

Stem Cell Modulators

Reprogramming
Self-Renewal
Differentiation
Cancer Stem Cells

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Biochemicals for Life Science Research

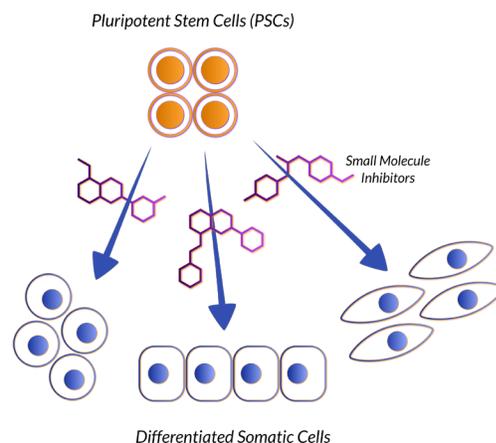


Influencing Stem Cell Biology with Small Molecules

Small molecules are playing an increasingly important role in the advancement of stem cell research and technology. They are versatile tools that have shown effectiveness in everything from somatic cell reprogramming to stem cell renewal to differentiation of pluripotent stem cells. They have increased the efficiency and speed at which cells move to and from pluripotency, unlocking new avenues of previously cost-prohibitive research. In some cases, small molecules have even helped somatic cells bypass the need to move to pluripotency altogether in a process called transdifferentiation.

As stem cell research tools, small molecules offer a variety of inherent benefits. They offer a high degree of control to researchers, as they are able to reversibly alter the function

of target proteins at precise points in time. Their synthesis routes are well developed and the compounds are well characterized, meaning that they are high in purity and low in variability between batches, both key factors in reproducibility. They are cost-effective relative to growth factors, and they are safer than using viral vectors that can introduce unwanted genetic material. Small molecules are playing an integral role in improving our understanding of stem cells, and enabling advancements in stem cell technology.



Reprogramming Somatic Cells With Small Molecules

ID	Name	Class	Description	Purity
A001001	A 83-01	TGF- β inhibitor	Enables Oct4-induced reprogramming in mouse fibroblasts.	$\geq 98\%$
A9602	Azacitidine (5-azacytidine)	DNMT inhibitor	Accelerates transition to pluripotency in some cell types.	$\geq 98\%$
A9603	5-Aza-2'-deoxycytidine (Decitabine)	DNMT inhibitor	DNMT inhibitor may enhance reprogramming efficiency, diminishing the number of cells that only reach partially reprogrammed states.	$\geq 98\%$
B349921	BIX-01294 TriHCl	HMT inhibitor	Enables reprogramming of some mouse cells to iPSCs without c-Myc and SOX2.	$\geq 98\%$
F5668	Forskolin	cAMP activator	In combination with other compounds, induces pluripotent stem cells from somatic cells in mice.	$\geq 98\%$
K1655	Kenpaullone	Inhibitor of GSK-3, CDK	Functionally replaces the reprogramming factor Klf4 while still yielding induced PSCs indistinguishable from murine ESCs.	$\geq 95\%$
P1202	PD-325901	MEK/ERK inhibitor	Promotes and increases efficiency of reprogramming in human somatic cells.	$\geq 98\%$
Q8016	Quercetin Dihydrate	Flavonoid	Promotes reprogramming of somatic cells.	$\geq 95\%$
R0161	Rapamycin	mTOR inhibitor	May enhance reprogramming efficiency.	$\geq 98\%$
R2400	RG-108	DNMT inhibitor	Accelerates transition to pluripotency in some cell types.	$\geq 98\%$
T6903	Tranylcypromine HCl	MAO inhibitor	Enables Oct4-induced reprogramming in mouse fibroblasts.	$\geq 98\%$
T6933	Trichostatin A	HDAC inhibitor	Establishes a ground state pluripotency in mouse iPS cells, erasing prior cell lineage "memory".	$\geq 98\%$
V0147	Valproic Acid Sodium	HDAC inhibitor	Enables Oct4 and Sox2 induced reprogramming in primary human fibroblasts, bypassing oncogenes c-Myc and Klf4.	$\geq 98\%$
V5734	Vorinostat (SAHA)	HDAC inhibitor	Promotes and increases efficiency of reprogramming in human and somatic cells in mice.	$\geq 98\%$

Reprogramming cells from a somatic state to a pluripotent one using methods that bypass the need for oncogenes and viral vectors has been a boon to the research community. Small molecules have been useful on two fronts when it comes to reprogramming. First, they have made the process itself faster and more efficient,

making it easier to generate desired cell types in vitro for disease modeling and other applications. This has been accomplished with epigenetic modifiers such as histone deacetylase inhibitors and DNA methyltransferase inhibitors. Small molecule antioxidant compounds reduce genome instability during reprogramming, when

oxidative stress levels are elevated, improving efficiency. Secondly, small molecules have been useful in helping researchers understand the underlying mechanisms of pluripotency itself, unlocking new possibilities for the treatment of disease.

Small Molecules Enhance Self Renewal

ID	Name	Class	Description	Purity
A2420	A-769662	AMPK activator	Maintains naïve pluripotent state in mouse ESCs through AMPK activation.	≥98%
A0918	N-Acetyl-L-Cysteine	Antioxidant	Reduces genome instability of iPSCs in combination with other antioxidants.	≥98%
A3208	AICAR	AMPK activator	Maintains naïve pluripotent state in mouse ESCs through AMPK activation.	≥98%
C9710	Cyclopamine	Hedgehog signaling inhibitor	Decreases proliferation in human mesenchymal stem cells, demonstrating the importance of Hh signaling during hMSC proliferation.	≥98%
G7443	GSK-429286A	ROCK inhibitor	Increases cloning efficiency of human PSCs. Improves cell maintenance by increasing resistance to senescence.	≥98%
N3310	Nicotinamide	N-methyltransferase inhibitor	Activates senescent muscle stem cells.	≥98%
P327212	Pifithrin- α -cyclic HBr	p53 inhibitor	Enhances proliferation of hematopoietic stem cells.	≥98%
P698583	Prostaglandin E2	EP activator	Improves survival and self-renewal of hematopoietic stem cells in mice.	≥99%
T3132	Thiazovivin	ROCK inhibitor	Enhances survival of human ESCs, potentially through the stabilization of E-cadherin signaling.	≥98%
Y1000	Y27632 2HCl	ROCK inhibitor	Reduces dissociation-induced apoptosis in embryonic and neural stem cells. Increases cloning efficiency.	≥98%

In order to support the expanding stem cell research field, improving the methodologies and technologies for maintaining stem cells in defined culture systems is critical. Additionally, research on the mechanisms of

self-renewal and stem cell preservation will enable the development of new stem cell applications. Small molecules have demonstrated the ability to improve the long term maintenance of stem cells, while others have shown

the potential to stimulate self-renewal. Small molecules might also improve stem cell survival by preventing apoptosis caused by imperfect stem cell manufacturing processes through the manipulation of signaling pathways.

Small Molecules Promote Differentiation

ID	Name	Class	Description	Purity
C291342	CHIR-99021	GSK3 inhibitor	Promotes differentiation in human PSCs to cardiomyocytes.	≥98%
D0260	DAPT	Notch inhibitor	Promotes differentiation in PSCs to insulin producing beta cells. Also shown to promote neuronal differentiation.	≥98%
D1693	Dexamethasone	Glucocorticoid	Promotes differentiation in human mesenchymal cells to multiple lineage types.	≥97%
F5668	Forskolin	cAMP activator	Improves transdifferentiation of human adult peripheral T cells into neurons.	≥98%
G1652	Genistein	Isoflavone phytochemical	Inhibits differentiation of adipocytes, possibly due to interactions with AMPK.	≥98%
I9060	IWP-2	Inhibitor of PORCN, WNT	Promotes differentiation in human PSCs to cardiomyocytes. Increases conversion of ES cells.	≥98%
K9600	KY-0211	WNT inhibitor	Promotes differentiation in human PSCs to cardiomyocytes.	≥98%
N3310	Nicotinamide	N-methyltransferase inhibitor	Promotes differentiation in human iPSCs, as well as in ES cells to mature neurons.	≥98%
P8370	Purmorphamine	Hedgehog activator	Promotes differentiation in induced PSCs to spinal motor neurons. Also promotes differentiation from human mesenchymal cells.	≥98%
R1885	Reversine	Inhibitor of MEK, AurK	Promotes differentiation in porcine stem cells to germ-like cells.	≥98%
S0500	SB-203580	p38 MAPK inhibitor	Promotes differentiation in human and mouse ES cells to cardiomyocytes.	≥98%
S0400	SB-431542	TGF- β inhibitor	Improves neuronal differentiation in vitro from human PSCs. Also enhances cardiomyocyte differentiation from mouse and human PSCs.	≥98%
S3343	Silibinin	Phytoestrogen flavonoid	Induces vascular differentiation from mouse ESCs, potentially by way of PI3K, STAT3, and AKT activation.	≥97%
R1780	trans-Retinoic Acid	RAR activator	Retinoids are involved in the regulation of differentiation. Promotes differentiation in induced PSCs to motoneurons.	≥98%
X0384	XAV-939	Inhibitor of TNKS, WNT	Promotes differentiation of cardiomyocytes from human PSCs.	≥95%

Manipulating developmental signaling pathways to induce differentiation in stem cells has far reaching implications in cancer research, neuroscience, and regenerative medicine. Key factors of successful induced differentiation include efficiency, reliability, and reproducibility. By this measure, small

molecules give researchers an excellent tool to maintain control over stem cells as they transition to other cell lineages of interest. Numerous signaling pathways have proven to be important in differentiation, including WNT, Notch, Hedgehog, and TGF- β . This process is rife with variables, includ-

ing the choice of initial pluripotent cell and desired cell lineage, the method of directing differentiation, the timing of introducing differentiation inducing tools, and potential combination effects with other small molecules. Understanding and optimizing differentiation is an ongoing effort.

Targeting Cancer Stem Cells With Small Molecules

ID	Name	Class	Description	Purity
A6234	Apigenin	Flavonoid	Suppresses stemness traits in TNBC cells, possibly due to decreased YAP/TAZ activity.	≥98%
C0267	Carnosol	Diterpene	Targets c-Met dependent pancreatic CSCs, down regulating pluripotency maintaining genes.	≥98%
C2947	Chlorpromazine HCl	Antipsychotic	Suppresses stemness traits in breast cancer CSCs, possibly due to the degradation of YAP (yes-associated protein).	≥98%
D5898	Doxycycline Monohydrate	Tetracycline antibiotic	Targets metabolic pathways by impairing mitochondrial function. Certain metabolotypic phenotypes may have a causitive role in maintaining stem traits in CSCs.	≥97%
E6234	Epigallocatechin Gallate	Flavonoid found in green tea	Inhibits the transcription and translation of genes that encode stemness markers such as Nanog, Oct4, Sox2, and CD44, thereby inhibiting CSC self-renewal.	≥98%
G4580	Glucosamine Hydrochloride	Inhibitor of STAT3	Reduces stemness of breast cancer CSCs by inhibiting the STAT3 pathway. STAT3 signaling contributes to the regulation of breast cancer CSCs.	≥96%
J3204	E-JIB-04	Inhibitor of Jumonji histone demethylases	Selectively targets colorectal cancer stem cells, reducing the self-renewal and stemness of those cells, perhaps due to interaction with WNT/ β -catenin signaling.	≥98%
J3205	Z-JIB-04	Inhibitor of Jumonji histone demethylases	Selectively targets colorectal cancer stem cells, reducing the self-renewal and stemness of those cells, perhaps due to interaction with WNT/ β -catenin signaling.	≥98%
M2076	Metformin HCl	AMPK activator	Targets metabolic pathways by inhibiting glycolysis. Certain metabolotypic phenotypes may have a causitive role in maintaining stem traits in CSCs.	≥98%
P0270	Parthenolide	Sesquiterpene lactone	Induces apoptosis in CSCs of nasopharyngeal carcinoma, perhaps due to COX-2 inhibition.	≥98%
S0168	Saractinib	Src inhibitor	Combined MEK-Src inhibition decreases tumor-initiating ovarian cancer cells.	≥98%
S1846	Selumetinib	MEK inhibitor	Combined MEK-Src inhibition decreases tumor-initiating ovarian cancer cells.	≥98%
V1769	Verapamil HCl	Calcium channel blocker	Inhibits pancreatic cancer tumor growth by targeting stem-like side population cells, and has a pro-apoptotic effect in gemcitabine resistant cells.	≥98%
W3576	Withaferin A	Steroid lactone	Targets c-Met dependent pancreatic CSCs, down regulating pluripotency maintaining genes.	≥98%

The concept of cancer stem cells (CSCs) is a relatively new idea in cancer research. Among all cancer cells found within a given tumor, some fraction exhibit stem-like traits and are responsible for tumor progression and maintenance. These cells are CSCs, and have the ability to generate the other cancer cell types. CSCs may be the first cancer cells to develop,

and could be the driving force behind metastasis and drug resistance. This would make CSCs crucial targets in combating cancer and explain why some cancer treatments fail. Although there is increasing evidence that CSCs exist, identifying and targeting them remains a challenge. The same signaling pathways that have been studied for their utility in stem cell research

(WNT, Notch, Hedgehog, etc.) can be useful in understanding and eliminating the stem-like qualities of CSCs. Other methods, such as targeting CSC metabolism, have also been explored. Small molecules targeting these pathways and functions will play an important role in providing clarity and solutions to this developing field.



About Us



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