Supplementary Table 1 *In vitro* neurogenesis (including neural differentiation, cell reprogramming and transdifferentiation) on 2D platforms

Initial cell	Target cel	l Transcriptio	Small	Soluble	Time	Conversion	Neuronal subtypes	Re
population	type	n factors	molecules	factors		efficiency (%)	(%)	f.
				(including				
				neurotrop				
				hic				
				factors,				
				growth				
				factors,				
				etc.)				
Mouse	Functional	Ascl1, Myt1l,	/	EGF,	Approxim	Approximatel	Glutamatergic,	[1]
embryonic	neurons	Brn2		bFGF	ately	y 20%	GABAergic,	
fibroblasts					8D-13D		excitatory cortical	
(MEFs)/mo							neurons (Tbr+:	
use							53%)	
postnatal								

tail-tip								
fibroblasts								
Human	Dopaminergic	Ascl1, Myt1l,	/	/	Approxim	Dopaminergic	(Approximately	[2]
embryonic	neurons	Brn2, Foxa2,			ately 28D	5%/Approxima	ately 20%)	
fibroblasts/		Lmx1a						
human fetal								
lung								
fibroblast								
cells								
Mouse tail	Midbrain	Ascl1, Pitx3,	/	FGF-8,	Approxim	9.10%	Dopaminergic	[3]
tip	dopaminergic	Lmx1a,		Shh	ately 18D			
fibroblasts	neurons	Nurr1,						
		Foxa2, EN1						
Human	Neurons	NeuroD2,	VPA,	BDNF,	Approxim	Approximatel	Glutamatergic,	[4]
fibroblasts		miR-9/9*,	db-cAMP	NT-3,	ately 30D	y	GABAergic	
		miR-124/Ne		bFGF		50%/Approxi		
		uroD2,				mately 80%		

		ASCL1, MYT11, miR-9/9*, miR-124						
Human	Neurons	/	VPA,	BDNF,	Approxim	Approximatel	Glutamatergic	(> [5]
fibroblasts			CHIR99021,	GDNF,	ately 14D	y 20%	80%), GABAer	gic
			Repsox,	NT-3,			(Approximately	
			forskolin,	bFGF			5%)	
			SP600125,					
			G06983,					
			Y-27632,					
			dorsomorphin,	,				
			cAMP					
MEFs	Neuronal cells	/	Forskolin,	bFGF,	Approxim	> 90%	Glutamatergic,	[6]
			ISX-9,	BDNF,	ately		GABAergic	
			CHIR99021,	GDNF	16D-20D			
			I-BET151					

Human fetal	Neuronal cells	Ascl1, Myt1l,	/	BDNF,	Approxim	2%-4%	Glutamatergic	[7]
fibroblasts/		Brn2,		GDNF,	ately		(~70%)	
human		NeuroD1		NT-3,	3W-4W			
postnatal				CNTF				
fibroblasts								
Human	Induced	Ascl1, Ngn2	SB431542,	Noggin,	Approxim	> 80%	Glutamatergic	[8]
postnatal	neurons		CHIR99021	BDNF,	ately 23D		(35%), GABAergic	
fibroblasts				GDNF,			(20%), serotonergic	
				NT-3			(5%)	
Human	Neuronal cells	/	VPA,	BDNF,	Approxim	Approximatel	Glutamatergic	[9]
adult			CHIR99021,	GDNF,	ately 12D	y 8%	(70%), cholinergic	
astrocytes			Repsox,	IGF			(7%)	
			forskolin,					
			I-Bet151, ISX-9					
Human fetal	Cholinergic	Ngn2	Forskolin,	BDNF,	Approxim	> 90%	Cholinergic (>90%)	[10]
lung	neurons		dorsomorphin	GDNF,	ately 14D			
fibroblasts				NT-3,				

				bFGF				
MEFs	Dopaminergic	Ascl1, Nurr1,	/	/	Approxim	Approximatel	Dopaminergic (85 ±	[11]
	neurons	Lmx1a			ately 16D	y 20%	4%)	
Postnatal	Neurons	MiR-124,	Forskolin	Noggin,	Approxim	Approximatel	Glutamatergic	[12]
human		Myt11, Brn2		BDNF,	ately 15D	y	(44%/28%)	
fibroblasts/a				GDNF,		50%/1.5%-11.		
dult human				bFGF		2%		
fibroblasts								
Human	Forebrain	/	cAMP,	BDNF,	Approxim	> 90%	GABAergic (>	[13]
pluripotent	GABA		compound E,	GDNF,	ately 25D		90%): CB	}
stem cells	interneurons		purmorphami	IGF-1			(Approximately	
(hPSCs)			ne/Shh				25%); SST	,
							(Approximately	
							15%); PV	-
							(Approximately	
							15%); nNOS (< 1%)	
Mouse	Induced	Ascl1, Myt1l,	/	-	Approxim	> 5%	Glutamatergic	[14]

hepatocytes	neurons	Brn2			ately 14D		(35/200 = 17.5%)	
Human	Forebrain	Ascl1 (five	/	BDNF,	Approxim	> 90%	GABAergic	[15]
embryonic	GABAergic	serine		GDNF,	ately 35D		$(84.5 \pm 3.5\%)$	
stem cells	neurons	residues are		NT-3,				
(hESCs)		substituted		IGF-1				
		with						
		alanine),						
		Dlx2, LHX6,						
		miR-124						
Human	Neurons	/	LDN193189,	BDNF,	Approxim	Approximatel	Glutamatergic (88.3	[16]
astrocytes			SB431542,	IGF-1,	ately 8D	y 65%	±4%), GABAergic	
			TTNPB, TZV,	NT-3			$(8.2\% \pm 1.5\%)$	
			CHIR99021,					
			VPA, DAPT,					
			SAG,					
			purmorphami					
			ne					

MEFs	Induced	Ascl1	/	BDNF,	Approxim	Glutamatergic	(Approximat	tely 40%)	[17]
	neurons			GDNF	ately 21D				
MEFs	Spinal motor	Ascl1, Brn2	, /	CNTF,	Approxim	Cholinergic	(5%-10%,	Hb9:	[18]
	neurons	Myt11, Lhx3,	,	BDNF,	ately 10D	GFP+/total M	EFs transduce	ed)	
		Hb9, Isl1,	,	GDNF					
		Ngn2							
MEFs	GABAergic	Ascl1, Foxg1,	, /	/	Approxim	Approximatel	GABAergio	(>	[19]
	neurons	Sox2, Dlx5	,		ately 21D	y 18%	80%):	GAD+	
		Lhx6					(Approxim	ately	
							90%),	GABA+	
							(Approxim	ately	
							90%),	PV	
							(Approxim	ately	
							90%)		
hESCs	Cortical	/	XAV939,	Shh,	Approxim	> 80%	GABAergio	-1	[20]
	interneuron		LDN193189,	BDNF,	ately 18D		cholinergic		
			SB431542	FGF-2					

hESCs/hPS	Neurons	Ngn2	/	BDNF,	Approxim	> 90%	Glutamatergic	[21]
Cs				NT-3	ately 21D			
hESCs	Neural	/	SB431542, AA,	Noggin,	Approxim	> 80%	Dopaminergic	[22]
	progenitors/n		CHIR99021,	BDNF,	ately 21D			
	eurons		db-cAMP/DA	GDNF,				
			PT, Y-27632	Shh				
hPSCs	GABAergic	Ascl1, Dlx2	/	BDNF	≥5W	93.2 ± 3.4%	GABAergic	[23]
	neurons					(Ascl1, Dlx2,	(Approximately	
						Myt1l-induce	90%)	
						d cells)		
hESCs	Neural cells	/	SB431542,	Noggin,	Approxim	>80%	Dopaminergic/mot	[24]
			cAMP,	BDNF,	ately 11D		oneurons	
			AA/RA, AA	Shh,				
				FGF-8,				
				GDNF,				
				TGF-β3/B				
				DNF, Shh				

hESCs	Dopamine	/	SB4315	542,	Shh,	Approxim	Approximatel	Dopaminergic	[25]
	neurons		LDN19	93189,	FGF-8,	ately 25D	y 75%	(Approximately	
			CHIR	99021,	BDNF,		(TH+/total	20%, TH+/FoxA2+)	
			purmo	orphami	GDNF,		cells)		
			ne,	DAPT,	TGF-β3				
			cAMP,	, AA					
hESCs	Cortical	/	Y-2763	32	Noggin	Approxim	Glutamatergic	(~60%)	[26]
	pyramidal					ately 44D			
	neurons								
Mouse	Functional	Ngn2/Dlx2	/		BDNF	Approxim	70.2% ±	Glutamatergic/GA	[27]
postnatal	neurons					ately 10D	6.3%/35.9% ±	BAergic	
astroglia							13.0%		
from the									
cerebral									
cortex									
Human	Neuronal cells	Sox2, Ascl1	/		/	Approxim	48% ± 9%	GABAergic	[28]
adult cortex						ately			

pericytes					5-6W				
Human fetal	Neurons	/	DAPT,	BDNF,	Approxim	Glutamatergic	(78%),	GABAergic	[29]
astrocytes			CHIR99021,	NT-3,	ately 14D	(2%), dopamin	ergic (1%	(o)	
			SB431542,	IGF-1					
			LDN193189,						
			Y-27632, AA						
Human	Neurons	/	CHIR99021,	BDNF,	Approxim	82.1% ± 1.6%	Glutan	natergic	[30]
newborn			LDN193189,	GDNF,	ately 14D		(89.1%	± 0.9%),	
foreskin			A83-01,	NT-3,			GABA	ergic (≤8%)	
fibroblasts			RG108,	IGF-1					
			dorsomorphin,						
			forskolin,						
			Y27632,						
			DAPT,						
			purmorphami						
			ne, ISX9,						
			P7C3-A20,						

		PD0325901						
hNPCs	Nociceptive /	CHIR99021,	FGF-2,	Approxim	75%	Nociceptors	(>	[31]
	sensory	LDN193189,	NGF,	ately 10D		60%)		
	neurons	SB431542,	BDNF,					
		DAPT,	GDNF					
		SU5402,						
		Y-27632						
hNPCs	CNS cortical /	LDN193189,	BDNF	Approxim	Approximatel	Cortical neurons	s (>	[32]
	neurons	SB431542,		ately 13D	y 70%	50%)		
		DAPT,						
		SU5402,						
		PD0235901,						
		XAV939,						
		Y-27632,						
		db-cAMP, AA						

The calculation methods for conversion efficiency are different in different articles (the main difference is whether the cell survival rate is considered). The references should be consulted for more detail. "Neuronal subtypes" represent the ratio of neurons with

specific subtypes to the converted neurons; if the data are not shown, then they were not mentioned in the article. If "conversion efficiency" and "neuronal subtypes" are merged into one table cell, then the data show the proportion of the specific neurons with specific subtypes induced from the initial cell types. AA: Ascorbic acid; BDNF: Brain-derived neurotrophic factor; bFGF: Basic fibroblast growth factor; cAMP: Cyclic AMP; CNTF: Ciliary neurotrophic factor; db-cAMP: Dibutyryl cAMP; EGF: Epidermal growth factor; GDNF: Glial cell line-derived neurotrophic factor; IGF: Insulin-like growth factor; NGF: Nerve growth factor; NT-3: Neurotrophin-3; RA: Retinoic acid; Shh: Sonic hedgehog; TGF-β3: Transforming growth factor b3; TZV: Thiazovivin; VPA: Valproic acid; /: None; conversion efficiency: The ratio of the target cell types to the initial cell types.

Supplementary Table 2 Small molecules applied in neural lineage induction

Compound	Mechanism of Action	Application	Ref.
SB431542	TGF-β1/ALK4/ALK5/A	Inhibits TGF-β	[8,24]
	LK7 inhibitor	signaling and induces	
		neuroepithelial	
		identity and	
		facilitates cell	
		reprogramming	
LDN193189	Inhibits BMP type1	Inhibits BMP	[20,29]
	receptors ALK2/ALK3	signaling and induces	
		neuroepithelial	
		identity (to replace	
		noggin)	
Dorsomorphin	Inhibits BMP type1	Suppresses	[10]
/compound C	receptors	BMP-mediated	
	ALK2/ALK3/ALK6	SMAD activation by	
		blocking BMP type I	
		receptor function	
CHIR99021/C	GSK3b inhibitor	Activates Wnt	[22,25,31]
T99021		signaling and induces	
		neural crest identity;	
		promotes neuronal	
		differentiation,	
		including axonal	
		outgrowth and	
		synapse formation;	
		facilitates D-V	
		pattering	

XAV939	A potent tankyrase	Inhibits Wnt [20,32]	
,41,707	1	signaling and induces	
	Wnt/b-catenin signaling	CNS lineages	
Forskolin	cAMP activator	Activates [10,12]	
		cAMP/PKA-CREB	
		signaling to promote	
		neural survival,	
		proliferation and	
		differentiation	
Dibutyryl-cA	PKA activator	Activates [22,32]	
MP		cAMP/PKA-CREB	
		signaling to promote	
		neural survival,	
		proliferation and	
		differentiation	
Purmorphami	A Smoothened receptor	Activates shh [13,25]	
ne	agonist	signaling and leads to	
		A-P pattering	
SAG	Potent Smoothened	Activates shh [16]	
	receptor agonist	signaling and leads to	
		A-P pattering	
ISX9	Mediates NeuroD	Induces neural [6]	
	reporter gene induction	induction by	
	via activation of Ca2+	increasing the	
	influx	expression of	
		transcription factor	
		NeuroD1	
Y27632	ROCK1 inhibitor	Improves cell [26]	
		viability	

Thiazovivin	ROCK inhibitor	Enhances stemness	[16]
		maintenance of ESCs	
		and cell	
		reprogramming	
		efficiency	
PD0235901	A selective and	Suppresses neural	[31,32]
	cell-permeable MEK	proliferation and	
	inhibitor	facilitates neural	
		differentiation	
SU5402	VEGFR2/FGFR/PDGFR/	Suppresses neural	[31,32]
	EGFR inhibitor	proliferation and	
		facilitates neural	
		differentiation	
DAPT	A potent g-secretase	Suppresses neural	[31,32]
	inhibitor that blocks	proliferation and	
	Notch signaling	facilitates neural	
		differentiation	
Compound E	A potent g-secretase	Suppresses neural	[13]
	inhibitor that blocks	proliferation and	
	Notch signaling	facilitates neural	
		differentiation	
Repsox	TGFbR-1/ALK5 inhibitor	Improves cell	[5,9]
		reprogramming	
		efficiency by	
		replacing the	
		transcription factor	
		Sox2	
I-BET151	A BET bromodomain	Promotes cell	[9]
	inhibitor that inhibits	reprogramming and	

	BRD4, BRD2, and BRD3	disrupts the gene	
		expression program	
		of initial cells	
TTNPB	RA analog and the	Promotes cell [16]	
	nuclear receptor RAR	reprogramming	
	agonist		
RA/all-trans-R	Natural agonist of RAR	Spinal cord [33,34]	
A	nuclear receptors; binds	patterning	
	to PPARb/d		
Valproic acid	Histone deacetylase	Promotes cell [4,5]	
	inhibitor	reprogramming	
Ascorbic	An endogenous	Plays a role in [22,24,29]	
acid/vitamin	antioxidant agent	neuronal	
С		differentiation and	
		maturation	
RG108	DNA methyltransferases	Promotes cell [30]	
	inhibitor	reprogramming	

ALK: Activin receptor-like kinase; BET: Bromodomain and extraterminal domain; BRD: Bromodomain-containing protein; BMP: Bone morphogenetic protein; cAMP: Cyclic-AMP; CNS: Central neural system; CREB: cAMP-responsive element binding; EGF: Epidermal growth factor; FGFR: Basic fibroblast growth factor receptor; GSK3b: Glycogen synthase kinase 3b; MEK: Mitogen-activated extracellular activated signal-regulated kinase; PKA: Protein kinase A; PDGFR: Platelet-derived growth factor receptor; PPAR: Peroxisome proliferator activated receptor; RA: Retinoic acid; RAR: Retinoic acid receptor; ROCK: Rho-associated coiled-coil containing kinases; Shh: Sonic hedgehog; TGF-β1: Transforming growth factor b1; VEGFR: Vascular endothelial growth factor receptor.

Supplementary Table 3 *In vitro* 3D neural differentiation and subsequent application

Cell Type	Biomaterials	Application	Ref.
Human neural	Matrigel	Disease Modeling (AD)	[35]
progenitor			
cells (hNPCs)			
hNPCs	Matrigel	Disease Modeling (AD)	[36]
hNPCs	Matrigel	Disease Modeling (AD)	[37]
Rat neural	Collagen I	NSC growth and	[38]
stem cells		differentiation	
(NSCs)			
Neural	Rat-tail	Tissue engineering (repair of	[39]
stem/progenit	collagen-based	facial nerve injuries, connected	
or cells	nerve conduits	8-mm facial nerve defects in	
	with anchored	rats)	
	bFGF		
Neural stem	Collagen I	Neural differentiation into	[40]
and		functional neuronal circuits	
progenitor			
cells isolated			
from			
embryonic rat			
cortical or			
subcortical			
neuroepitheli			
um			
Rat primary	Collagen I	Investigation of the	[41]
neural		proliferation and	
precursor cell		differentiation of NPCs	

expansion,

differentiation

Mouse Nunc Lab-Tek Evaluation of the role of ECM [42]

embryonic II tissue-grade proteins on mESC

stem cells polystyrene differentiation into neural and

(mESCs) chamber slides glial lineages in vitro

were coated

with either

type-I collagen

(collagen-1),

gelatin,

laminin,

poly-d-lysine

(PDL) or

fibronectin;

collagen-1,

Matrigel,

gelatin,

hyaluronic acid

and a synthetic

peptide-RAD1

6-II seeded in

the same slides

Mouse Collagen - Survival, proliferation, and [43]

embryonic, hyaluronan differentiation into neurons

postnatal, and

adult neural

stem/progenit

or cells

Rat NPCs	Collagen-cetux	Tissue engineering (spinal [44]
	imab, an EGFR	cord injury)
	antagonist	
Rat NPCs	Sodium	Tissue engineering (traumatic [45]
	hyaluronate	brain injury)
	collagen	
	scaffold loaded	
	with bFGF	
Rat NPCs	A collagen	Tissue engineering (spinal [46]
	microchannel	cord injury repair)
	scaffold	
	carrying	
	paclitaxel-lipos	
	omes	
Rat NPCs	RADA16-IKVA	Tissue engineering (traumatic [47]
	V	brain injury)
	(AcN-RADAR	
	ADARADARA	
	DAIKVAV-CO	
	NH2) (purity >	
	85%)	
Rat	RADA16-RGD	Tissue engineering (sciatic [48]
NPCs/NSCs	(Ac-(RADA)4-	nerve defect, intracerebral
	DGDRGDS)	hemorrhage, and spinal cord
	and	transection)
	RADA16-IKVA	
	V	
	(Ac-(RADA)4-	
	RIKVAV)	

Rat neural	PuraMatrix	Tissue engineering (brai	n ^[49]
stem/progenit		injury)	
or cells			
Human fetal	Laminin	Survival and neurona	al ^[50]
NPCs	1-functionalize	differentiation of hNPCs	
	d PuraMatrix		
Neonatal	Poly (L-lactic	NSC differentiation an	d ^[51]
mouse	acid) (PLLA)	neurite outgrowth	
cerebellum	nano/micro		
C17.2 stem	fibrous		
cells	scaffolds		
Neonatal	PLLA	NSC differentiation an	d ^[52]
mouse	nanofibrous	neurite outgrowth	
cerebellum	scaffold		
C17.2 stem			
cells			
Human	Electrically	NSC differentiation an	d ^[53]
SH-SY5Y	polarized	neurite outgrowth	
neuroblastom	PLLA aligned		
a cells; rat	nanofibers		
embryonic			
cortical			
neurons			
Rat NSCs	PEG-RGD-TnC	Survival, growth an	d ^[54]
		differentiation of NSCs	
mNSCs (fetal	Star-PEG-hepa	Tissue engineering (PD)	[55]
midbrain-deri	rin hydrogel		
ved)			
Human	PEG hydrogels	hNSC neurite extension an	d ^[56]

induced		neural differentiation	
pluripotent			
stem cells			
(iPSCs)			
derived			
human NSCs			
(hNSCs)			
mESCs	Poly (lactic - co	Neural differentiation	[57]
	- glycolic acid)		
	(PLGA)		
	scaffolds		
Rat NSCs and	PLGA polymer	Tissue engineering (transection	[58]
Schwann cells	scaffold	spinal cord injury)	
hNSCs	Polypyrrole	Neural differentiation	[59]
	(PPy)		
Rat	PPy/SWCNT	Improvement of the	[60]
pheochromoc	films	electrode-neural tissue	
ytoma (PC12)		interface	
cells			
Rat PC12 cells	PPy/PDLLA	Tissue engineering (rat sciatic	[61]
	conduit	nerve defect)	
Mouse	Single-walled	Neural differentiation	[62]
embryonic	carbon		
NSCs	nanotube		
	(SWCNT)-pol		
	yelectrolyte		
	multilayer thin		
	films		
Rat embryonic	Chondroitin	Neuron-enriched network	[63]

NPCs	sulfate/MWC	formation
	NT scaffold	
Rat Schwann	Collagen	Cell survival and morphology [64]
cells	I-Matrigel	
	composite	
	scaffolds	
Neuronal and	PLGA/MWCN	Cell survival and proliferation [65]
glial cells from	Ts nanofibrous	
rat cerebral	scaffolds	
cortices		
iNSCs derived	PLGA-PEG	Tissue engineering (spinal [66]
from mouse	scaffolds	cord injury, SCI)
embryonic		
fibroblasts		
(MEFs)		
PC12 cells	Lysine-doped	Tissue engineering (nerve [67]
	PPy/RSSP/PL	transection)
	LA/NGF	
Rat Schwann	Erythropoietin	Tissue engineering (sciatic [68]
cells	controlled-rele	nerve defect)
	asing	
	PLA/MWCNT	
	s/gelatin	
	nanofibrils	

AD: Alzheimer's disease; bFGF: Basic fibroblast growth factor; EGFR: Epidermal growth factor receptor; ESC: Embryonic stem cell; iPSC: Induced pluripotent stem cell; MEF: Mouse embryonic fibroblast; MWCNT: Multiwalled carbon nanotube; NGF: Nerve growth factor; NPC: Neural progenitor cell; NSC: Neural stem cell; PD: Parkinson's disease; PDL:

Poly-D-lysine; PDLLA, poly (D, L-lactic acid); PEG: Poly (ethylene glycol); PLA: Poly (lactic acid); PLGA: Poly (lactic-co-glycolic acid); PLLA: Poly (L-lactic acid); PPy: Polypyrrole; RSSP: Regenerated spider silk protein; SWCNT: Single-walled carbon nanotube; TnC: tenascin-R.

Supplementary Table 4 Microarray-based screening in 2D or 3D platforms

2D/3	Substrate	Interme	Extracellular signals	Spo	Patterning	Cell type	Demonstrati	Referen
D		diates/3		ts	methods		on	ce
		D gels						
2D	Epoxy-coated glass	Dip-coat	25 different acrylate,	1728	The larger	Human	hESC growth	[69]
	slides	ed in 4	diacrylate, dimethacrylate		format	ESCs	and	
		vol%	and triacrylate monomers		CMP9B or	(hESCs)	differentiatio	
		pHEMA			CMP6B pins		n	
					with a Pixsys			
					5500 robot			
2D	Epoxy-coated glass	4 v/w %	Acrylate polymers (16	1728	A robotic pin	Human	hEB cell	[70]
	slides	pHEMA	major monomers were		printer	embryoid	adhesion	
			mixed pairwise with 6			body (hEB)		
			minor monomers in the			cells		
			following ratios: 100/0,					
			90/10, 85/15, 80/20,					
			75/25 and 70/30)					

2D	Glass slides	3-(trimet	32 different combinations 256	SpotArray 24	Mouse ESC	Maintenance [71]
		hoxysily	of five ECM molecules	equipped with	(mESCs),	of primary
		l)-propy	(collagen I, collagen III,	Stealth SMP	primary rat	rat
		1	collagen IV, laminin and	3.0 split pins	hepatocytes	hepatocyte
		methacr	fibronectin)			phenotype,
		ylate;				differentiatio
		polyacr				n of mESCs
		ylamide				toward an
		gel				early hepatic
						fate
2D	4-well plates	PEG	ECM proteins and Notch 2016	A robotic	Mouse NSCs	The roles of [72]
		hydroge	signaling proteins	spotter	(mNSCs)	integrin and
		ls		equipped with		Notch
				an 8-pin head		signaling in
						NSC fate and
						niche-depen
						dent NSC

							regulation	
2D	Glass slides	Aldehy	44 signaling combinations	352	Noncontact	Primary	Neural	[73]
		de-deriv	containing ECM		arrayer for	human	specification	
		atized	components and putative		printing	NPCs	and	
		slides	signaling factors that			(hNPCs)	differentiatio	
			promote neurogenesis and				n	
			gliogenesis and prevent or					
			elevate both					
2D	Microscope slides	NaOH	ECM proteins, growth	6400	SpotArray 24	hPSCs	Cell	[74]
		etching,	factors, small molecules		with		attachment,	
		methacr	and glycans		TeleChem		growth and	
		ylate			SMP3 pins		proliferation	
		silanizat			spaced 9 mm			
		ion,			apart to print			
		glutaral			the arrayed			
		dehyde			cellular			
		activatio			microenviron			

			n, and				ment slides			
			fabricati							
			on of							
			polyacr							
			ylamide							
			gel pads							
			on							
			slides							
2D	Agarose-coate	ed	2%	190 combinations	of 10	1140	Microcontact	Long-term	Neural	[75]
	glass slides		Agarose	ECM proteins			printed arrays	neuroepithel	differentiatio	
								ial stem cells	n toward	
								(Lt-NES)	TH ⁺ neurons	
3D	PDMS mem	brane	Chitosa	32 protein combina	ations of	96	Pipettes	Bone	Cell	[76]
	with holl	lowed	n	5 ECM and	cell-cell			marrow-deri	adhesion,	
	array		solution	contact-mediating				ved	proliferation	
				proteins, including	g human			mesenchyma	and	
				fibronectin, vitr	onectin,			1 stem cells	osteogenic	

			type	I	collagen,				(BMSCs)	differentiatio	
			ameloger	nin	and					n	
			E-cadher	in							
3D	Poly	Alginate	/			200	MicroSy	\mathbf{S}^{TM}	mESCs	Cell	[77]
	(styrene-co-maleic					or	5100-4SQ	2		proliferation	
	anhydride)					400	nonconta	act		and neural	
	(PS-MA) treated						microarr	ayer		differentiatio	
	glass slides									n	
3D	Four-well cell	PEG	Combina	tions	of ECM	2016	A	DNA	Human	MSC	[78]
	culture plate	hydroge	proteins	with	growth		spotter	with	MSCs	differentiatio	
		ls	factors	and	signaling		solid pir	ns was	(hMSCs),	n and	
			factors; s	stiffness	s could be		used to	spot	mNSCs	self-renewal	
			adjusted	by	hydrogels		different			of NSCs	
			with sh	iear n	noduli of		protein				
			~1-50 kP	a			solutions	s on			
							micropil	lars of			
							a				

					microfabricate				
					d silicon				
					stamp, which				
					were pressed				
					against a thin				
					layer of PEG				
					hydrogel				
3D	1536-well	PEG	Combinations of ECM	1024	Nanolitre-rang	mESCs	Colony	[79]	
	plates/glass slides	gels	proteins, cell-cell		e liquid		formation		
			interaction proteins,		handling robot		and		
			soluble factors, different		equipped with		self-renewal		
			matrix mechanical		small-volume				
			properties, and matrix		dispensing				
			mechanical properties		tips				
3D	Standard cell	Polystyr	/	96	Liquid	Human	Cellular	[80]	
	culture dishes and	ene or		or	handling	NSCs	growth		
	multiwell plates	poly-L-l		384	robots	(hNSCs)	profile,		

		actic								morphology,	
		acid								cell-matrix	
		(PLLA)								interaction,	
										gene	
										expression	
										and voltage	
										gated	
										calcium	
										channel	
										function	
3D	PS-MA treated	Alginate	/			384	MicrosSys		hNP cell line	Cell viability	[81]
	glass slides						5100-4SQ		ReNcell VM	for toxicity	
							microcontact	t		·	
							microarray				
							spotter				
3D	3-(trimethoxysilyl)	Methacr	Combinations	of	ECM	288	SpotBot	3	hMSCs	Osteogenic	[82]
	propyl	ylated	proteins and BN	ЛРs			contact			differentiatio	

	methacrylate	gelatin				microarra	ayer		n	
	treated glass slides					with	four			
						pinheads				
3D	Poly (maleic	Alginate	/		NM	S+		hNP cell line	Cell viability	[83]
	anhydride	and				Microarra	ayer	ReNcell VM	and	
	alt-1-octadecene)-c	growth							high-through	
	oated micropillar	factor							put	
	chips	reduced							assessment	
		Matrigel							of	
									lineage-speci	
									fic	
									differentiatio	
									n	
3D	Polystyrene	Matrigel	24-compound	library	532	MicroSys	3	hNP cell line	Cell viability	[84]
	microchips with		consisting of	approved		5100-4SQ	<u>)</u>	ReNcell VM	and	
	micropillars or		drugs, heavy m	netals, and		nonconta	ct		proliferation	
	microwells		pesticides			robotic			for toxicity	

						microarray			
						spotting			
						system			
3D	PS-MA-treated	Collage	27 compounds	for	1080	MicroSys	MCF7 or	Cell viability	[85]
	glass slide	n or	hepatotoxicity assess	ment		5100-4SQ	Hep3B cells	for toxicity	
		alginate				microarray			
		gels				spotter			
						equipped with			
						an extended			
						head			
3D	Polydopamine-coa	Matrigel	Combinations of	12	532	MicroSys	hNP cell line	hNPC	[86]
	ted polystyrene		soluble different	iation		5100-4SQ	ReNcell VM	differentiatio	
	chips		factors			noncontact		n	
						robotic			
						microarray			
						spotting			
						system			

EB: Embryoid body; ECM: Extracellular matrix; ESC: Embryonic stem cell; MSC: Mesenchymal stem cell; NM: Not mentioned; NPC: Neural progenitor cell; NSC: Neural stem cell; PDMS: Poly(dimethylsiloxane); PEG: Poly(ethylene glycol); PLLA: Poly(L-lactic acid); pHEMA, poly(hydroxyethyl methacrylate); PS-MA: Poly(styrene-co-maleic anhydride).

- 277 Ladewig J, Mertens J, Kesavan J, Doerr J, Poppe D, Glaue F, Herms S, Wernet P, Kögler G, Müller FJ, Koch P, Brüstle O. Small molecules enable highly efficient neuronal conversion of human fibroblasts. *Nat Methods* 2012; **9**: 575-578 [PMID: 22484851 DOI: 10.1038/nmeth.1972]
- 278 Liu ML, Zang T, Zou Y, Chang JC, Gibson JR, Huber KM, Zhang CL. Small molecules enable neurogenin 2 to efficiently convert human fibroblasts into cholinergic neurons. *Nat Commun* 2013; **4**: 2183 [PMID: 23873306 DOI: 10.1038/ncomms3183]
- 279 **Ambasudhan R**, Talantova M, Coleman R, Yuan X, Zhu S, Lipton SA, Ding S. Direct reprogramming of adult human fibroblasts to functional neurons under defined conditions. *Cell Stem Cell* 2011; **9**: 113-118 [PMID: 21802386 DOI: 10.1016/j.stem.2011.07.002]
- 280 Chanda S, Ang CE, Davila J, Pak C, Mall M, Lee QY, Ahlenius H, Jung SW, Südhof TC, Wernig M. Generation of induced neuronal cells by the single reprogramming factor ASCL1. *Stem Cell Reports* 2014; **3**: 282-296 [PMID: 25254342 DOI: 10.1016/j.stemcr.2014.05.020]
- 281 Espuny-Camacho I, Michelsen KA, Gall D, Linaro D, Hasche A, Bonnefont J, Bali C, Orduz D, Bilheu A, Herpoel A, Lambert N, Gaspard N, Péron S, Schiffmann SN, Giugliano M, Gaillard A, Vanderhaeghen P. Pyramidal neurons derived from human pluripotent stem cells integrate efficiently into mouse brain circuits in vivo. *Neuron* 2013; 77: 440-456 [PMID: 23395372 DOI: 10.1016/j.neuron.2012.12.011]

- **Karow M**, Sánchez R, Schichor C, Masserdotti G, Ortega F, Heinrich C, Gascón S, Khan MA, Lie DC, Dellavalle A, Cossu G, Goldbrunner R, Götz M, Berninger B. Reprogramming of pericyte-derived cells of the adult human brain into induced neuronal cells. *Cell Stem Cell* 2012; **11**: 471-476 [PMID: 23040476 DOI: 10.1016/j.stem.2012.07.007]
- **Yin JC**, Zhang L, Ma NX, Wang Y, Lee G, Hou XY, Lei ZF, Zhang FY, Dong FP, Wu GY, Chen G. Chemical Conversion of Human Fetal Astrocytes into Neurons through Modulation of Multiple Signaling Pathways. *Stem Cell Reports* 2019; **12**: 488-501 [PMID: 30745031 DOI: 10.1016/j.stemcr.2019.01.003]
- **Wichterle H**, Lieberam I, Porter JA, Jessell TM. Directed differentiation of embryonic stem cells into motor neurons. *Cell* 2002; **110**: 385-397 [PMID: 12176325 DOI: 10.1016/s0092-8674(02)00835-8]
- **Ma F**, Zhu T, Xu F, Wang Z, Zheng Y, Tang Q, Chen L, Shen Y, Zhu J. Neural stem/progenitor cells on collagen with anchored basic fibroblast growth factor as potential natural nerve conduits for facial nerve regeneration. *Acta Biomater* 2017; **50**: 188-197 [PMID: 27940160 DOI: 10.1016/j.actbio.2016.11.064]
- **Li X**, Xiao Z, Han J, Chen L, Xiao H, Ma F, Hou X, Li X, Sun J, Ding W, Zhao Y, Chen B, Dai J. Promotion of neuronal differentiation of neural progenitor cells by using EGFR antibody functionalized collagen scaffolds for spinal cord injury repair. *Biomaterials* 2013; **34**: 5107-5116 [PMID: 23591390 DOI: 10.1016/j.biomaterials.2013.03.062]
- **Aligholi H**, Rezayat SM, Azari H, Ejtemaei Mehr S, Akbari M, Modarres Mousavi SM, Attari F, Alipour F, Hassanzadeh G, Gorji A. Preparing neural stem/progenitor cells in PuraMatrix hydrogel for transplantation after brain injury in rats: A comparative methodological study. *Brain Res* 2016; **1642**: 197-208 [PMID: 27038753 DOI: 10.1016/j.brainres.2016.03.043]

- **Ortinau S**, Schmich J, Block S, Liedmann A, Jonas L, Weiss DG, Helm CA, Rolfs A, Frech MJ. Effect of 3D-scaffold formation on differentiation and survival in human neural progenitor cells. *Biomed Eng Online* 2010; **9**: 70 [PMID: 21070668 DOI: 10.1186/1475-925X-9-70]
- **Yang F**, Murugan R, Ramakrishna S, Wang X, Ma YX, Wang S. Fabrication of nano-structured porous PLLA scaffold intended for nerve tissue engineering. *Biomaterials* 2004; **25**: 1891-1900 [PMID: 14738853 DOI: 10.1016/j.biomaterials.2003.08.062]
- **Lv ZJ**, Liu Y, Miao H, Leng ZQ, Guo JH, Liu J. Effects of multiwalled carbon nanotubes on electrospun poly(lactide-co-glycolide)-based nanocomposite scaffolds on neural cells proliferation. *J Biomed Mater Res B Appl Biomater* 2017; **105**: 934-943 [PMID: 26849161 DOI: 10.1002/jbm.b.33620]
- **Liu** C, Huang Y, Pang M, Yang Y, Li S, Liu L, Shu T, Zhou W, Wang X, Rong L, Liu B. Tissue-engineered regeneration of completely transected spinal cord using induced neural stem cells and gelatin-electrospun poly (lactide-co-glycolide)/polyethylene glycol scaffolds. *PLoS One* 2015; **10**: e0117709 [PMID: 25803031 DOI: 10.1371/journal.pone.0117709]
- **Zhang H**, Wang K, Xing Y, Yu Q. Lysine-doped polypyrrole/spider silk protein/poly(l-lactic) acid containing nerve growth factor composite fibers for neural application. *Mater Sci Eng C Mater Biol Appl* 2015; **56**: 564-573 [PMID: 26249628 DOI: 10.1016/j.msec.2015.06.024]
- **Salehi M**, Naseri-Nosar M, Ebrahimi-Barough S, Nourani M, Khojasteh A, Hamidieh AA, Amani A, Farzamfar S, Ai J. Sciatic nerve regeneration by transplantation of Schwann cells *via* erythropoietin controlled-releasing polylactic acid/multiwalled carbon

nanotubes/gelatin nanofibrils neural guidance conduit. *J Biomed Mater Res B Appl Biomater* 2018; **106**: 1463-1476 [PMID: 28675568 DOI: 10.1002/jbm.b.33952]

Yang J, Mei Y, Hook AL, Taylor M, Urquhart AJ, Bogatyrev SR, Langer R, Anderson DG, Davies MC, Alexander MR. Polymer surface functionalities that control human embryoid body cell adhesion revealed by high throughput surface characterization of combinatorial material microarrays. *Biomaterials* 2010; **31**: 8827-8838 [PMID: 20832108 DOI: 10.1016/j.biomaterials.2010.08.028]

Flaim CJ, Chien S, Bhatia SN. An extracellular matrix microarray for probing cellular differentiation. *Nat Methods* 2005; **2**: 119-125 [PMID: 15782209 DOI: 10.1038/nmeth736]

Roccio M, Gobaa S, Lutolf MP. High-throughput clonal analysis of neural stem cells in microarrayed artificial niches. *Integr Biol (Camb)* 2012; **4**: 391-400 [PMID: 22307554 DOI: 10.1039/c2ib00070a]

Lopes D, Fernandes C, Nóbrega JM, Patrício SG, Oliveira MB, Mano JF. Screening of perfused combinatorial 3D microenvironments for cell culture. *Acta Biomater* 2019; **96**: 222-236 [PMID: 31255663 DOI: 10.1016/j.actbio.2019.06.047]

Cheng K, Lai Y, Kisaalita WS. Three-dimensional polymer scaffolds for high throughput cell-based assay systems. *Biomaterials* 2008; **29**: 2802-2812 [PMID: 18405966 DOI: 10.1016/j.biomaterials.2008.03.015]

Meli L, Barbosa HS, Hickey AM, Gasimli L, Nierode G, Diogo MM, Linhardt RJ, Cabral JM, Dordick JS. Three dimensional cellular microarray platform for human neural stem cell differentiation and toxicology. *Stem Cell Res* 2014; **13**: 36-47 [PMID: 24816401 DOI: 10.1016/j.scr.2014.04.004]

- **Dolatshahi-Pirouz A**, Nikkhah M, Gaharwar AK, Hashmi B, Guermani E, Aliabadi H, Camci-Unal G, Ferrante T, Foss M, Ingber DE, Khademhosseini A. A combinatorial cell-laden gel microarray for inducing osteogenic differentiation of human mesenchymal stem cells. *Sci Rep* 2014; **4**: 3896 [PMID: 24473466 DOI: 10.1038/srep03896]
- **Lee MY**, Kumar RA, Sukumaran SM, Hogg MG, Clark DS, Dordick JS. Three-dimensional cellular microarray for high-throughput toxicology assays. *Proc Natl Acad Sci U S A* 2008; **105**: 59-63 [PMID: 18160535 DOI: 10.1073/pnas.0708756105]