PEPROTECH®
OUR SUPPORT, YOUR DISCOVERY

biogems
A PeproTech Brand

Small Molecules in Stem Cell and Cellular Reprogramming Research

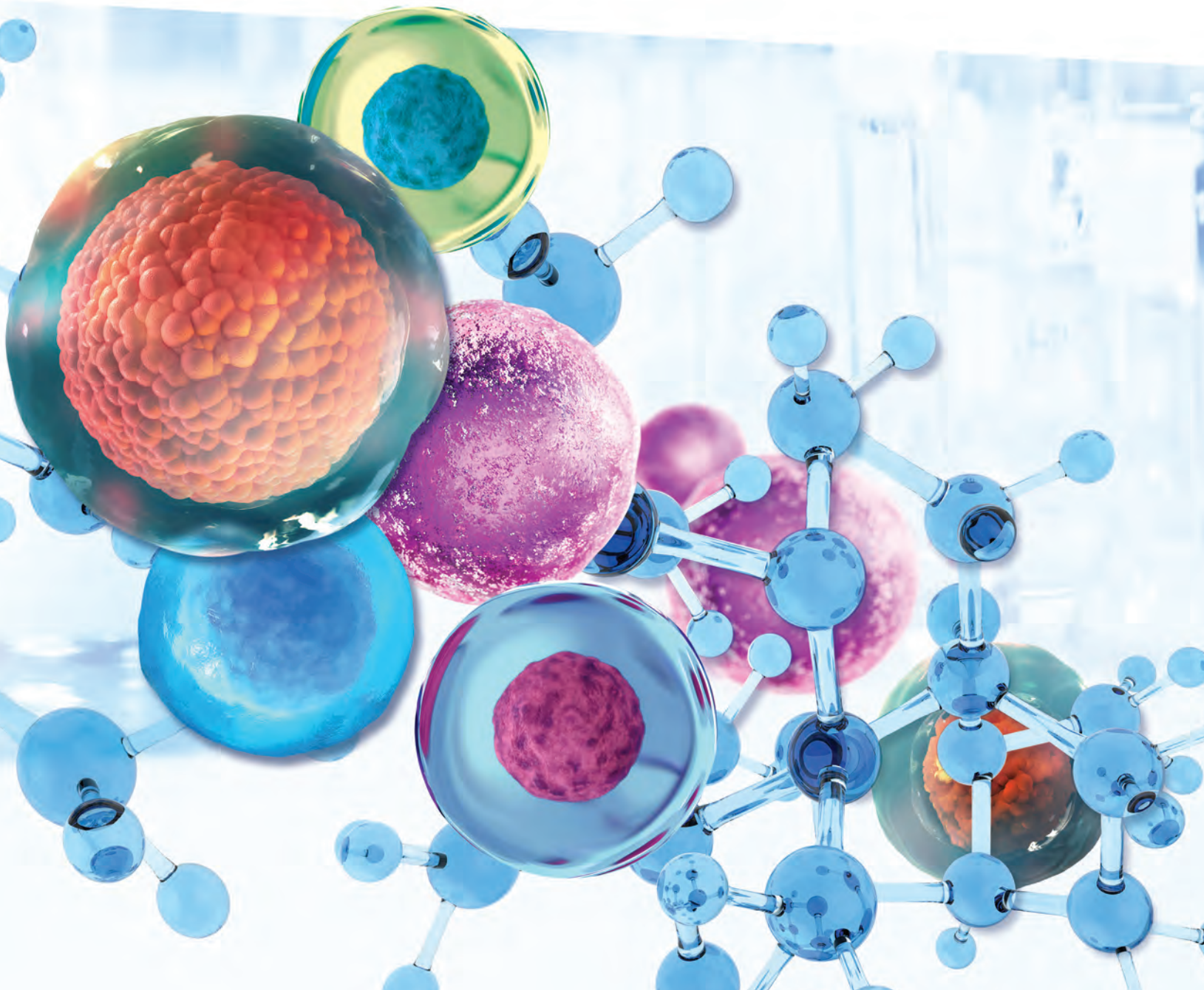


Table of Contents

Stem Cell Maintenance and Self-Renewal

In order to maintain pluripotency, embryonic stem cells (ESCs) are commonly cultured in the presence of feeder cells, serum and growth factors. Several growth factors crucial to maintaining pluripotency have been identified. For the culturing of mouse ESCs (mESCs) these include Leukemia inhibitory factor (LIF) and bone morphogenetic protein (BMP), whereas fibroblast growth factor 2 (FGF-2, FGF-basic) and Transforming Growth Factor-β (TGF-β) are essential for the culturing of human ESCs (hESCs). Furthermore, Wnt signaling was also determined to be important for the maintenance of both mESCs and hESCs.

In order to alleviate the introduction of possible experimental variability and pathogenic contamination that can stem from the use of feeder cells and serum, protocols have been developed to exclude such components. Small molecules are valuable components in feeder-free and serum-free conditions, due to having chemically-defined formulations, higher levels of purity, increased lot-to-lot consistency, and biological effects that are usually rapid, reversible and dose-dependent.

Small molecules can maintain pluripotency by either inhibiting pathways responsible for the induction of differentiation (e.g. MEK-ERK and Ras-GAP), or activating pathways that promote self-renewal (e.g. Wnt).

Small molecules can often boost efficacy by targeting a single component involved in several pathways. This is exemplified by several small molecules, such as CHIR 99021 and SB 216763, that regulate Wnt/β-catenin and Hedgehog signaling by inhibiting glycogen synthase kinase-3β (GSK-3β).

The addition of small molecules, whether alone or in combination with other reagents, can also aid in decreasing the sensitivity to enzymatic dissociation often associated with the passaging of hESC cultures.

References:

1. Choi, Y., & Nam, T. G. (2012). Chemical biology in stem cell research. *Archives of pharmacal research,* 35(2), 281-297.
2. Schmole, A. C., Hubner, R., Beller, M., Rolfs, A., & J Frech, M. (2013). Small molecules in stem cell research. *Current pharmaceutical biotechnology,* 14(1), 36-45.
3. Zhang, Y., Li, W., Laurent, T., & Ding, S. (2012). Small molecules, big roles–the chemical manipulation of stem cell fate and somatic cell reprogramming. *J Cell Sci,* 125(23), 5609-5620.

NAME	CAS # CAT. #	FUNCTION	EFFECT	CELL SYSTEM	REFERENCE
Bisindolylmaleimide 1i	133052-90-1 1331975	GSK-3β inhibitor	Enhances ESC self-renewal	mESCs	Bone, H.K. *Chem. Biol.* (2009) 16: 15
BIO	667463-62-9 6676296	GSK-3β inhibitor Activates Wnt signaling followed by Oct3/4 expression	Maintains ESC self-renewal	hESCs/ mESCs	Sato, N. *Nat. Med.* (2004) 10: 55
All-Trans Retinoic Acid	32-79-4 3027949	Retinoid pathway activator	Maintains feeder-independent self-renewal	mESCs	Chen, L. *Stem Cells* (2008) 26: 1858
Pluripotin	302-79-4 8393780	RasGAP and ERK1 inhibitor	Promotes self-renewal	mESCs	Chen, S., *PNAS U.S.A.* (2006) 103: 17266
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor	Together: Promote self-renewal	mESCs	Ying, Q.-L. *Nature* (2008) 453: 519
SU 5402	215543-92-3 2159233	VEGFR and FGFR inhibitor			
PD 184352	212631-79-3	MEK inhibitor			
PD 0325901	391210-10-9 3911091	MEK inhibitor	Blocks differentiation pathway of mESCs	mESCs	Ying, Q.-L. *Nature* (2008) 453: 519
Pinacidil	85371-64-8	Potassium channel activator	Enhances ESCs survival	hESCs	Barbaric, I. *Stem Cell Res.* (2010) 5: 104
Pyrintegrin	1228445-38-2 1223824	β1 integrin activator	Enhances hESCs survival after enzymatic dissociation	hESCs	Xu, Y. *PNAS U.S.A.* (2010) 107: 8129
ID 8	147591-46-6 1474669	DYRK pathway inhibitor	Sustains self-renewal and pluripotency	mESCs	Miyabayashi, T. *Biosci. Biotechnol. Biochem.* (2008) 72: 1242
Y-27632	129830-38-2 1293823	ROCK inhibitor	Together: Allows expansion without feeders or matrices	hESCs	Krawetz, R. *Tissue Eng. Part C: Methods* (2009) 16: 573
Rapamycin	53123-88-9 5318893	mTOR inhibitor			
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor	Stimulates proliferation and self-renewal of HSCs	hHSCs/ mHSCs	Bug, G. *Cancer Res.* (2005) 65: 2537
16,16-dimethyl PGE2	39746-25-3	Competitive inhibitor of 15-hydroxy PGDH	Prevents differentiation and preserves self-renewal	hHSCs	Hagedorn, E.J. *Exp. Cell Res.* (2014) 329: 220
WH-4-023	837422-57-8 83712-25	Selective Lck and Src inhibitor	Together: Supports self-renewal of naïve hESCs	hESCs	Theunissen, T.W. *Cell Stem Cell* (2014) 15: 471
PD 0325901	391210-10-9 3911091	Selective MEK/ERK inhibitor			
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor			
SB 590885	405554-55-4	B-Raf inhibitor			
(-)-Blebbistatin	856925-71-8 8567182	Non-muscle myosin II (NM II) ATPase inhibitor	Improves cell survival and cloning efficiency	hESCs	Chen, G. *Cell Stem Cell* (2010) 7: 240
Garcinol	78824-30-3 7883034	Histone cetyltransferase (HAT) inhibitor	Promotes *ex vivo* expansion of hESCs		
Endo-IWR-1	7883-03-4 1128234	Wnt pathway inhibitor; AXIN2 stabilizer	Together: Maintains mouse epiblast SCs and hESCs self-renewal	hESCs mouse epiblast SCs	Kim, H. *Nat. Commu.* (2013) 4: 2403
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor			
PD 98059	167869-21-8 1672186	Selective MEK/ERK pathway inhibitor	Enhances the growth and self-renewal of mESCs	mESCs	Qi, X. *PNAS U.S.A.* (2004) 101: 6027
Rosiglitazone	122320-73-4 1227342	Peroxisome proliferator-activated receptor γ (PPARγ) activator	Stimulates mENSCs proliferation and inhibits neuronal differentiation	mENSCs	Bragina, O. *Neurosci. Lett.* (2010) 482: 81
SAG	912545-86-9 9128694	Hedgehog pathway activator; Activates Smoothened (SMO)	Induces proliferation and survival of neuronal and glial precursors	mENSCs	Qi, X. *PNAS U.S.A.* (2004) 101: 6027
SB 203580	869185-85-3 8698538	p38 MAPK inhibitor	Enhances the growth and self-renewal of mESCs	mESCs	Kirby, L.A. *PloS one* (2012) 7: e39329
SB 216763	280744-09-4 2800944	WNT pathway activator; Inhibits GSK-3α and GSK-3β	Maintains mESCs in an undifferentiated, pluripotent state when co-cultured with MEFs	mESCs	Desbordes, S.C. *Cell Stem Cell* (2008) 2: 602
Sinomenine	6080-33-7 6083373	Anti-inflammatory plant alkaloid	Promotes self-renewal in cultured hESCs and mESCs	hESCs/ mESCs	Desbordes, S.C. *Cell Stem Cell* (2008) 2: 602

BioGems Catalog Number

NAME	CAS # CAT. #	FUNCTION	EFFECT	CELL SYSTEM	REFERENCE
Gatifloxacin	112811-59-3 1125931	Antibiotic	Promotes self-renewal in cultured hESCs and mESCs	hESCs/ mESCs	Ware, C.B. *Cell Stem Cell* (2009) 4: 359
Sodium Butyrate	156-54-7 1565474	Epigenetic modifier; Inhibits histone deacetylase	Supports self-renewal of hESCs and mESCs	hESCs/ mESCs	Csaszar, E. *Cell Stem Cell* (2012) 10: 218
StemRegenin 1	1227633-49-9 1224999	Aryl hydrocarbon receptor (AHR) antagonist	Promotes maintenance and expansion of hHSCs in culture	hHSCs	Choi, K.-M., *J. Biosci. Bioeng.* (2008) 105: 586
L-Ascorbic Acid	50-81-7 5088177	Antioxidant; Reducing agent	Supports proliferation of MSCs	MSCs	Huang, X. *Leukemia.* (2016) 30: 144
OAC-1	300586-90-7 3009078	Oct4 activator	Mediates *ex vivo* expansion of cord blood CD34+ hematopoietic stem and progenitor cells	HSCs	Qi, X. PNAS U.S.A. (2004) 101: 6027
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor	Together: Maintains undifferentiated mESCs	mESCs	Ying, Q.-L. *Nature* (2008) 453: 519
PD 0325901	391210-10-9 3911091	MEK inhibitor			Ying, Q.-L. *Nature* (2008) 453: 519
PD 173074	219580-11-7 2191178	Tyrosine kinase and FGFR inhibitor	Maintains the undifferentiated state of mESCs	mESCs	Chaurasia, P. *J. Clin. Invest.* 124.6 (2014): 2378
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor	Mediates *ex vivo* expansion of cord blood CD34+ hematopoietic stem and progenitor cells	Human cord blood HSCs	Dutta, D. *Stem Cells* (2011) 29: 618
Gö 6983	133053-19-7 1331975	PKC inhibitor	Inhibits differentiation and maintains pluripotency in mESCs	mESCs	Li, W. *Cell Stem Cell* (2009) 4: 16
A 83-01	909910-43-6 9094360	TGF-β1 receptor, ALK4, ALK5 and ALK7 inhibitor	Together: Supports long-term self renewal of riPSCs	riPSCs	
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor			
PD 0325901	391210-10-9 3911091	MEK inhibitor			

BioGems Catalog Number

Chemically Induced Pluripotent Stem Cells (iPSCs)

The use of hESCs in research and for therapeutic applications is a controversial issue due to a combination of religious, political and ethical considerations. This has led researchers to concentrate on adult stem cells as a source of pluripotent cells; however, working with these cells has several drawbacks that limit their use for practical purposes. A breakthrough discovery by Yamanaka generated iPSCs from somatic cells by the forced ectopic expression of four transcription factors (TFs), Oct4, Sox2, KLF4 and c-Myc (termed OSKM) by viral transduction. This new source of pluripotent cells opened new avenues for the research of regenerative medicine, disease modeling and drug discovery.

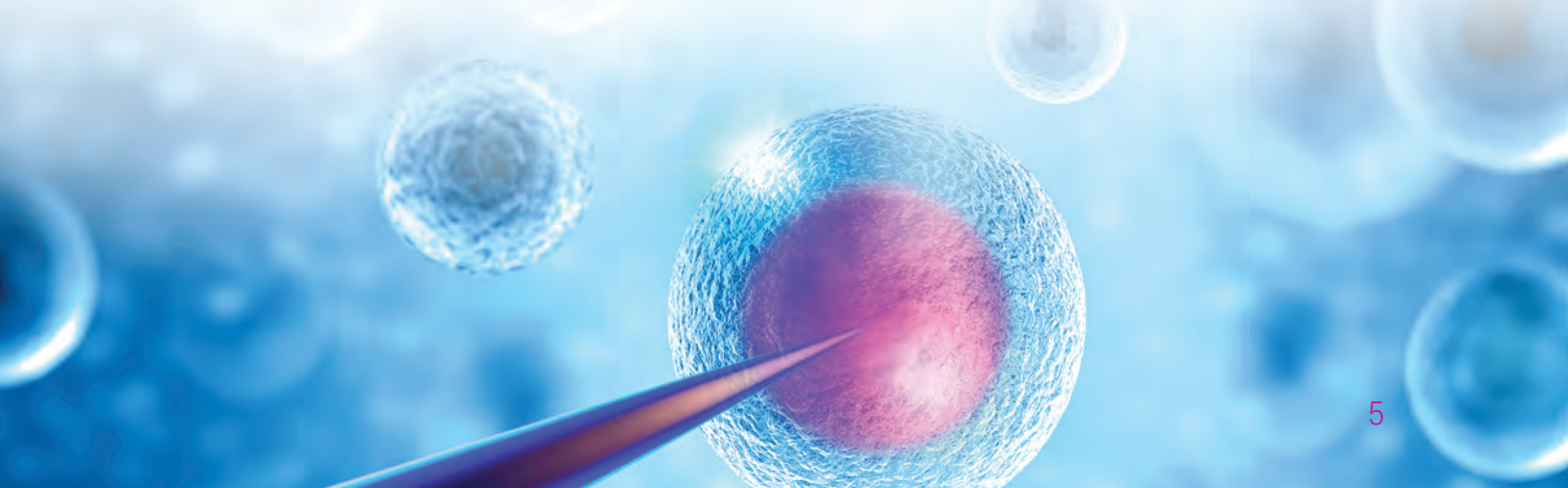
The use of iPSCs introduces a major safety concern related to possible tumorigenicity from viral integration of transcription factors and transgene alterations. This concern has led to the development of alternate methods for DNA-free induction of iPSCs and the introduction of external DNA sequences through non-integrative vectors. These methods, however, lack the efficiency and stability required for practical purposes.

Since small molecules have the ability to modulate gene expression through the regulation of epigenetic mechanisms, they can be used to replace some of the Yamanaka TFs and improve efficiency. This improvement has been demonstrated by numerous published studies that have successfully used small molecules to replace one or more of the Yamanaka TFs.

Another major improvement to the Yamanaka method came in 2013 with the development of a chemical-only induction of pluripotency. This chemical substitution allowed for a more efficient generation of iPSCs, bringing the method closer to the requirements of clinical applications.

References:

1. Ebrahimi, B. (2016). Chemical-only reprogramming to pluripotency. *Frontiers in Biology,* 11(2), 75-84.
2. Hou, P., Li, Y., Zhang, X., et al., & Deng, H. (2013). Pluripotent stem cells induced from mouse somatic cells by small-molecule compounds. *Science,* 341(6146), 651-654.
3. Lin, T., & Wu, S. (2015). Reprogramming with small molecules instead of exogenous transcription factors. *Stem cells international,* 2015.
4. Takahashi, K., & Yamanaka, S. (2006). Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell,* 126(4), 663-676.
5. Zhang, Y., Li, W., Laurent, T., & Ding, S. (2012). Small molecules, big roles–the chemical manipulation of stem cell fate and somatic cell reprogramming. *J Cell Sci,* 125(23), 5609-5620.



NAME	CAS # CAT. #	FUNCTION	EFFECT	REQUIRED TRANSCRIPTION FACTORS	HOST	REFERENCE
SB 431542	301836-41-9 3014193	TGF-β1 receptor, ALK4, ALK5 and ALK7 inhibitor	Replaces Sox2 in the reprogramming of MEFs to iPSCs	Oct4, KLF4, and c-Myc	Mouse	Ichida, J.K. *Cell Stem Cell* (2009) 5: 491
(+)-Bay K8644	98791-67-4 9876741	L-type calcium channel agonist	Together: Replace Sox2 and c-Myc in the reprogramming of MEFs to iPSCs	Oct4 and KLF4	Mouse	Shi, Y. *Cell Stem Cell* (2008) 3: 568
BIX-01294	1392399-03-9 1806425	G9a histone methyltransferase inhibitor				
3-Deazaneplanocin A	102052-95-9 1029595	Histone EZH2 lysine methyltransferase inhibitor	Together: Enable chemical reprogramming (without genetic factors) of MEFs to iPSCs		Mouse	Hou, P. *Science* (2013) 341: 651
CHIR 99021	102052-95-9 2520691	GSK-3β inhibitor				
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase				
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor				
Tranylcpromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor				
E-616452	446859-33-2 4463325	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5				
TTNPB	71441-28-6 7142861	Retinoic acid receptor ligand				
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase	Replaces Oct4 in the reprogramming of MEFs to iPSCs	Sox2, KLF4, and c-Myc	Mouse	Hou, P. *Science* (2013) 341: 651
D 4476	301836-43-1	Activin/NODAL/TGF-β pathway inhibitor; Inhibits CK1, ALK5 and p38 MAPK	Replaces Oct4 in the reprogramming of mouse fibroblasts to iPSCs	Sox2, KLF4, and c-Myc	Mouse	Hou, P. *Science* (2013) 341: 651
DBZ	209984-56-5	Notch pathway inhibitor; Inhibits γ-secretase	Replaces KLF4 and c-Myc in the reprogramming of human keratinocytes to iPSCs	Sox2 and Oct4	Human	Ichida, J.K. *Nat. Chem. Biol.* (2014) 10: 632
Kenpaullone	142273-20-9 1422097	WNT pathway activator; GSK-3β inhibitor	Replaces KLF4 in the reprogramming of MEFs to iPSCs	Oct4, Sox2, and c-Myc	Mouse	Lyssiotis, C.A. *Proc. Natl. Acad. Sci. U.S.A.* (2009) 106: 8912
LY-364947	396129-53-6 3965362	Activin/BMP/TGF-β pathway inhibitor; Inhibits ALK5	Together: Replace SOX2 in the reprogramming of MEFs to iPSCs	Oct4, KLF4, and c-Myc	Mouse	Ichida, J.K. *Cell Stem Cell* (2009) 5: 491
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor				
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor	Replaces KLF4, and c-Myc in the reprogramming of human fibroblasts to iPSCs	Oct4 and Sox2	Human	Huangfu, D. *Nat. Biotechnol.* (2008) 26: 1269
PP1	172889-26-8	Tyrosine kinase inhibitor; Inhibits LCK, FYN, HCK, and SRC	Replaces Sox2 in the reprogramming of MEFs to iPSCs	Oct4, KLF4, and c-Myc	Mouse	Staerk, J. *Angew. Chem. Int. Ed.* (2011) 50: 5734
PD 0325901	391210-10-9 3911091	MEK/ERK pathway inhibitor; Inhibits MEK	Together: Replace Sox2, KLF4, and c-Myc in the reprogramming of human epidermal keratinocytes to iPSCs	Oct4	Human	Zhu, S. *Cell Stem Cell* (2010) 7: 651
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor				
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor				
A 83-01	909910-43-6 9094360	Activin/NODAL/TGF-β pathway inhibitor				
PS48	1180676-32-7	Phosphoinositide-dependent protein kinase 1 (PDK1)				
Sodium Butyrate	156-54-7 1565474	Epigenetic modifier; Inhibits histone deacetylase				

NAME	CAS # CAT. #	FUNCTION	EFFECT	REQUIRED TRANSCRIPTION FACTORS	HOST	REFERENCE
Tranylcypromine	1986-47-6	Lysine-specific demethylase 1 (LSD1) inhibitor	Together: Replace Sox2 and c-Myc in the reprogramming of human keratinocytes to iPSCs	Oct4 and KLF4	Human	Li, W. *Stem Cells* (2009) 27: 2992
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor				
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor	Together: Enable chemical reprogramming (without genetic factors) of iPSC from neural stem cells from the ectoderm		Mouse	Ye, J. *Cell Res.* (2016) 26: 34
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor				
E 616452	446859-33-2 4463325	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5				
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor				
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase				
EPZ 004777	1338466-77-5	Protein methyltransferase DOT1L inhibitor				
Ch 55	110368-33-7	Synthetic analog of retinoic acid				
3-Deazaneplanocin A	102052-95-9 1029595	Histone EZH2 lysine methyltransferase inhibitor				
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor	Together: Enable chemical reprogramming (without genetic factors) of iPSC from small intestinal epithelial cells from the endoderm		Mouse	Ye, J. *Cell Res.* (2016) 26: 34
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor				
E 616452	446859-33-2 4463325	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5				
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor				
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase				
AM 580	102121-60-8 1026081	Retinoic acid receptor agonist				
3-Deazaneplanocin A	102052-95-9 1029595	Histone EZH2 lysine methyltransferase inhibitor				
CHIR99021	252917-06-9 2520691	WNT pathway activator; Inhibits GSK-3β	Together: Enable chemical reprogramming (without genetic factors) of fibroblasts into induced neural stem cell-like cells		Mouse	Zhang, M. *Cell Stem Cell* (2016) 18: 653
LDN 193189	1062368-24-4 1062443	Activin/BMP/TGF-β pathway inhibitor				
A 83-01	909910-43-6 9094360	Activin/NODAL/TGF-β pathway inhibitor				
Hh-Ag1.5	612542-14-0	Hedgehog pathway activator				
All-Trans Retinoic Acid	302-79-4 3027949	Retinoid pathway activator				
SMER28	307538-42-7	Autophagy small-molecule enhancer (SMER)				
RG 108	48208-26-0 4822608	DNA methyltransferase (DNMT) inhibitor				
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor				
BIX-01294	1392399-03-9 1806425	G9a histone methyltransferase inhibitor	Replaces Sox2 and c-Myc in the reprogramming of neural progenitor cells to iPSCs	Oct3/4 and KLF4	Mouse	Shi, Y. Cell *Stem Cell* (2008) 2: 525
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor	Together: Replaces Sox2, KLF4, and c-Myc in the reprogramming of MEFs to iPSCs	Oct4	Mouse	Li, Y. *Cell Res.* (2011) 21: 196
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor				
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor				
E 616452	446859-33-2 4463325	Activin/NODAL/TGF-β inhibitor; Inhibits ALK5				

BioGems Catalog Number

NAME	CAS # CAT. #	FUNCTION	EFFECT	REQUIRED TRANSCRIPTION FACTORS	HOST	REFERENCE
AMI-5	17372-87-1	Protein Methyltransferase (PRMT) Inhibitor	Together: Replaces Sox2, KLF4, and c-Myc in the reprogramming of MEFs to iPSCs	Oct4	Mouse	Yuan, X. *Stem Cells* (2011) 29: 549
A 83-01	909910-43-6 9094360	Activin/NODAL/TGF-β pathway inhibitor				
25-hydroxy Cholesterol	2140-46-7 2144674	Hedgehog Pathway Activator	Replaces Sox2, KLF4 and c-Myc in the reprogramming of MEFs to iPSCs	Oct4	Mouse	Moon, J-H. *Cell Res.* (2011) 21: 1305
Purmorphamine	483367-10-8 4831086	Hedgehog Pathway Activator	Replaces Sox2, KLF4 and c-Myc in the reprogramming of MEFs to iPSCs	Oct4	Mouse	Moon, J-H. *Cell Res.* (2011) 21: 1305
3-Deazaneplanocin A	102052-95-9 1029595	Histone EZH2 lysine methyltransferase inhibitor	Together: Enables chemical reprogramming (without genetic factors) of MEFs to iPSCs		Mouse	Long, Y. *Cell Res.* (2015) 25: 1171
CHIR 99021	102052-95-9 2520691	GSK-3β inhibitor				
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase				
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor				
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor				
E-616452	446859-33-2 4463325	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5				
TTNPB	71441-28-6 7142861	Retinoic acid receptor ligand				
BrdU	59-14-3 5911439	Thymidine analog				
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor	Together: Enables chemical reprogramming (without genetic factors) of MEFs to iPSCs (but at low frequency)		Mouse	Long, Y. *Cell Res.* (2015) 25: 1171
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase				
E-616452	446859-33-2 4463325	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5				
BrdU	59-14-3 5911439	Thymidine analog				
3-Deazaneplanocin A	102052-95-9 1029595	Histone EZH2 lysine methyltransferase inhibitor	Together: Enables chemical reprogramming (without genetic factors) of MEFs to iPSCs		Mouse	Zhao, Y. *Cell* (2015) 163: 1678
CHIR 99021	102052-95-9 2520691	GSK-3β inhibitior				
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase				
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor				
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor				
E-616452	446859-33-2 4463325	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5				
TTNPB	71441-28-6 7142861	Retinoic acid receptor ligand				
EPZ 004777	1338466-77-5	DOT1L methyltransferase inhibitor				
AM 580	102121-60-8 1026081	Retinoic acid receptor agonist				
SGC 0946	1561178-17-3	DOT1L methyltransferase inhibitor				
5-Aza-2'-deoxycytidine	2353-33-5	Cytosine analog, DNA methyltransferase inhibitor				

BioGems Catalog Number

Improving Reprogramming Efficiency

The use of induced pluripotent stem cells (iPSCs) rather than ESCs avoids those ethical issues often associated with the use of hESCs and holds several advantages including the availability to "endlessly" generate genetically matching cells, which is important for disease modeling and stem cell transplantation.

The low level of conversion efficiency of the original Yamanaka method, which is approximately 0.1% for mESCs and 0.01% for hESCs, became an obstacle for practical applications using iPSCs.

Since basic mechanisms are similar between ESCs and iPSCs, the small molecules that affect fundamental pathways in ESCs have similar effects in iPSCs. Small molecules can be used alone or in combination cocktails that simultaneously target several pathways and processes to enhance reprogramming efficiency.

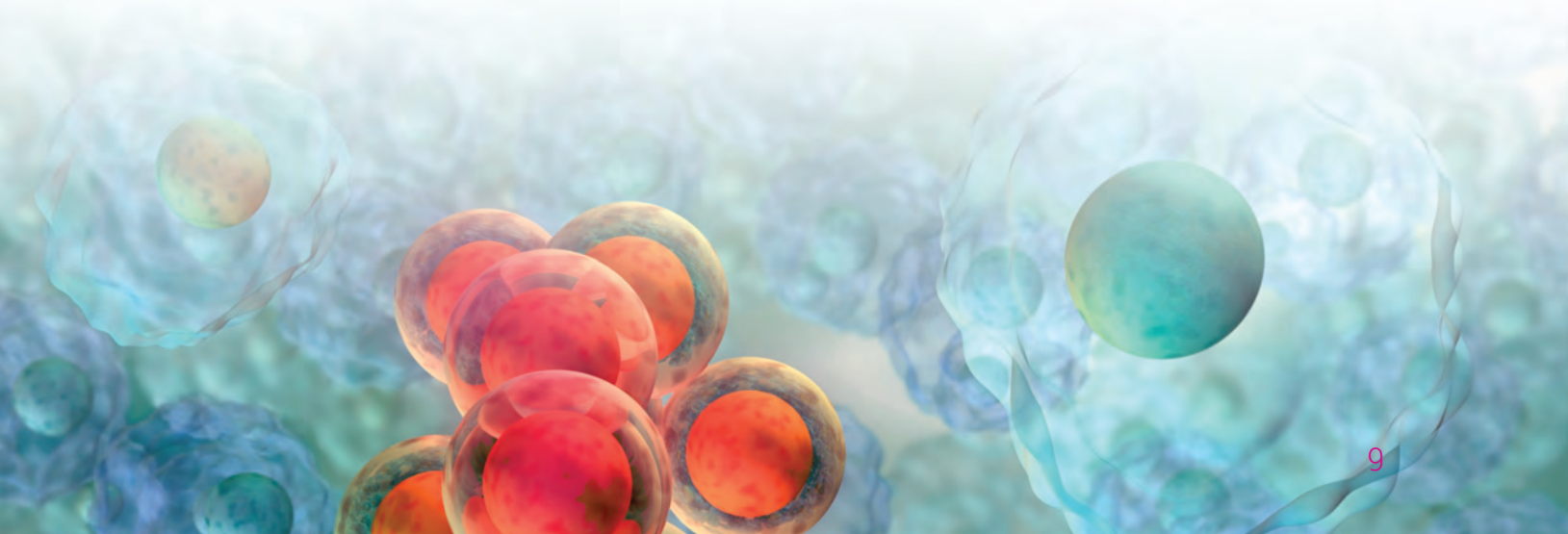
Small molecules can be used to enhance reprogramming efficiency by targeting various cellular processes through:

- Enzymes, such as histone deacetylases, histone demethylases, and DNA methyltransferases. These enzymes influence cells at the level of transcription to cause epigenetic modifications.
- Signaling pathways, such as the Wnt and TGF-β.
- The regulation of cell senescence, which can lead to low efficiency in cellular reprogramming.

Efforts are underway to discover new small molecules that can further improve reprogramming efficiency.

References:

1. Lin, T., & Wu, S. (2015). Reprogramming with small molecules instead of exogenous transcription factors. *Stem cells international*, 2015.
2. Masip, M., Veiga, A., Belmonte, J. C. I., & Simón, C. (2010). Reprogramming with defined factors: from induced pluripotency to induced transdifferentiation. *Molecular human reproduction,* 16(11), 856-868.
3. Schmole, A. C., Hubner, R., Beller, M., Rolfs, A., & J Frech, M. (2013). Small molecules in stem cell research. *Current pharmaceutical biotechnology,* 14(1), 36-45.



NAME	CAS # CAT. #	FUNCTION	EFFECT	SPECIES	REFERENCE
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor	Increases reprogramming efficiency >100-fold	Mouse/ Human	Huangfu, D. *Nat. Biotechnol.* (2008) 26: 795
Suberoylanilide Hydroxamic Acid	149647-78-9 1497894	Histone deacetylase (HDAC) inhibitor	Increases reprogramming efficiency >10-fold	Mouse	Huangfu, D. *Nat. Biotechnol.* (2008) 26: 795
Trichostatin A	58880-19-6 5881960	Histone deacetylase (HDAC) inhibitor	Increases reprogramming efficiency >10-fold	Mouse	Huangfu, D. *Nat. Biotechnol.* (2008) 26: 795
Sodium Butyrate	156-54-7 1565474	Histone deacetylase (HDAC) inhibitor	Increases reprogramming efficiency 100-fold	Mouse/ Human	Mali, P. *Stem Cells* (2010) 28: 713
AM 580	102121-60-8 1026081	Retinoic acid receptor agonist	Increases reprogramming efficiency ~200-fold	Mouse	Wang, Q., *Cell Res.* (2011) 21: 1424
3-Deazaneplanocin A	102052-95-9 1029595	Epigenetic modulator, Inhibits histone EZH2 lysine methyltransferase	Increases reprogramming efficiency 65-fold	Mouse	Hou, P. *Science* (2013) 341: 651
TTNPB	102052-95-9 7142861	Retinoic acid receptor ligand	Increases reprogramming efficiency 40-fold	Mouse	Hou, P. *Science* (2013) 341: 651
SB 431542	301836-41-9 3014193	TGF-β1 receptor, ALK4, ALK5 and ALK7 inhibitor	Together: Increases reprogramming efficiency ~200-fold	Human	Lin, T. *Nat. Methods* (2009) 6: 805
Thiazovivin	1226056-71-8 1227180	ROCK inhibitor			
PD 0325901	391210-10-9 3911091	Selective MEK/ERK inhibitor			
A 83-01	909910-43-6 9094360	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5, ALK4, and ALK7	Increases reprogramming efficiency 7-fold	Human	Zhu, S. *Cell Stem Cell* 7.6 (2010) 7:651
RSC-133	1418131-46-0	DNA methyltransferase (DMNT) and HDAC inhibitor	Increases reprogramming efficiency 3-fold	Human	Lee, J. *Angew. Chem. Int. Ed.* (2012) 51: 12509
Tranylcypromine	1986-47-6 1984764	Histone demethylation inhibitor	Increases reprogramming efficiency 3-fold	Mouse	Li, W. *Stem Cells* (2009) 27: 2992
Rapamycin	53123-88-9 5318893	mTOR inhibitor	Increases reprogramming efficiency 5-fold	Mouse	Chen, T., *Aging Cell* (2011) 10: 908
8-Bromo-cAMP	76939-46-3 2354843	cAMP analog; Protein kinase A (PKA) activator	Increases reprogramming efficiency 6.5-fold	Human	Wang, Q., *Cell Res.* (2011) 21: 1424
N-Oxalylglycine	5262-39-5	Prolyl-4-hydroxylase inhibitor	Increases reprogramming efficiency 3.5-fold	Human	Zhu, S. *Cell Stem Cell* (2010) 7: 651
OAC-1	300586-90-7 3009078	Oct4 activator	Increases reprogramming efficiency ~20-fold	Mouse	Li, W., *Proc. Natl. Acad. Sci. U.S.A.* (2012) 109: 20853
5-Azacytidine	320-67-2 3206727	DNA methyltransferase (DMNT) inhibitor	Increases reprogramming efficiency ~4-fold	Mouse	Mikkelsen, T.S. *Nature* (2008) 454: 49
bpV(HOpic)	722494-26-0	PTP and PTEN inhibitor	Together: Increases reprogramming efficiency	Mouse	Liao, J. *Mol. Ther.* (2013) 21: 1242
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor			
Gö 6983	133053-19-7 1331975	PKC inhibitor	Enhances reprogramming efficiency	Mouse	Dutta, D. *Stem Cells* (2011) 29: 618
HA-100	210297-47-5 2104759	Protein kinase inhibitor; Inhibits PKA, PKC, and PKG	Together: Increases reprogramming efficiency	Human	Yu, J. *PloS one* (2011) 6: e17557
PD 0325901	391210-10-9 3911091	Selective MEK/ERK inhibitor			
CHIR99021	252917-06-9 2520691	WNT pathway activator; Inhibits GSK-3β			
A83-01	909910-43-6 9094360	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5, ALK4, and ALK7			
L-Ascorbic Acid	50-81-7 5088177	Antioxidant; Reducing agent	Increases reprogramming efficiency	Mouse/ Human	Esteban, M.A. *Cell Stem Cell* (2010) 6: 71-79
Quercetin	117-39-5	mTOR, PI3K/AKT, NF-kB, and tyrosine kinase pathway inhibitor; Inhibits PI3K and SRC kinase	Increases reprogramming efficiency	Human	Zhu, S. *Cell Stem Cell* (2010) 7: 651-655

NAME	CAS # CAT. #	FUNCTION	EFFECT	SPECIES	REFERENCE
RG 108	48208-26-0 4822608	Epigenetic modifier; Inhibits DNA methyltransferase (DNMT)	Increases reprogramming efficiency	Mouse/ Human	Shi, Y. *Cell Stem Cell* (2008) 3: 568-574
Thiazovivin	1226056-71-8 1227180	ROCK inhibitor	Increases reprogramming efficiency	Human	Hu, K. *Blood* (2011) 117: e109-e119
Cyclic Pifithrin-α	511296-88-1 5118819	p53 Inhibitor	Increases reprogramming efficiency	Mouse	Liao, J. *Mol. Ther.* (2013) 21: 1242-1250

BioGems Catalog Number

Chemical Transdifferentiation

Regenerative medicine, which can replace lost or damaged cells in a variety of tissues and organs, requires sufficient amounts of the desired competent cells for transplantation. Such cells can be obtained by reprogramming somatic cells into pluripotent stem cells (PSCs), which can then be differentiated into the desired functional cells. Transdifferentiation, which refers to the direct lineage reprogramming of one specialized somatic cell-type into another without passing through the pluripotent state, holds several advantages over the PSC-based strategies, including higher efficiency and improved safety.

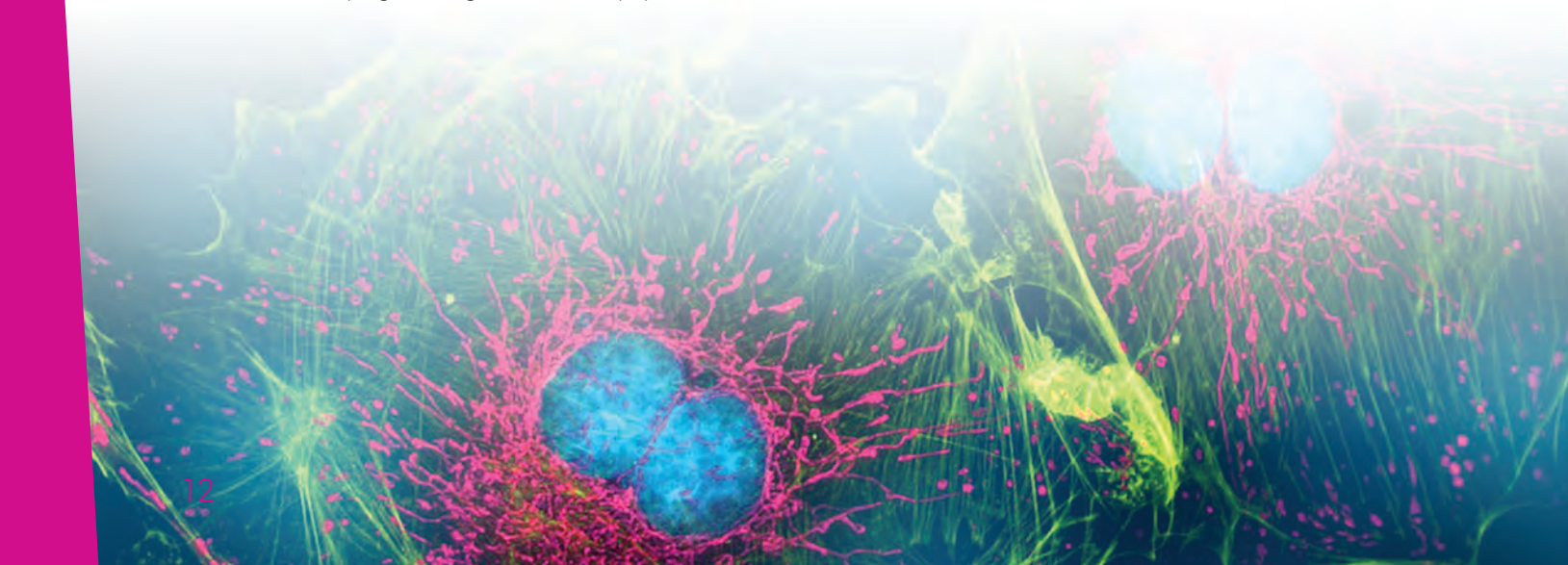
Changes in cellular fate involve a profound change in gene transcription, which is regulated predominantly by TFs. Thus, forced expression of tissue-specific TFs can be used to induce transdifferentiation of a variety of somatic cells within the same germ layer, and even across germ layers.

Although small molecules were initially used to boost and facilitate TF-based transdifferentiation, further development in the field has enabled transdifferentiation of various cell-types using a mixture of small molecules, growth factors, and transient overexpression of the Yamanaka OSKM TFs. This method removes the need for prolonged, forced expression of these TFs that is required with inducing pluripotency.

The complete avoidance of TF use has recently been demonstrated in the use of a defined combination of small molecules and growth factors.

References:

1. Xie, M., Tang, S., Li, K., & Ding, S. (2017). Pharmacological Reprogramming of Somatic Cells for Regenerative Medicine. *Accounts of Chemical Research*. 50 (5), 1202–1211.
2. Xu, J., Du, Y., & Deng, H. (2015). Direct lineage reprogramming: strategies, mechanisms, and applications. *Cell stem cell*, 16(2), 119-134.
3. Xu, A., & Cheng, L. (2016). Chemical transdifferentiation: closer to regenerative medicine. *Frontiers of medicine,* 10(2), 152-165.
4. Zhang, Y., Li, W., Laurent, T., & Ding, S. (2012). Small molecules, big roles–the chemical manipulation of stem cell fate and somatic cell reprogramming. *J Cell Sci,* 125(23), 5609-5620.



NAME	CAS # CAT. #	FUNCTION	STARTING CELLS	TARGET CELLS	REQUIRED TRANSCRIPION FACTORS	REQUIRED CYTOKINES	REFERENCE
RepSox	446859-33-2 4463325	Activin/NODAL/TGF-β; Inhibits ALK5	Human Fibroblasts	Mature neurons		BDNF GDNF NT-3	Hu, W. *Cell Stem Cell* (2015) 17: 204
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase					
SP 600125	129-56-6 1295666	c-Jun N-terminal kinase (JNK) inhibitor					
Gö 6983	133053-19-7 1331975	PKC inhibitor					
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor					
SB 431542	301836-41-9 3014193	TGF-β1 receptor; ALK4, ALK5 and ALK7 inhibitor	Mouse Fibroblasts	Mature neurons		BDNF GDNF	Li, X. *Cell Stem Cell* (2015) 17: 195)
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor					
ISX-9	832115-62-5	Inducer of neural differentiation					
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase					
I-BET151	1300031-49-5	Bromodomain and extra terminal (BET) proteins family inhibitor					
Dexamethasone	50-02-2 5000222	Glucocorticoid pathway activator; Activates glucocorticoid receptor	Mouse Pancreatic cells	Hepatocytes			Shen, C-N. *Nat. Cell Biol.* (2000) 2: 879
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase	Human Fetal lung fibroblasts	Cholinergic neurons			Liu, M-L. *Nat. Commu.* (2013) 4:2183
PD 0325901	391210-10-9 3911091	MEK/ERK pathway inhibitor; Inhibits MEK	Human iPSC	Naïve or "mouse ESC-like" pluripotent state		LIF FGF-basic TGF-β1	Hanna, J. *Proc. Natl. Acad. Sci. U.S.A.* (2010) 107: 9222
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor					
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase					
SP 600125	129-56-6 1295666	c-Jun N-terminal kinase (JNK) inhibitor					
SB 203580	152121-47-6 1524762	p38 MAPK inhibitor					
AS-8351	796-42-9 7964296	Histone demethylase inhibitor	Human fetal lung fibroblasts	Cardiomyocytes		Activin A BMP-4 VEGF	Cao, N. *Science* (2016) 352: 1216
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitior					
A 83-01	909910-43-6 9094360	Activin/NODAL/TGF-β pathway inhibitor					
BIX 01294	1392399-03-9 1806425	G9a histone methyltransferase inhibitor					
SC-1	839707-37-8 8393780	PI3K and MEK/ERK pathway inhibitor					
Y 27632	129830-38-2 1293823	RHO/ROCK pathway inhibitor; Inhibits ROCK1 and ROCK2					
OAC2	6019-39-2 6013929	Oct4-activating compound					
SU 16f	251356-45-3 2514536	Platelet-derived growth factor receptor β (PDGFRβ) inhibitor					
JNJ 10198409	627518-40-5 6274058	Platelet-derived growth factor receptor tyrosine kinase (PDGF-RTK) inhibitor					
Bexarotene	153559-49-0	High-affinity retinoid X receptor (RXR) agonist	Mouse Myoblasts	Brown adipocyte-like cells (BAT)			Nie, B. *Cell Rep.* (2017) 18: 624

BioGems Catalog Number

NAME	CAS # CAT. #	FUNCTION	STARTING CELLS	TARGET CELLS	REQUIRED TRANSCRIPION FACTORS	REQUIRED CYTOKINES	REFERENCE
5-Azacytidine	320-67-2 3206727	Epigenetic modifier; Inhibits DNA methyltransferase (DNMT)	Human Fibroblasts	Pancreatic β-like cells			Pennarossa, G. *Proc. Natl. Acad. Sci. U.S.A.* (2013) 110: 8948
All-Trans Retinoic Acid	302-79-4 3027949	Retinoid pathway activator					
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor	Human urinary cells and Mouse Fibroblasts	Chemical-induced Neural Progenitor Cells (ciNPCs)		EGF FGF-basic	Cheng, L. *Cell Res.* (2014) 24: 665
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor					
E 616452	446859-33-2 4463325	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5					
Sodium Butyrate	156-54-7 1565474	Epigenetic modifier; Inhibits histone deacetylase	Human urinary cells and Mouse Fibroblasts	Chemical-induced Neural Progenitor Cells (ciNPCs)		EGF FGF-basic	Cheng, L. *Cell Res.* (2014) 24: 665
Lithium Chloride	7447-41-8						
SB 431542	301836-41-9 3014193	TGF-β1 receptor, ALK4, ALK5 and ALK7 inhibitor					
Trichostatin A	58880-19-6 5881960	Class I, II, and IV Histone deacetylase (HDAC) inhibitors	Human urinary cells and Mouse Fibroblasts	Chemical-induced Neural Progenitor Cells (ciNPCs)		EGF FGF-basic	Cheng, L. *Cell Res.* (2014) 24: 665
Lithium Carbonate	554-13-2						
Tranilast	53902-12-8	Anti-inflammatory and immunomodulatory effects					
LDN 193189	1062368-24-4 1062443	Activin/BMP/TGF-β pathway inhibitor; Inhibits ALK1, ALK2, ALK3, and ALK6	Human cortical astrocytes	Functional neurons		BDNF NT-3 IGF-1	Zhang, L. *Cell Stem Cell* (2015) 17: 735
SB 431542	301836-41-9 3014193	TGF-β1 receptor, ALK4, ALK5 and ALK7 inhibitor					
TTNPB	71441-28-6 7142861	Retinoic acid receptor ligand					
Thiazovivin	1226056-71-8 1227180	ROCK inhibitor					
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor					
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor					
DAPT	208255-80-5 2088055	Notch pathway inhibitor; Inhibits γ-Secretase					
SAG	912545-86-9 9128694	Hedgehog pathway activator; Activates Smoothened (SMO)					
Purmorphamine	483367-10-8 4831086	Hedgehog Pathway Activator; Activates Smoothened (SMO)					
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor	Mouse Neonatal and adult astrocytes	DCX + neuroblasts and Tuj1+ or NeuN + neurons		Sonic Hedgehog (Shh), BDNF, GDNF, FGF-8 FGF-basic	Cheng, Lin *Cell Res.* (2015) 25: 1269
E 616452	446859-33-2 4463325	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5					
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor	Mouse Fibroblasts	Chemical-induced cardiomyocyte like cells (CiCMs)		LIF GDF-15/MIC-1 G-CSF	Fu, Y. *Cell Res.* (2015) 25: 1013
E 616452	446859-33-2 4463325	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5					
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase					
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor					
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor					

BioGems Catalog Number

NAME	CAS # CAT. #	FUNCTION	STARTING CELLS	TARGET CELLS	REQUIRED TRANSCRIPION FACTORS	REQUIRED CYTOKINES	REFERENCE
TTNPB	71441-28-6 7142861	Retinoic acid receptor ligand	Mouse Fibroblasts	Chemical-induced cardiomyocyte like cells (CiCMs)		LIF GDF-15/ MIC-1 G-CSF	Fu, Y. *Cell Res.* (2015) 25: 1013
L-Ascorbic Acid	50-81-7 5088177	Antioxidant; Reducing agent					
Rolipram	61413-54-5 6145453	cAMP pathway activator; Inhibits type 4 cyclic nucleotide phospho-diesterases (PDE4)					
PD 0325901	391210-10-9 3911091	MEK/ERK pathway inhibitor; Inhibits MEK					
E 616452	446859-33-2 4463325	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5	Mouse Fibroblasts	Cardiomyocytes progenitors		FGF-basic	Han, X. *Cell Res.* (2017) 27: 386
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor					
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor					
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase					
SB 431542	301836-41-9 3014193	TGF-β1 receptor, ALK4, ALK5 and ALK7 inhibitor					
Dorsomorphin	866405-64-3 8666430	BMP and AMPK pathway inhibitor; Inhibits ALK2, ALK3, ALK6, and AMPK					
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor					
E 616452	446859-33-2 4463325	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5	Mouse Fibroblasts	Neuronal/glial progenitors		FGF-basic	Han, X. *Cell Res.* (2017) 27: 386
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor					
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor					
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase					
A 83-01	909910-43-6 9094360	Activin/NODAL/TGF-β pathway inhibitor					
Valproic Acid	1069-66-5 1066656	Histone deacetylase (HDAC) inhibitor					
E 616452	446859-33-2 4463325	Activin/NODAL/TGF-β pathway inhibitor; Inhibits ALK5	Mouse Fibroblasts	Adipocytes progenitors		FGF-basic	Han, X. *Cell Res.* (2017) 27: 386
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor					
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor					
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase					
Nicotinamide	98-92-0 9899208	Poly (ADP-ribose) polymerase (PARP-1) inhibitor	Human Fibroblasts	Insulin Expressing Clusters		FGF-basic IGF-I	Pereyra-Bonnet, F. *PloS one* (2014) 9: e100369
Exendine-4	914454-01-6	Peptide agonist of the glucagon-like peptide 1 (GLP-1) receptor					
SB 431542	301836-41-9 3014193	TGF-β1 receptor, ALK4, ALK5 and ALK7 inhibitor	Mouse Fibroblasts	Cardiomyocytes	Oct4	BMP-4	Wang, H. *Cell Rep.* (2014) 6: 951
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor					
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor					
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase					

BioGems Catalog Number

NAME	CAS # CAT. #	FUNCTION	STARTING CELLS	TARGET CELLS	REQUIRED TRANSCRIPION FACTORS	REQUIRED CYTOKINES	REFERENCE
A 83-01	909910-43-6 9094360	Activin/NODAL/TGF-β pathway inhibitor	Human Embryonic fibroblasts	Cardyomyocytes Endothelial cells Smooth muscle cells	Oct4, KLF4, Sox2, and c-Myc		Zhu, S. *Cell Res.* (2014) 24: 126
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor					
Sodium Butyrate	156-54-7 1565474	Epigenetic modifier; Inhibits histone deacetylase					
1-Oleoyl Lysophosphatidic Acid	22556-62-3 2256236	Lysophosphatidic acid (LPA)1 and LPA2 agonist	Mouse Embryonic fibroblasts	Mature Pancreatic-like Cells	Oct4, KLF4, Sox2, and c-Myc		Xie, M. *Acc. Chem. Res.* (2017) 50: 1202
Rolipram	61413-54-5 6145453	cAMP pathway activator; Inhibits type 4 cyclic nucleotide phosphodiesterases (PDE4)					
SP 600125	129-56-6 1295666	c-Jun N-terminal kinase (JNK) inhibitor					
JAK Inhibitor I	457081-03-7 4570371	JAK/STAT pathway inhibitor; Inhibits JAK1, JAK2, and JAK3					
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor					
SU 5402	215543-92-3 2159233	VEGFR and FGFR inhibitor					
LiCl	7447-41-8		Embryonic fibroblasts	Mature Mouse Pancreatic like cells	Oct4, KLF4, Sox2, and c-Myc	Activin A	Li, K. *Cell stem cell* (2014) 14: 228
BIX 01294	1392399-03-9	G9a histone methyltransferase inhibitor					
2-Phospho-L-ascorbic Acid Trisodium Salt	66170-10-3	A stable ascorbic acid derivative					
All-Trans Retinoic Acid	302-79-4 3027949	Retinoid pathway activator					
A 83-01	909910-43-6 9094360	Activin/NODAL/TGF-β pathway inhibitor					
LDE225	1218778-77-8	Hedgehog signaling pathway inhibitor					
SB 203580	152121-47-6 1524762	p38 Mitogen-activated protein kinase (MAPK) inhibitor					
RG 108	48208-26-0 4822608	Epigenetic modifier; Inhibits DNA methyltransferase (DNMT)	Human Fibroblasts	Pancreatic β-like cells	Oct4	FGF-basic EGF KGF (FGF-7) FGF-10 Activin A	Zhu, S. *Nat. Commun.* (2016) 7: 10080
Thiazovivin	1226056-71-8 1227180	ROCK inhibitor					
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor					
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor					
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase					
Nicotinamide	98-92-0 9899208	Poly (ADP-ribose) polymerase (PARP-1) inhibitor					
Exendine-4	914454-01-6	Glucagon-like peptide 1 (GLP-1) receptor agonist					
Sodium Butyrate	156-54-7 1565474	Epigenetic modifier; Inhibits histone deacetylase					
5'-N-Ethylcarboxa-	35920-39-9	Adenosine receptors agonist					

NAME	CAS # CAT. #	FUNCTION	STARTING CELLS	TARGET CELLS	REQUIRED TRANSCRIPION FACTORS	REQUIRED CYTOKINES	REFERENCE
All-Trans Retinoic Acid	302-79-4 3027949	Retinoid pathway activator	Human Fibroblasts	Pancreatic β-like cells	Oct4	FGF-basic EGF KGF (FGF-7) FGF-10 Activin A	Zhu, S. *Nat. Commun.* (2016) 7: 10080
A 83-01	909910-43-6 9094360	Activin/NODAL/TGF-β pathway inhibitor					
Compound E	209986-17-4	Notch pathway inhibitor					
GDC-0449	879085-55-9	Smoothened (SMO) antagonist					
LDN193189 (Hydrochloride)	1062368-62-0 1066208	BMP pathway inhibitor; Inhibits ALK1, ALK2, ALK3, and ALK6					
TPPB	497259-23-1	Protein Kinase C (PKC) activator					
Nicotinamide	98-92-0 9899208	Poly (ADP-ribose) polymerase (PARP-1) inhibitor					
L-Ascorbic Acid	50-81-7 5088177	Antioxidant; Reducing agent					
Bay K8644	98791-67-4 9876741	L-type calcium channel inhibitor					
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor	Mouse Fibroblasts	Cardiomyocytes	Oct4	BMP-4 PDGF-BB	Wang, H. *Cell Rep.* (2014) 6: 951
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor					
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase					
SB 431542	301836-41-9 3014193	TGF-β1 receptor, ALK4, ALK5 and ALK7 inhibitor					
Valproic Acid	1069-66-5	Histone deacetylase (HDAC) inhibitor	Neonatal and adult astrocytes	DCX$^+$ neuroblasts and Tuj1$^+$ or NeuN$^+$ neurons		BDNF, GDNF FGF-8 FGF-basic Sonic Hedgehog (Shh)	Cheng, Lin *Cell Res.* (2015) 25: 1269
E 616452	446859-33-2	Activin/Nodal/TGF-β pathway inhibitor; Inhibits ALK5					
LDN 193189	1062368-24-4 1062443	Activin/BMP/TGF-β pathway inhibitor; Inhibits ALK1, ALK2, ALK3, and ALK6	Mouse Fibroblasts	Neural Stem cells		FGF-basic	Zhang, M. *Cell Stem Cell* (2016) 18: 653
A 83-01	909910-43-6 9094360	Activin/NODAL/TGF-β pathway inhibitor					
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor					
Hh-Ag1.5	612542-14-0	Hedgehog pathway activator					
All-Trans Retinoic Acid	302-79-4 3027949	Retinoid pathway activator					
RG 108	48208-26-0 4822608	Epigenetic modifier; Inhibits DNA methyltransferase (DNMT)					
Tranylcypromine	1986-47-6 1984764	Lysine-specific demethylase 1 (LSD1) inhibitor					
SMER 28	307538-42-7	Autophagy small-molecule enhancer (SMER)					
Rosiglitazone	122320-73-4 1227342	PPARγ activator	Human Fibroblasts	Brown adipocytes			Takeda, Y. *Sci. Rep.* (2017) 7:4304
Triiodothyronine	5817-39-0	Thyroid hormone receptors agonist					
Dexamethasone	50-02-2 5000222	Glucocorticoid pathway activator					
IBMX	28822-58-4 2885842	A general inhibitor of cyclic nucleotide phosphodiesterases					

BioGems Catalog Number

NAME	CAS # CAT. #	FUNCTION	STARTING CELLS	TARGET CELLS	REQUIRED TRANSCRIPION FACTORS	REQUIRED CYTOKINES	REFERENCE
CHIR 99021	252917-06-9 2520691	GSK-3β inhibitor	Human Fibroblasts	Brown adipocytes		FGF-basic	Takeda, Y. *Sci. Rep.* (2017) 7:4304
PD 0325901	391210-10-9 3911091	MEK/ERK pathway inhibitor; Inhibits MEK					
SB 431542	301836-41-9 3014193	TGF-β1 receptor, ALK4, ALK5 and ALK7 inhibitor					
LDN 193189	1062368-24-4 1062443	Activin/BMP/TGF-β pathway inhibitor					
Pifithrin-α	63208-82-2	p53 inhibitor					
Dorsomorphin	866405-64-3 8666430	BMP and AMPK pathway inhibitor; Inhibits ALK2, ALK3, ALK6, and AMPK					
Forskolin	66575-29-9 6652995	cAMP activator; Activates adenylyl cyclase					

BioGems Catalog Number

Notes

Notes

OUR QUALITY
YOUR DEDICATION

PEPROTECH®
OUR SUPPORT, YOUR DISCOVERY

5 Crescent Avenue, P.O. Box 275
Rocky Hill, NJ 08553
Tel: 800.436.9910
Fax: 609.497.0321
sales@peprotech.com, www.peprotech.com

biogems
A PeproTech Brand

31238 Via Colinas, Suite A3
Westlake Village, CA 91362
Tel: 800.493.5868, 818.338.3312
Fax: 818.338.3316
info@bio-gems.com, www.bio-gems.com