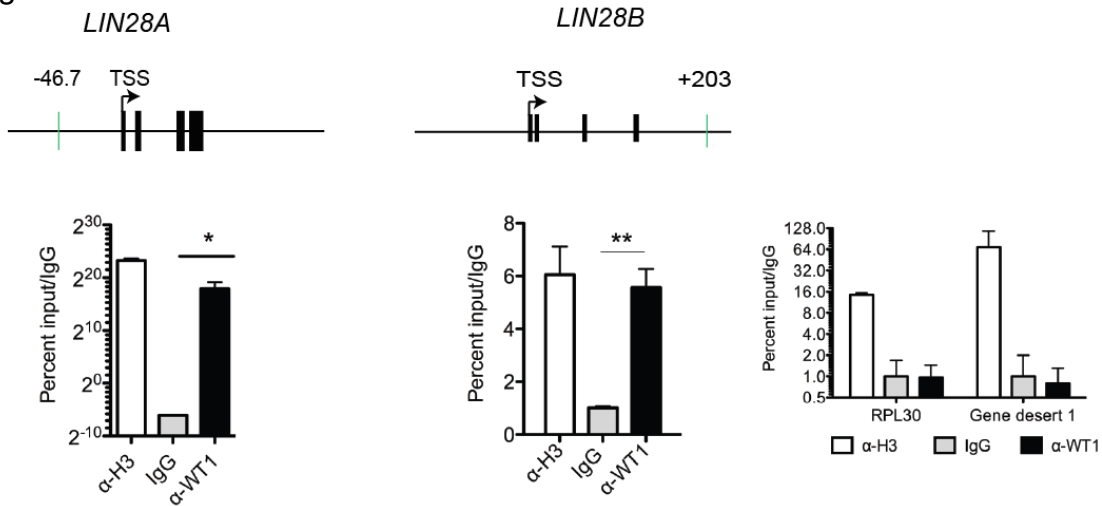
Fig. S5. WT1 ChIP-qRT-PCR on LIN28A and B genomic regions. Genomic PCR was performed on regions identified to contain WT1 consensus DNA-binding elements (green line) from *in silico* analysis. Bars represent the mean of three biologic replicates. Statistical significance was assessed by ANOVA, * p<0.05, **p<0.01. **b)** Expression of LIN28 (A and B), WT1 (C and D), and BASP1 (E and F) in CML patients. In the left panels, each bar represents a single patient. Right panels are averages of all patients for each group, with significance determined by ANOVA, ***p<0.001.

Figure S6
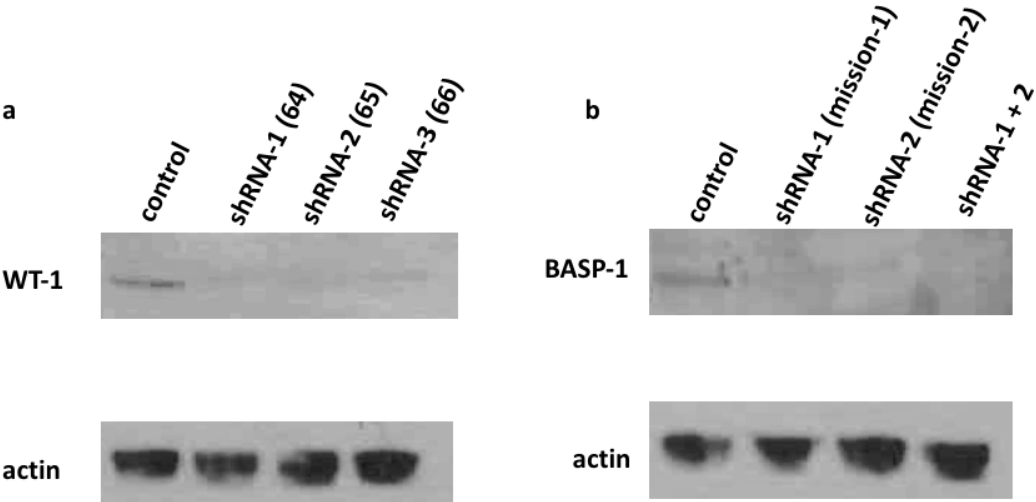
Fig. S6. The shRNAs used in the study reduce expression of the expected proteins **a)** WT-1 protein level in MEF was reduced by three different shRNA sequences (Sigma Mission®), while the housekeeping gene actin is unaffected. **b)** BASP-1 protein level in MEF cells was reduced by two different shRNA sequences (Sigma Mission®) separately and in combination.

Table S1

	Light chain	Heavy chain
SoxAb1	`----CDR1--->    <--CDR2-->    <---CDR3----` `QSVSSTY.....___GAS.......___QQCGDSPQT`	`----CDR1--->    <--CDR2-->    <---CDR3----` `GFYFPGYW....___VYPGDSHT..___ARQGASSTSYDY`
SoxAb2	`----CDR1--->    <--CDR2-->    <---CDR3---` `-SGSIASGY....___END.......___QSTGDNYQPI`	`----CDR1--->    <--CDR2-->    <---CDR3----` `GGTFSSYA....___IIPIFGTA..___ATVLGLVKTFGVEPHGGRFGMDV`
OctAb1	`----CDR1--->    <--CDR2-->    <---CDR3----` `QGISDH......___AAS.......___QQANSFPLT`	`----CDR1--->    <--CDR2-->    <---CDR3----` `GFTFSSYS....___ISSSSSYI..___AREFIVPAAMSFYYYYGMDV`
OctAb2	`----CDR1--->    <--CDR2-->    <---CDR3----` `QSVSSSY.....___GAS.......___QQYGSSLT`	`----CDR1--->    <--CDR2-->    <---CDR3----` `GFSVSSNF....___FYPDGRT...___TTATMPNNCDS`

Table S2

	Transcriptome correlation	AP	SSEA1 (IF)	Sox2 (IF,RNAseq)	Oct4 (IF, RNAseq)	Nanog (IF, RNAseq)	Differentiate to 3 germ layers
SoxAb1	0.96, 0.96	+	+	+,+	+,+	+,+	+
SoxAb2	0.96, 0.97	+	+	+,+	+,+	+,+	+
OctAb1	0.94, 0.96	+	+	+,+	+,+	+,+	+
OctAb2	0.94, 0.96	+	+	+,+	+,+	+,+	+
Basp1Kd + KOM #1	0.99, 0.96	+	+	+,+	+,+	+,+	+
Basp1Kd + KOM #2	0.97, 0.97	+	+	+,+	+,+	+,+	+
Wt1 + KOM #1	.97, 0.96	+	+	+,+	+,+	+,+	+
Wt1 + KOM #2	0.97, 0.96	+	+	+,+	+,+	+,+	+
Lin28 Esrrb + KOM	not tested	+	+	+,+	+,+	+,+	+
Lin28 Esrrb + KO	not tested	+	+	+,+	+,+	+,+	+
Esrrb + KOM	not tested	+	+	+,+	+,+	+,+	+
Esrrb + KO	not tested	+	+	+,+	+,+	+,+	+