

Supplementary Information

Small molecule-induced cellular conversion

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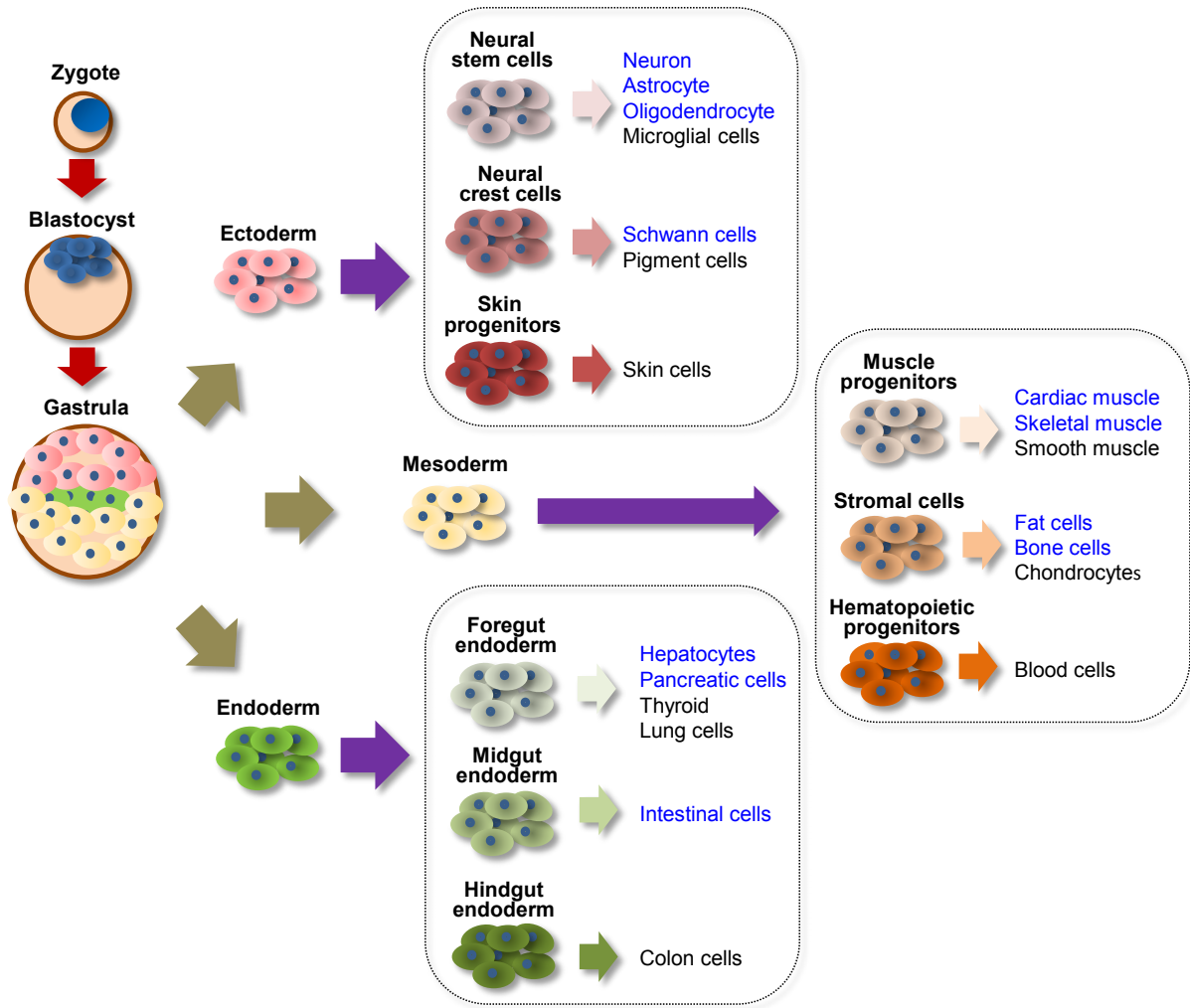
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⁺Two authors contribute equally to this work.

^{*}co-correspondence

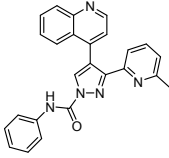
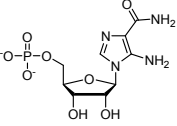
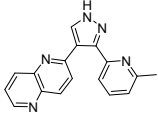
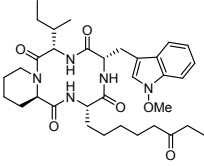
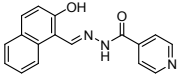
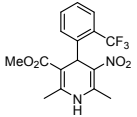
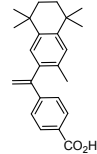
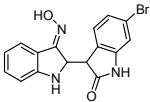
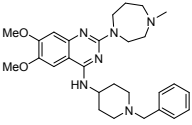
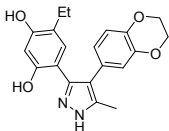
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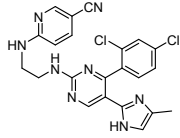


Supplementary Figure S1. A simplified scheme of differentiation of three germ layers into their subsequent lineages. We have considered only some popular cell types and their differentiation traces to give an insight into the cellular conversion. Lineages depicted in blue color are those mentioned in this review.

Supplementary Table S1. Summary of small molecules, described in this review, that induce cell conversion.

Name	Structure	Target	Use and Comments	References and Figure ^a
A83-01		An inhibitor of TGF- β type 1 receptor ALK4/5/7	Used for converting fibroblasts into neural stem-like cells and cardiac cells.	Neural stem-like cells: Fig 12; ref 33 Cardiogenesis: Fig 14; ref 38
AICAR		An activator of AMP-activated protein kinase (AMPK)	Used for astroglial differentiation from neural stem cells.	Astroglial cells: Fig 10; ref 29
Alk5i II		An inhibitor of TGF- β RI kinase	Used for the conversion of pancreatic progenitors into endocrine cells and β -cells.	Endocrine cell and β -cells: Fig 19; ref 48
Apicidin		An inhibitor of histone deacetylase (HDAC)	Used for converting oligodendrocyte precursor cells into neural stem-like cells.	Neural stem-like cells: Fig 11; ref 31
AS8351		An inhibitor of histone demethylase	Used for converting fibroblasts into cardiac cells.	Cardiogenesis: Fig 14; ref 38
Bay K8644		An activator of calcium channel	Used for converting gastric epithelial cells into endodermal progenitors.	Endodermal progenitors: Fig 18; ref 46
Bexarotene		An agonist of the retinoic acid X receptor	Used for converting myoblasts into adipocytes.	Adipogenesis: Fig 15; ref 41
BIO (6-bromoindirubin-3-oxine)		An inhibitor of GSK-3 β	Used for cardiac mesoderm and endoderm induction from pluripotent stem cells.	Cardiogenesis: Fig 13; refs 35, 36 Endoderm: ref 44
BIX01294		An inhibitor of histone methyltransferase	Used for converting fibroblasts into cardiac cells. Used for converting gastric epithelial cells into endodermal progenitors.	Cardiogenesis: Fig 14; ref 38 Endodermal progenitors: Fig 18; ref 46
CCT-018159		An inhibitor of heat shock protein 90 (Hsp90) ATPase activity	Used for hepatic induction from pluripotent stem cells.	Hepatocytes: ref 50

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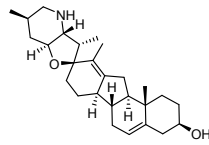


An inhibitor of glycogen synthase kinase 3 β (GSK-3 β)

Activates the Wnt signaling pathway. Used for the generation of cardiac, skeletal muscle, neuronal and osteocyte cells. Used for endoderm induction from pluripotent stem cells.

Neurogenesis: Figs 7, 9, 12; refs 22, 28, 32, 33
Schwann cells: ref 30
Cardiogenesis: Figs 13, 14; refs 35, 36, 37, 38, 39
Skeletal muscle: ref 40
Osteogenesis: Fig 16; ref 42
Endoderm: Figs 19, 20; refs 43, 48, 49

Cyclopamine

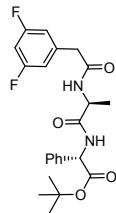


An inhibitor of hedgehog signaling pathway

Used for converting pluripotent stem cells into bone cells.

Osteogenesis: Fig 16; ref 42

DAPT

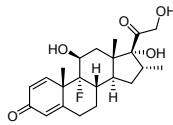


An inhibitor of γ -secretase

Used for converting astrocytes into neuronal cells.

Neurogenesis: Fig 9; ref 28

Dexamethasone

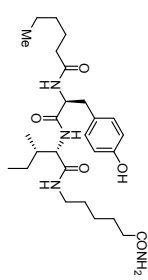


An agonist of glucocorticoid receptor

Used for the modulation of the proliferation and functional maturation of hepatocytes.

Hepatocytes: Fig 20; ref 49

Dihexa

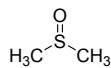


An agonist of hepatocyte growth factor receptor

Used for the functional maturation of hepatocytes.

Hepatocytes: Fig 20; ref 49

Dimehtyl sulfoxide (DMSO)

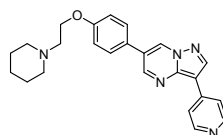


Pleotropic targets

Used for the hepatic specific induction and progenitor generation from the endoderm.

Hepatocytes: Fig 20; ref 49

Dorsomorphin

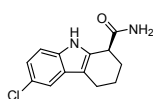


An inhibitor of AMP-activated protein kinase (AMPK)

Used for converting fibroblasts into neuronal cells.

Neurogenesis: Fig 7; ref 22

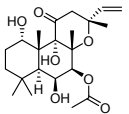
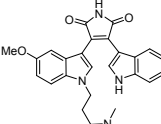
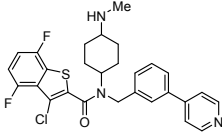
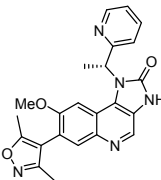
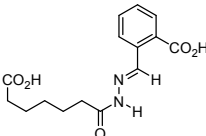
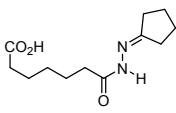
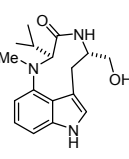
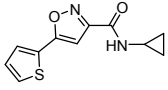
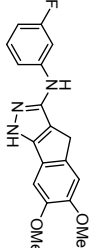
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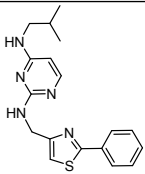
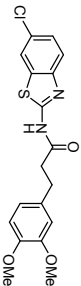
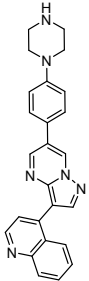
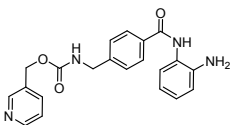
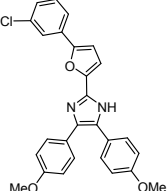
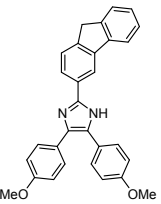
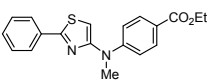
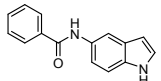
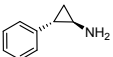


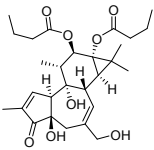
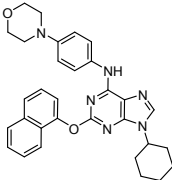
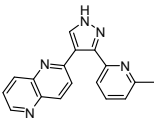
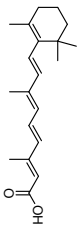
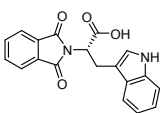
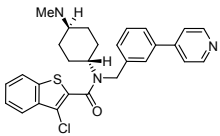
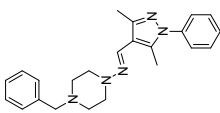
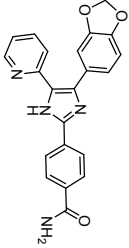
a selective inhibitor of sirtuin 1 (SIRT1)

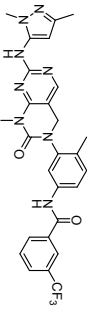

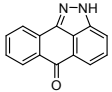
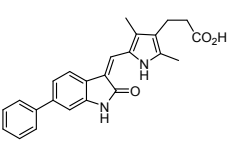
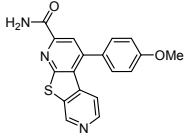
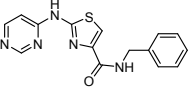
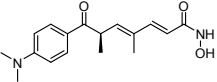
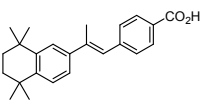
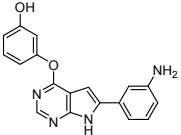
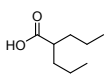
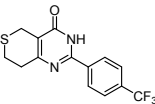
Used for neuronal differentiation from pluripotent stem cells.

Neurogenesis: Figs 8B and C; ref 26

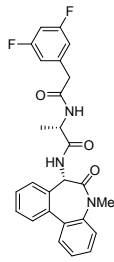
Forskolin		An activator of adenylate cyclase	Used for converting fibroblasts into neuronal and cardiac cells. Used for converting epidermal neural crest cells to Schwann cells.	Neurogenesis: Fig 7; ref 22 Schwann cells: ref 30 Cardiogenesis: refs 37, 39
GO6983		An inhibitor of protein kinase C (PKC)	Used for converting fibroblasts into neuronal cells.	Neurogenesis: Fig 7; ref 22
Hh-Ag 1.5		An agonist of smoothened	Used for converting fibroblasts into neural stem-like cells.	Neural stem-like cells: Fig 12; ref 33
I-BET151		An inhibitor of bromodomain and extra-terminal motif protein (BET) family	Used for converting fibroblasts into neurons.	Neurogenesis: ref 23
IDE1		An activator of TGF- β signaling pathway	Used for converting ESCs into the definitive endoderm.	Definitive endoderm: Fig 17; ref 45
IDE2		An activator of TGF- β signaling pathway	Used for converting ESCs into the definitive endoderm.	Definitive endoderm: Fig 17; ref 45
(-)-Indolactam V		An activator of protein kinase C (PKC)	Used for converting ESCs into the definitive endoderm Used for converting the definitive endoderm into pancreatic progenitors.	Pancreatic progenitors: Fig 17; refs 45, 47
ISX9		Unknown	Used for neuronal differentiation from hippocampal neural progenitor cells (HCNs), P19 cells, and mouse fibroblasts. Accelerates Neurogenesis: through inducing the Ca ²⁺ influx into the nucleus.	Neurogenesis: Fig 4; refs 18, 23
JNJ10198409		An inhibitor of the platelet-derived growth factor	Used for converting fibroblasts into cardiac cells.	Cardiogenesis: Fig 14; ref 38

KHS101		An inhibitor of transforming acidic coiled-coil containing protein 3 (TACC3)	Used for neural differentiation from hippocampal neural progenitor cells (HCNs). Accelerates neurogenesis through negative regulation of the cell cycle.	Neurogenesis: Fig 3; ref 17
KY0211		An inhibitor of Wnt signaling pathway	Used for cardiac differentiation from mesoderm.	Cardiogenesis: Fig 13; ref 36
LDN193189		An inhibitor of BMP type 1 receptor ALK2/3	Used for converting astrocytes into neurons. Used for converting fibroblasts into neural stem-like cells. Used for the generation of pancreatic progenitors from definitive endoderm	Neurogenesis: Fig 9; ref 28 Neural stem-like cells: Fig 12; ref 33 Pancreatic progenitors: Fig 19; ref 48
MS-275 (Entinostat)		An inhibitor of histone deacetylase (HDAC)	Used for converting oligodendrocyte precursor cells into neural stem-like cells.	Neural stem-like cells: Fig 11; ref 31
Neurodazine (Nz)		Unknown	Used for neuronal differentiation from myoblasts, pluripotent stem cells, NIH3T3 fibroblasts and neuroblastoma cells. Accelerates neuronal differentiation by activating Wnt and Shh signaling pathways.	Neurogenesis: Figs 5, 6, 8A; refs 7, 13, 21, 25
Neurodazole (Nzl)		Unknown	Used for neuronal differentiation from pluripotent stem cells, NIH3T3 fibroblasts and neuroblastoma cells. Induces neuronal differentiation by activating Wnt and Shh signaling pathways.	Neurogenesis: Fig 6, refs 13, 21 Fig 8A; ref 25
Neuropathiazol		Unknown	Used for neuronal differentiation from hippocampal neural progenitor cells (HCNs).	Neurogenesis: Fig 2; ref 16
OAC2		An activator of pluripotency factor Oct4	Used for converting fibroblasts into cardiac cells.	Cardiogenesis: Fig 14; ref 38
Parnate		An inhibitor of histone demethylase	Used for converting fibroblasts into neuronal stem-like and cardiac cells.	Neural stem-like cells: Fig 12; ref 33 Cardiogenesis: refs 37, 39

PDBu		An activator of PKC	Used for the generation of pancreatic progenitors from definitive endoderm,	Pancreatic progenitors: Fig 19; ref 48
Purmorphamine		An agonist for smoothened	Used for converting astrocytes into neuronal cells.	Neurogenesis: Fig 9; ref 28
Repsox		An inhibitor of the TGF-β type 1 receptor ALK5	Used for converting fibroblasts into neural and cardiac cells. Used for the conversion of fibroblasts into neural progenitors.	Neurogenesis: Fig 7; ref 22 Neural progenitors: ref 32 Cardiogenesis: ref 39
Retinoic acid		An activator of retinoic signaling pathway	A well-known Neurogenesis: inducer Used for converting epidermal neural crest cells into Schwann cells. Used for converting fibroblasts into neural stem-like cells. Used for generation of pancreatic progenitors from definitive endoderm, pancreatic maturation and endocrine cells generation.	Schwann cells: ref 30 Neural stem-like cells: Fig 12; ref 33 Pancreatic progenitors & endocrine cell: Fig 19; ref 48
RG108		An inhibitor of DNA methyltransferase	Used for converting fibroblasts into neural stem-like cells and cardiac cells. Used for converting gastric epithelial cells into endodermal progenitors.	Neural stem-like cells: Fig 12; ref 33 Endodermal progenitors: Fig 18; ref 46
SAG		A smoothened agonist	Used for converting astrocytes into neuronal cells. Used for converting pluripotent stem cells into bone cells. Activates hedgehog signaling pathway.	Neurogenesis: Fig 9; ref 28 Osteogenesis: Fig 16; ref 42
SANT1		A smoothened antagonist	Used for the generation of pancreatic progenitors from definitive endoderm, pancreatic maturation and endocrine cell generation.	Pancreatic progenitors & endocrine cells: Fig 19; ref 48
SB431542		An inhibitor of TGF-β/activin signaling pathway	Used for converting astrocytes into neurons. Used for converting epidermal neural crest cells to Schwann cells. Used for the conversion of fibroblasts into cardiomyocytes. Used for gastric epithelial cell reprogramming to endodermal progenitors.	Neurogenesis: Fig 9; ref 28 Schwann cells: ref 30 Cardiogenesis: ref 37 Endodermal progenitor: Fig 18; ref 46

SC1		A dual inhibitor of Ras-GAP and ERK1	Used for converting fibroblasts into cardiac cells	Cardiogenesis: Fig 14; ref 38
SMER28		An inhibitor of DNA methyltransferases	Used for converting fibroblasts into neural stem-like cells.	Neural stem-like cells: Fig 12; ref 33
SP600125		An inhibitor of c-Jun N-terminal kinase (JNK)	Used for converting fibroblasts into neuronal cells.	Neurogenesis: Fig 7; ref 22
SU16F		An inhibitor of the platelet-derived growth factor	Used for converting fibroblasts into cardiac cells.	Cardiogenesis: Fig 14; ref 38
TH		Helioxanthin-derivative	Used for converting pluripotent stem cells into bone cells.	Osteogenesis: Fig 16; ref 42
Thiazovivin		An inhibitor of Rho-associated protein kinase (ROCK)	Used for converting astrocytes into neuronal cells	Neurogenesis: Fig 9; ref 28
TSA (Trichostatin A)		An inhibitor of histone deacetylase (HDAC)	Used for converting oligodendrocyte precursor cells into neural stem-like cells.	Neural stem-like cells: Fig 11; ref 31
TTNPB		An agonist of retinoic acid receptor	Used for converting astrocytes into neurons. Used for converting fibroblasts into cardiac cells	Neurogenesis: Fig 9; ref 28 Cardiogenesis: ref 39
TWS119		An inhibitor of glycogen synthase kinase 3β (GSK-3β)	Activates the Wnt signaling pathway Used for neuronal differentiation from pluripotent stem cells.	Neurogenesis: Fig 2; ref 15
Valproic acid (VPA)		An inhibitor of histone deacetylase (HDAC)	Used for converting fibroblasts into neuronal and cardiac cells as well as neural progenitor cells. Used for converting astrocytes into neuronal cells.	Neurogenesis: Figs 7, 9; refs 22, 28, 32 Cardiogenesis: ref 39
XAV939		An inhibitor of Wnt signaling pathway	Used for cardiac differentiation from mesoderm.	Cardiogenesis: Fig 13; ref 36

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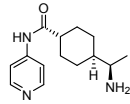


An inhibitor of γ -secretase

Used for endocrine cell generation from pancreatic progenitors.

Endocrine cells:
Fig 19; ref 48

Y-27632



An inhibitor of Rho-associated protein kinase (ROCK)

Used for converting fibroblasts into neuronal and cardiac cells.

Neurogenesis:
Fig 7; ref 22
Cardiogenesis:
Fig 14; ref 38

^arefs in the text.