Supplements

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Method

Search strings and selection strategy

The electronic databases PubMed, Scopus and Web of Science were searched using the following terms: PubMed: (("Urinary Bladder"[Mesh] OR urotheli* OR transitional) AND ("Organoids"[Mesh] OR "Spheroids, Cellular"[Mesh]) AND ("Cell Line, Tumour"[Mesh] OR "Cell Line, Transformed"[Mesh] OR "Cell Line"[Mesh])) ; Scopus: TITLE-ABS-KEY((bladder OR vesicle OR urotheli* OR transitional) AND (organoid OR organ OR urospher* OR sphere* OR spheroid* OR 3D OR 3-D OR 3 dimension* OR 3-dimension* OR multilayer* OR multi-layer* OR "multi layer*") AND ("cell line*" OR "secondary culture" OR grow*)); Web of Science: (("bladder" OR "vesicle*" OR "urotheli*" OR "transitional") AND ("organoid" OR "organ" OR "urospher*" OR "sphere*" OR "spheroid*" OR "3D" OR "3-D" OR "3 dimension*" OR "3-dimension*" OR "multilayer*" OR "multi-layer*" OR "multi layer*") AND ("cell line*" OR "secondary culture" OR "grow*")). The search were limited to articles published from January 2000 to April 2022 and to English.

After removing duplicates, 525 articles were retrieved for inclusion; 52 articles were eliminated after evaluating search results. Following screening, the authors reviewed 473 and evaluated for inclusion in our review using the following exclusion criteria: focus on 3D brachytherapy,

3D ultrasound, 3D radiotherapy, 3D PET and CT images, immunohistochemical 3D reconstruction, 3D modelling from anatomical images, non-UC cell lines non-original research/or review, and those non-English and which full-text articles were not available. Our study ultimately contained 195 articles.

Methods	forced floating			liquid overlay						membrane-like structure	ALI	scaffold	microfluidic chip	rotary	>1 method							
	ULA	HD	polyHEMA	MC	collagen	Matrigel	stroma	agarose	bacto agar	CAM					ULA+Coll	ULA+M	ULA+coll+fibronectin	MC+HD+coll	ULA+MC	HD+VM	HD+A	Coll+M
Grade 1:																						
RT4	(1–6)	(7)	(8–10)		(7,11)	(12,13)	(14,15)	(16–19)				(20)	(21)	(22)						(7)		
SW780	(23)																					
MGHU3	(24)							(25–27)						(28)								
SW780						(29)							(21)									
Grade 2:																						
RT112	(6)					(30)	(14,15)	(18,19,25–27,31–38)		(39)	(40)											
5637	(41)		(8–10)		(11)	(30)	(42)	(43,44)	(45)			(20)	(21)	(46)								
UMUC1					(11)																	
647V			(47)																			
Grade 3:																						
SBT31A	(48)																					
T24	(6,24,48–50)		(47)		(7,11,51,52)	(13,53,54)		(18,27,38,43,44,55–59)		(39)			(21,52,60,61)	(46,62)		(63)		(64)	(65)	(7)	(66)	(67)
EJ28							(14,15)								(68)							
BFTC905	(41)																					
BFTC909	(41)																					
MGHU1					(69)																	
UMUC3					(70)	(13,71)		(72,73)					(21)								(66)	
UMUC9															(74)							
J82	(5)		(10)			(54,71)		(18,19,38,59,73,75)					(21)	(46)								(67)
HT1376								(27)														
AY-27								(25,26,76)														
Hu1703He								(77)														

Grade 4:																						
UMUC14								(27)							(74)							
253J								(27)							(74)		(78)					
253JBV						(53)							(21)				(78)					
TCCSUP	(5)					(54)																
EJ138														(79)								
Unknown grade:																						
UMUC13															(74)							
UMUC18															(74)							
TUM06			(80)																			
TUM07			(80,81)																			
TUM24			(81)																			
TUM25			(80)																			
OBR			(47)																			
SCABER					(11)																	
MB49								(55)														
MB49I								(55,82)													(82)	
Normal:																						
UROtsa	(5,83)				(51)			(75)														
SVHUC1	(50)		(10)			(54,71)																
HBEP								(84,85)			(84,85)											
HBLAK								(40,84–86)			(40,84,85,87)											
NHUC																						
NHU								(18,38,59)														

Table 1: Several approaches used to develop 3D UC culture in various UC cell lines. Methylcellulose(MC); hanging drop (HD); collagen (Coll); ultra low attachment dish/plate (ULA); Matrigel (M); vesical mimic (VM); hanging drop + agarose (HD+A); poly 2-hydroxyethyl methacrylate (Poly HEMA); chicken chorionic allantoic membrane (CAM).

Supplements	Factors	Ref.
Growth factor	ascorbic acid	(14,88)
	ferrous sulphate	(14)
	hydrocortisone	(5,14,72,83)
	TGFb-1	(47)
	EGF	(5,41,47,50,54,66,83,89)
	insulin	(5,50,66,72,80,83,89)
	bFGF	(41,50,72,89)
	2-b-mercaptoethanol	(80,90)
	glutamine	(51,80)
	sodium pyruvate	(31,80)
	non-essential amino acid	(80)
	selenium	(5,83)
	transferrin	(5,83)
	triiodothyronine	(5,83)
	bovine serum albumin	(90)
	B27	(41,89)
	N2	(89)
	F12	(91)
	human gastrin I	(89)
	Glutamax	(89,90)
	N-acetyl-l-cysteine	(89)
	Noggin	(89)
	R-spondin	(89)
	Heregulin	(92)
Differentiation factor	PD153035	(93)
	Troglitazone	(93)
	calcium	
	FOXA1 (knock-in)	(11)
	GATA3 (knock-in)	(11)
	rosiglitazone	(11)
	urine (filter-sterilized)	(40,84,85,87)
Pluripotent maintenance	CHIR 99021	(90)
Special media	CnT PR media	(40,84,85,87)
	CnT PR 3D media	(40,84,85,87)
	DMEM/F12	(5,83,90)
	keratinocyte serum free media	(66)
	RPMI/Ham's F12	(41)
Coculture	HUVECs	(52,88)
	fibroblast	(64)
	rat tail collagen	(11)
	mice embryonic bladder mesenchyme	(11)
	B-lymphocyte	(54)

Table 2: Various supplements used in media for 3D culturing of UC cells.

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