Qkine

Growth factors for

Organoids

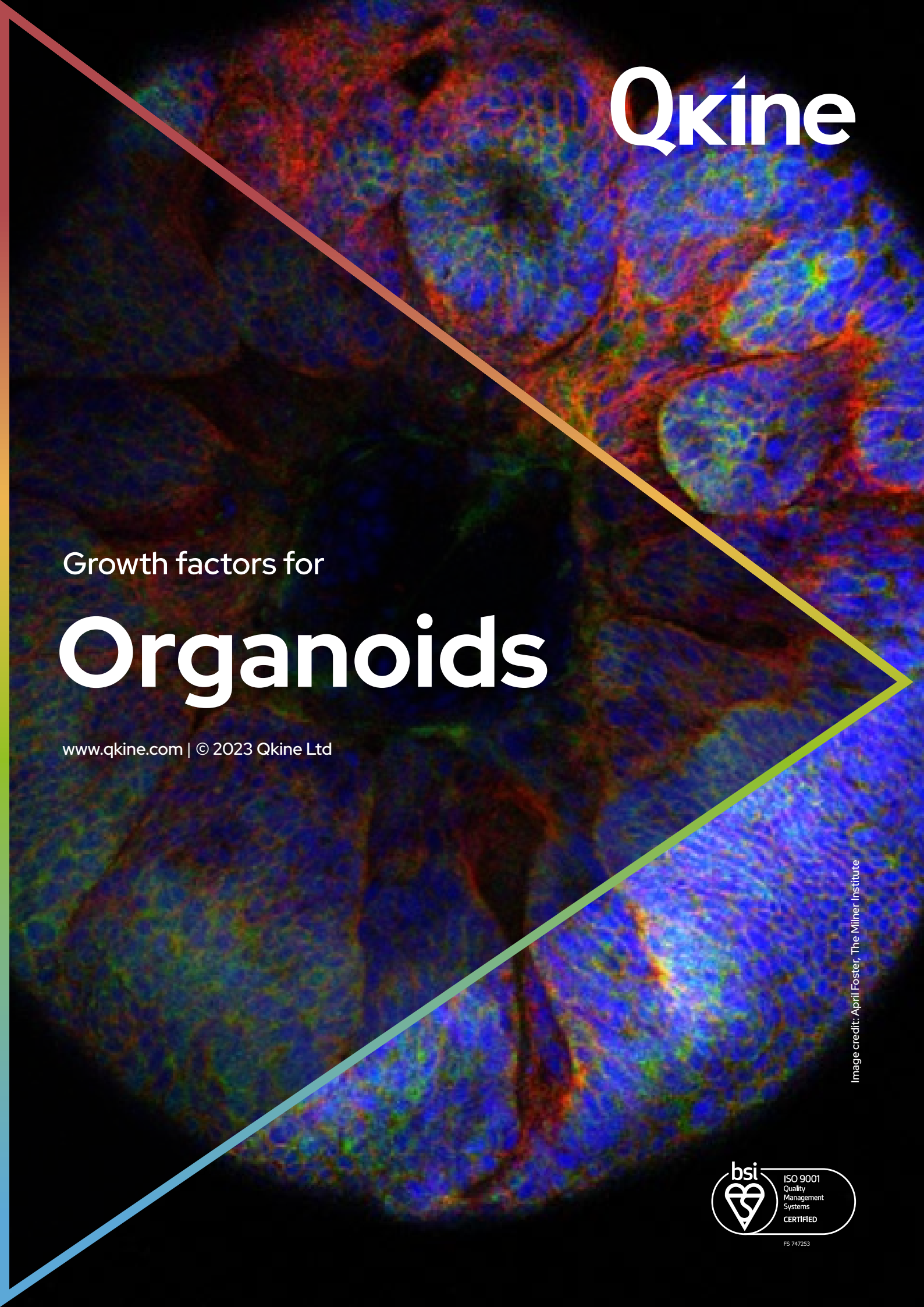

Image credit: April Foster, The Milner Institute

Stem cells are undifferentiated cells with the capacity to self-renew or differentiate into specialized cell types of the body. There are different types of stem cells such as embryonic stem cells and adult stem cells. As they are involved in the development and the maintenance of the organ size, they reside in a defined microenvironment, known as the stem cell niche, in various tissues. Several tissue engineering studies have attempted to mimic the stem cell niche using soluble growth factors, extracellular matrices, and other cues, contributing to the evolution of more complex cultures such as organoids.

An organoid is a three-dimensional (3D) structure derived from stem cells which mimics the key function, structure, and biology of an organ or a tissue. In contrast to traditional 2D cell culture models, Organoid models can replicate the intricate spatial architecture and the physiological responses of in vivo differentiated tissue enabling the investigation of the biologically relevant cell-to-cell and cell-matrix interactions.

Organoids are derived from induced pluripotent stem cells (iPSCs), embryonic stem cells (ESCs) or tissue-derived cells in conditions that promote their self-organization and differentiation into specific cell types. By creating the cellular microenvironments using matrices, and providing appropriate growth factors, organoids can develop into complex structures that resemble miniaturized organs.

For example, intestinal organoids have been shown to self-organize themselves into a crypt-villus architecture while hepatic organoids have been shown to express tissue-specific markers like MRP4. Since their discovery, organoids have gained a significant interest as a valuable tool to study human development, disease modelling, and personalized medicine.

Their ability to mimic different tissues and facilitate the investigation of complex physiological systems ex vivo, contributes to their potential in pre-clinical drug-screening models.

Hence, organoids are expected to bridge the gap between in vivo and in vitro studies for targeted therapies reducing the study costs and time, and the use of animal models.

However, it is important to note the ethical considerations, technical challenges, and regulatory aspects that need to be addressed as their applications progress.

> "Organoids are self-organizing 3D cultures that present an alternative to conventional platforms, while retaining the benefits of both conventional 2D cell lines and *in vivo* animal models."
>
> Kim, Koo and Clevers, 2022

In this brochure, key organoid types will be discussed, along with suggested protocols, focusing on the key growth factors and cytokines required.

References

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Yi, S.A. et al. (2021) 'Bioengineering Approaches for the Advanced Organoid Research', Advanced Materials, 33(45). Available at: https://doi.org/10.1002/ADMA.202007949.

Zhao, Z. et al. (2022) 'Organoids', Nature Reviews Methods Primers 2022 2:1, 2(1), pp. 1–21. Available at: https://doi.org/10.1038/s43586-022-00174-y.

Trust Qkine for your organoid cultures

High-quality growth factors are essential for the development and maintenance of robust, reproducible, and physiologically relevant organoid cultures. Therefore, it is crucial to use growth factors from reliable sources with stringent quality control measures ensuring the purity, stability, and bioactivity of the growth factors. Choosing an animal-free supplier guarantees that there are no contaminating endogenous growth factors, allowing scientists to have confidence in their cell culture.

Qkine manufactures bioactive animal-free recombinant proteins at an ISO9001:2015 certified facility based in Cambridge, UK. Qkine combines proprietary production processes with protein engineering technology to tackle fundamental biological, quality, and scale-up challenges to provide more reliable tools for research and bio-manufacturing.

As leaders in protein innovation, approximately 30% of our catalogue is made of unique products. We have developed a portfolio of stable and protein tag-free growth factors aimed at increasing reproducibility and scaling-up your organoid research.

Why choose Qkine?

Manufactured in Cambridge, UK

Animal-free and carrier-protein free

In stock for fast worldwide delivery

Bulk quantities available for large scale applications

High purity and protein tag-free

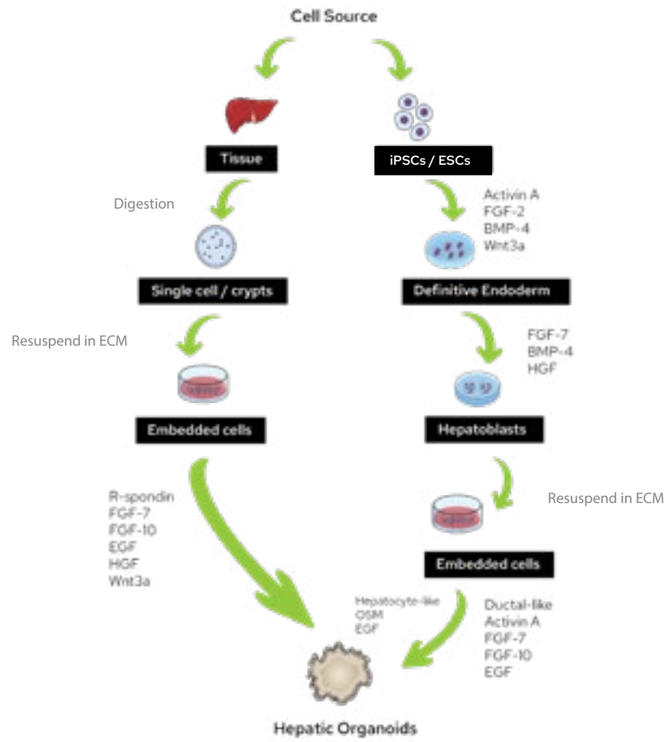
ISO 9001:2015 accredited facility

Highly bioactive

Innovative engineered protein forms available

Hepatic organoids

The utilization and implementation of hepatic organoids hold immense potential in advancing the field of hepatic research. These organoids have transformed the culture and maintenance of liver cells, particularly hepatocytes, which tend to exhibit significant dedifferentiation in conventional cultures. Hepatic organoids are typically cultured within an extracellular matrix supplemented with a combination of growth factors, facilitating the formation and differentiation of hepatic organoids. The expression of albumin (ALB) is assessed to confirm successful hepatic differentiation. The establishment of hepatic organoids has enabled the disease modeling and the investigation of gene and cell therapy in liver cancer and alcohol-associated liver disease.



Product code	Description
Qk001	Human/mouse Activin A
Qk005	Human/mouse Activin A PLUS
Qk035	Follistatin-resistant Activin A
Qk038	Human BMP-4
Qk011	Human EGF protein
Qk025	Human FGF-2 (bFGF) 145 aa
Qk027	Human FGF-2 (bFGF) 154 aa
Qk052	Thermostable FGF2-G3 145 aa

Product code	Description
Qk053	Thermostable FGF2-G3 154 aa
Qk046	Human KGF (FGF-7)
Qk003	Human/rat/bovine/porcine FGF-10
Qk013	Human HGF (NK1)
Qk049	Human Oncostatin M (OSM) protein
Qk031	Human R-spondin 1 LR5
Qk006	Human R-spondin 1
Qk032	Human R-spondin 3

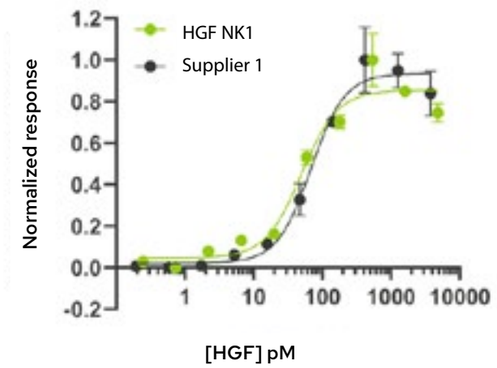
Further reading

Broutier L, Andersson-Rolf A, Hindley CJ, et al. Culture and establishment of self-renewing human and mouse adult liver and pancreas 3D organoids and their genetic manipulation. Nat Protoc. 2016;11(9):1724-1743.
Caiazza C, Parisi S, Caiazzo M. Liver Organoids: Updates on Disease Modeling and Biomedical Applications. Biology (Basel). 2021;10(9):835.
Nuciforo S, Heim MH. Organoids to model liver disease. JHEP Rep. 2020;3(1):100198. Published 2020 Oct 22.

Recombinant HGF (NK1) protein

For hepatic organoids

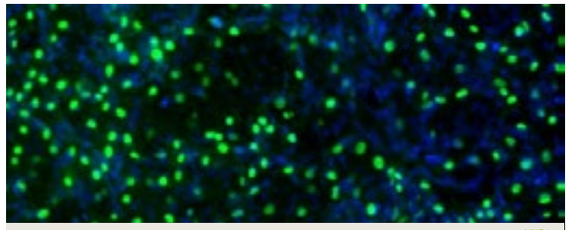
Recombinant human HGF protein is a potent, high-purity NK1 isoform of human hepatocyte growth factor (HGF). This protein promotes efficient differentiation of human iPSCs to hepatocyte-like cells at just 10 ng/ml with homogeneous expression of the hepatic marker, HNF4α. This animal-free 20 kDa naturally occurring isoform of HGF is suitable for chemically defined media and reproducible scale-up.



Full-length HGF protein domains

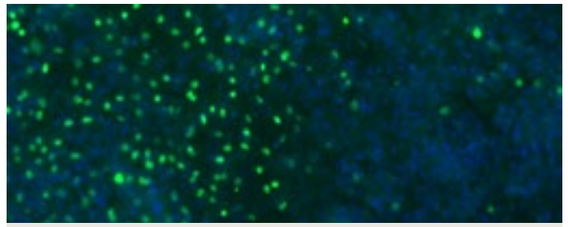
NK1 isoform

Highly pure, animal-free, protein with extensive biochemical and quantitative bioactivity data to ensure reproducible and scalable stem cell differentiation. Luciferase assay shows HGF (NK1) (Qk013) has equivalent bioactivity to full-length HGF (mammalian expression system) from other suppliers.



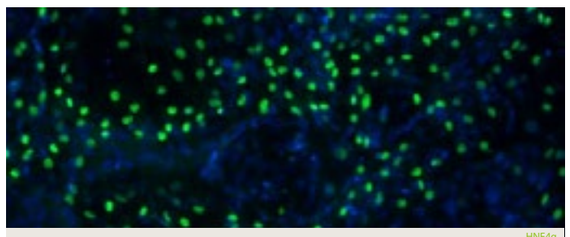
Qk013 HGF (NK1) 10ng/ml

HNF4α
DAPI
10 x



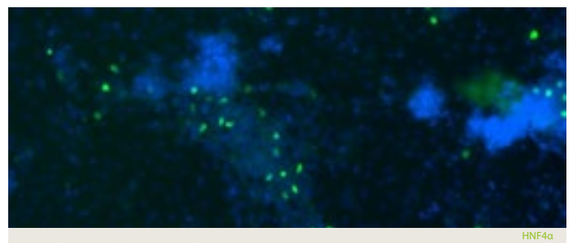
Qk013 HGF (NK1) 40ng/ml

HNF4α
DAPI
10 x



Supplier x HGF 10 ng/ml

HNF4α
DAPI
10 x



Supplier x HGF 40 ng/ml

HNF4α
DAPI
10 x

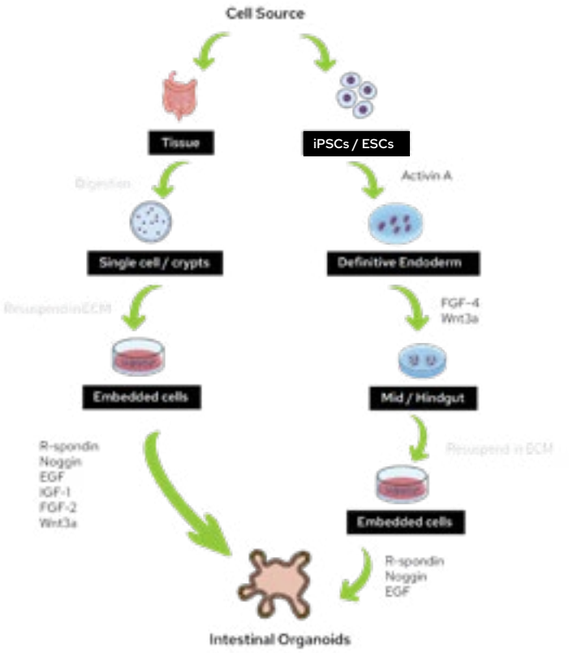
HGF (NK1) promotes efficient differentiation of human iPSCs to hepatocyte-like cells at just 10 ng/ml with highly homogeneous expression of the hepatic marker, HNF4α.

Learn more about human HGF (NK1) protein by visiting our website or scanning the QR code with your smartphone.

Product code	Description
Qk013	Human HGF (NK1)
Qk060	Bovine HGF (NK1)
Qk061	Porcine HGF (NK1)

Intestinal organoids

Intestinal organoids are one of the first organoids to have been successfully established in vitro. Intestinal organoids comprise of several intestinal cell types, including enterocytes, goblet cells, Paneth cells, enteroendocrine cells, and intestinal stem cells. These cells self-organize themselves to form a crypt-villus architecture that closely resembles that of the intestine. The intestinal crypts express markers such as the intestinal stem cell marker, Lgr5, and the enterocyte marker, villin. They have been shown to perform many of the key functions such as secretion of mucus and gut hormonal regulation and have been widely used for intestinal disease modeling, including inflammatory bowel disease and colorectal cancer. The development of intestinal organoids has made a significant contribution to organoid research and has formed the foundation for other tissue-specific organoid discoveries such as liver organoids.



Product code	Description
Qk001	Human/mouse Activin A
Qk005	Human/mouse Activin A PLUS
Qk035	Follistatin-resistant Activin A
Qk011	Human EGF protein
Qk025	Human FGF-2 (bFGF) 145 aa
Qk027	Human FGF-2 (bFGF) 154 aa
Qk052	Thermostable FGF2-G3 145 aa
Qk053	Thermostable FGF2-G3 154 aa

Product code	Description
Qk004	Human FGF-4
Qk041	Human/bovine/porcine IGF-1 LR3
Qk047	Human/bovine/porcine IGF-1
Qk034	Human noggin
Qk033	Mouse/rat noggin
Qk031	Human R-spondin 1 LR5
Qk006	Human R-spondin 1
Qk032	Human R-spondin 3

Further reading

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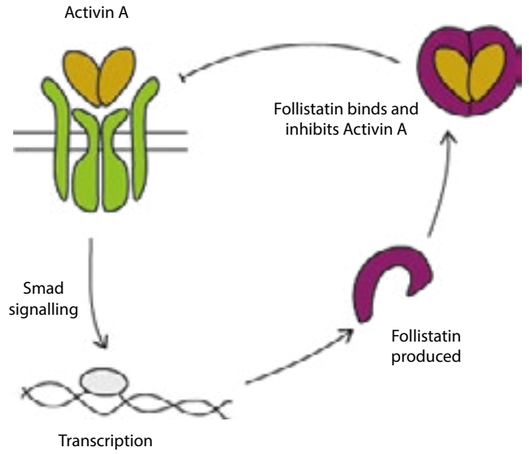
Pioneering proteins

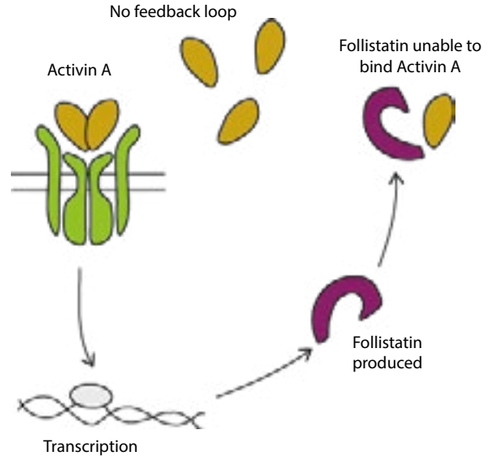
Follistatin-resistant Activin A protein for lung organoids

Follistatin-resistant activin A protein (FRACTA) has been engineered to prevent binding to the natural inhibitor, follistatin. In vivo, the activity of Activin A is regulated by follistatin, a high-affinity inhibitor; consequently, activin A activity fluctuates in stem cell culture, due to accumulation and inhibiton of follistatin. FRACTA has equivalent bioactivity to wild-type activin A but does not bind follistatin so is resistant to feedback inhibition. FRACTA is a high purity, animal-free, and carrier-protein free, 26 kDa dimer comprising engineered mature domain of activin A protein.

Follistatin inhibits Activin A



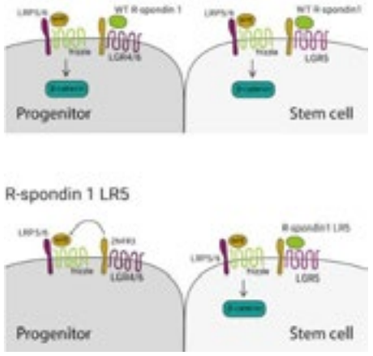
Removing inhibition by follistatin



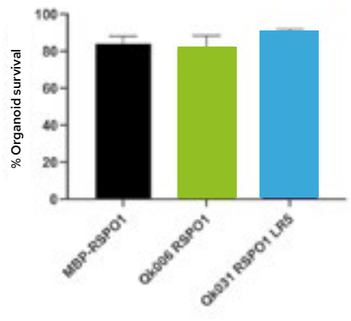
R-spondin 1 LR5 protein for intestinal organoids

Recombinant human R-spondin 1 LR5 protein is engineered to bind to the LGR5 receptor on intestinal stem cells with high affinity. As LGR5 is specifically expressed by the stem cell population of the lower intestinal crypt in organoid cultures and not the transit amplifying cells, the engineered R-spondin 1 LR5 activates Wnt signalling only in LGR5+ stem cell population in comparison to the wild-type version. R-spondin 1 LR5 has been tested in intestinal organoid culture and supports organoid survival and growth.

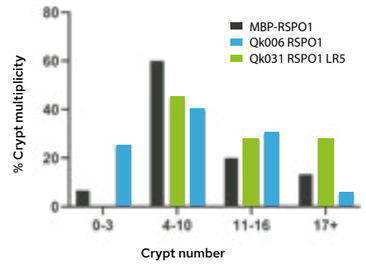
Specificity to LGR5+ stem cells



Organoid survival is maintained



Crypt multiplicity is maintained



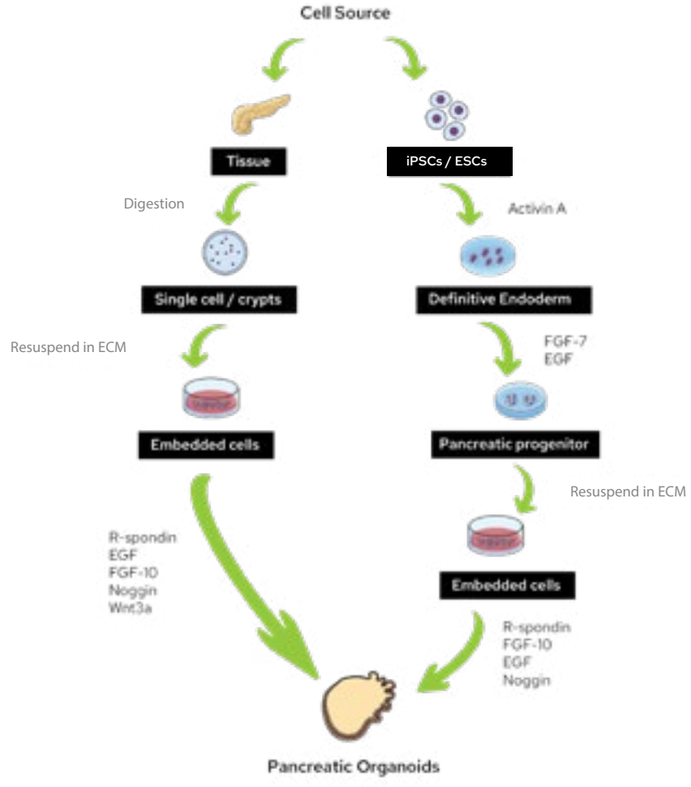
All organoid data from the laboratory of Marc de la Roche and reproduced with permission (© Marc de la Roche, 2020).

Learn more about our pioneering proteins by visiting our website or scanning the QR code with your smartphone.

Product code	Description
Qk035	Follistatin-resistant Activin A
Qk031	R-spondin 1 LR5

Pancreatic organoids

Pancreatic organoids are generated to mimic the pancreatic ductal system. They are composed of tissue-specific cell types including pancreatic ductal cells, acinar cells, and endocrine cells that are organized to form complex pancreatic structures. Cells within pancreatic organoids express key markers such as ductal marker, KRT19, and pancreatic progenitor marker, PDX1. The establishment of pancreatic organoids has great potential to study pancreatic regeneration, repair mechanisms, and the development of targeted therapies for pancreatic disorders. For example, multiple studies are investigating pancreatic stem cell transplantation and cell therapy to replace the insulin-producing beta cells in patients with Type I diabetes.



Product code	Description
Qk001	Human/mouse Activin A
Qk005	Human/mouse Activin A PLUS
Qk035	Follistatin-resistant Activin A
Qk011	Human EGF protein
Qk046	Human KGF (FGF-7)
Qk003	Human/rat/bovine/porcine FGF-10

Product code	Description
Qk034	Human noggin
Qk033	Mouse/rat noggin
Qk031	Human R-spondin 1 LR5
Qk006	Human R-spondin 1
Qk032	Human R-spondin 3

Further reading

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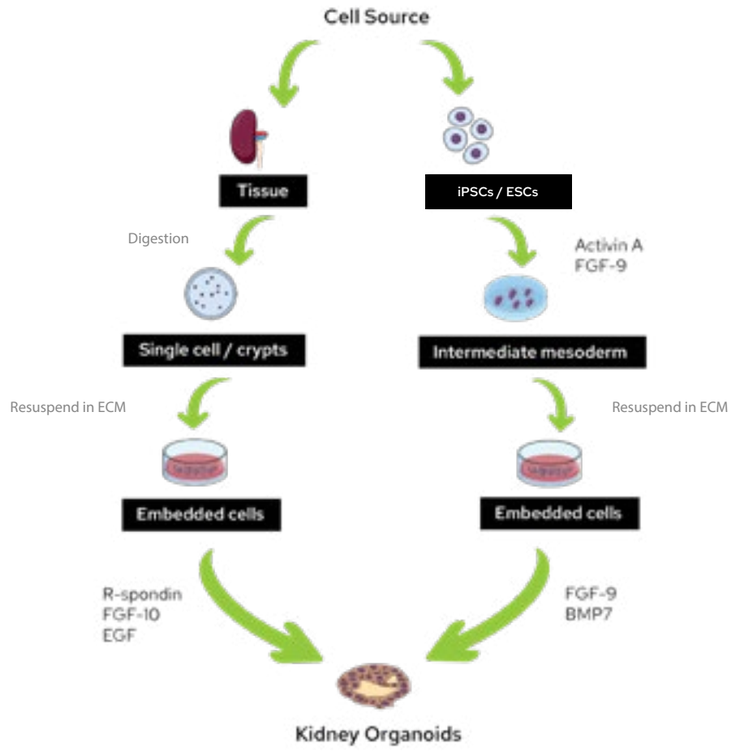
Shi X, Li Y, Yuan Q, et al. Integrated profiling of human pancreatic cancer organoids reveals chromatin accessibility features associated with drug

Kidney organoids

The recent progress in organoid technology has facilitated the generation of kidney organoids to mimic the structure and function of the kidney, a vital organ responsible for waste regulation. These developed kidney organoids consist of tissue-specific cell types that are arranged to form the intricate cellular architecture of tubules, nephrons, and associated mesenchyme networks. Kidney organoids demonstrate the expression of key markers such as E-cadherin (ECAD) and podocalyxin (PODXL) in the distal tubules and podocytes, respectively. Previous studies focusing on kidney-related research have proved challenging due to limited physiologically relevant kidney models. However, kidney organoids present a promising solution to overcome these challenges for kidney-related investigations and applications.



Product code	Description
Qk001	Human/mouse Activin A
Qk005	Human/mouse Activin A PLUS
Qk035	Follistatin-resistant Activin A
Qk011	Human EGF protein
Qk039	Human FGF-9

Product code	Description
Qk003	Human/rat/bovine/porcine FGF-10
Qk031	Human R-spondin 1 LR5
Qk006	Human R-spondin 1
Qk032	Human R-spondin 3

Further reading

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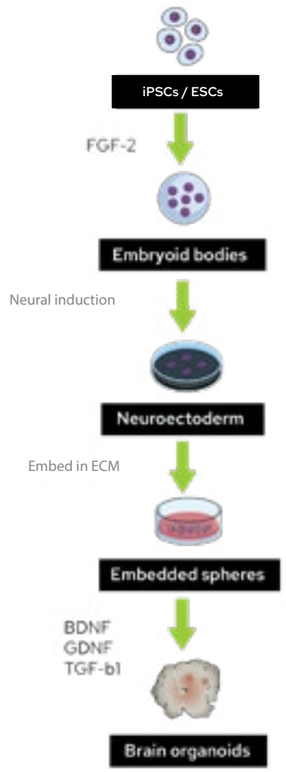
Sander V, Przepiorski A, Crunk AE, Hukriede NA, Holm TM, Davidson AJ. Protocol for Large-Scale Production of Kidney Organoids from Human Pluripotent Stem Cells. STAR Protoc. 2020;1(3):100150. Published 2020 Oct 29. doi:10.1016/j.xpro.2020.100150

Neural organoids

Neural organoids, also known as cerebral organoids, are composed of tissue-specific cell types including glial cells, neurons, and other brain cells, that are arranged to form complex neural networks that mimic the developmental processes and structural organization of the brain. Cells within neural organoids have been shown to express key markers such as the neuronal marker class III beta-tubulin (Tuj1) or the apical progenitor marker, PAX6. The capacity of neural organoids to model neurodegenerative disorders such as Alzheimer's and Parkinson's diseases has facilitated the investigation of regenerative medicine of injured neurons and the development of potential stem cell treatments.



Product code	Description
Qk050	Human BDNF
Qk025	Human FGF-2 (bFGF) 145 aa
Qk027	Human FGF-2 (bFGF) 154 aa
Qk052	Thermostable FGF2-G3 145 aa

Product code	Description
Qk053	Thermostable FGF2-G3 154 aa
Qk051	Human GDNF
Qk010	Human/bovine/porcine TGF-β1 PLUS

Further reading

Monzel AS, Smits LM, Hemmer K, et al. Derivation of Human Midbrain-Specific Organoids from Neuroepithelial Stem Cells. Stem Cell Reports. 2017;8(5):1144-1154.

Lancaster MA, Renner M, Martin CA, Wenzel D, Bicknell LS, Hurles ME, Homfray T, Penninger JM, Jackson AP, Knoblich JA. Cerebral organoids model human brain development and microcephaly. Nature. 2013 Sep 19;501(7467):373-9.

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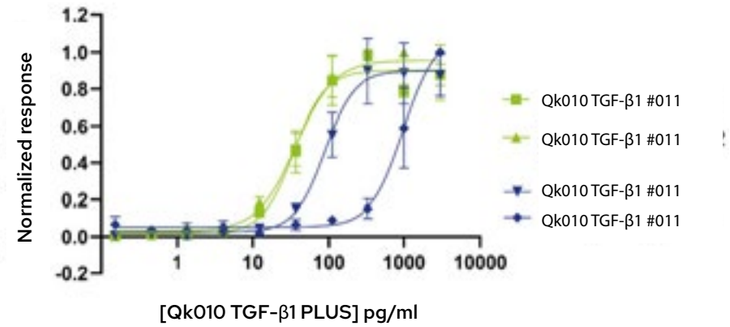
Recombinant TGF-β1 protein

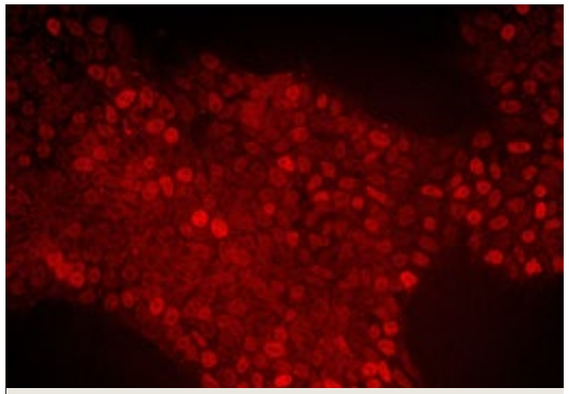
For neural organoids

Qkine TGF-β1 PLUS protein is the first entirely animal-free recombinant human transforming growth factor beta 1 (TGF-β1) protein for highly reproducible results and compatible with chemically defined stem cell media and organoid cultures. TGF-β1 is used extensively in the E8 media for induced pluripotent stem cell (iPSC), embryonic stem cell (ESC), and organoid cultures. This protein is a high-purity, animal-free, and carrier-protein free 24 kDa dimer comprising an optimized mature domain of TGF-β1 protein.

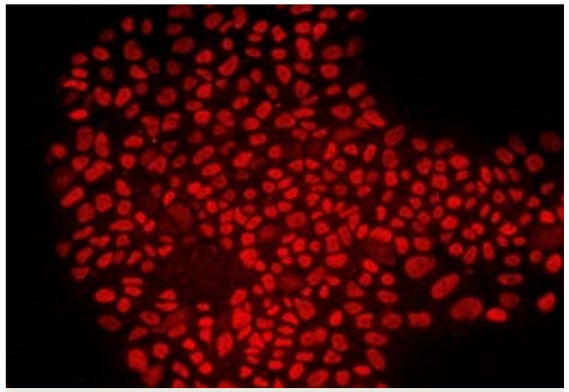


- Suitable for chemically defined stem cell media
- Animal origin-free manufacturing process
- High-purity protein with expceptional lot-to-lot consistency

Highly pure, animal-free, protein with extensive biochemical and quantitative bioactivity data to ensure reproducible and scalable stem cell maintenance. Quantitative luciferase reporter assays show TGF-β1 PLUS (Qk010) has consistently high bioactivity when compared directly to TGF-β1 produced in mammalian expression systems from two other suppliers.



Supplier 1 (mammalian expressed) NANOG



Qkine TGF-β1 PLUS (Qk010) NANOG

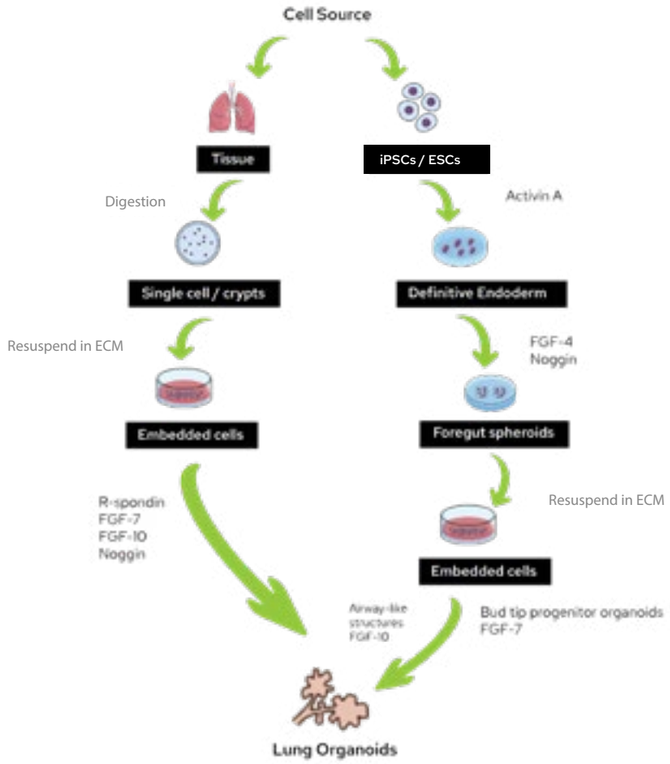
Comparison between Qkine TGF-β1 PLUS (animal-free) and mammalian expressed TGF-β1 sourced from another supplier. TGF-β1 PLUS promotes efficient maintenance of iPSCs at 1 ng/ml, with highly homogeneous expression of the pluripotency marker Nanog.

Learn more about human TGF-β1 protein by visiting our website or scanning the QR code with your smartphone.

Product code	Description
Qk010	Human TGF-β1 PLUS

Lung organoids

Lung organoids have the potential to be used as a powerful tool for high-throughput drug screening and development as they provide the capacity to study complex respiratory-related processes and diseases. Lung organoids have been shown to contain several tissue-specific cell types including lung epithelial cells, endothelial cells, and mesenchymal cells. These organoids structurally resemble the branching architecture of the alveolar and airway regions within the lung. By employing lung organoids, researchers gain access to robust 3D model systems that closely resemble lung tissue, facilitating the study of airway-related conditions such as chronic obstructive pulmonary disease (COPD) and the recent Covid-19 disease.



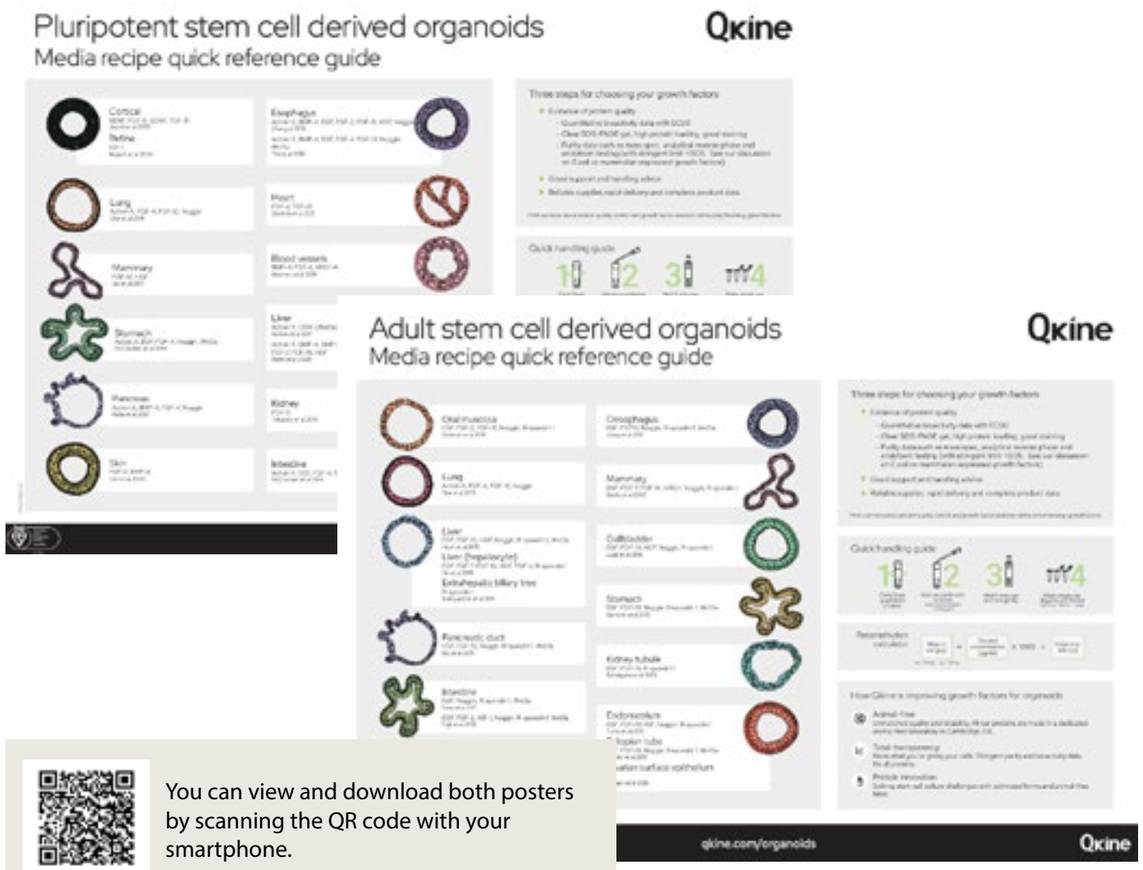
Product code	Description
Qk001	Human/mouse Activin A
Qk005	Human/mouse Activin A PLUS
Qk035	Follistatin-resistant Activin A
Qk004	Human FGF-4
Qk046	Human KGF (FGF-7)
Qk003	Human/rat/bovine/porcine FGF-10

Product code	Description
Qk034	Human noggin
Qk033	Mouse/rat noggin
Qk031	Human R-spondin 1 LR5
Qk006	Human R-spondin 1
Qk032	Human R-spondin 3

Further reading

Miller AJ, Dye BR, Ferrer-Torres D, et al. Generation of lung organoids from human pluripotent stem cells in vitro. Nat Protoc. 2019;14(2):518-540.
Li Z, Yu L, Chen D, Meng Z, Chen W, Huang W. Protocol for generation of lung adenocarcinoma organoids from clinical samples. STAR Protoc. 2020;2(1):100239.
Paolicelli G, Luca A, Jose SS, et al. Using Lung Organoids to Investigate Epithelial Barrier Complexity and IL-17 Signaling During Respiratory Infection. Front Immunol. 2019;10:323.

Related resources



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Setting the standard in bioactive protein manufacturing

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USA (toll free): 1-866 877 2185.

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