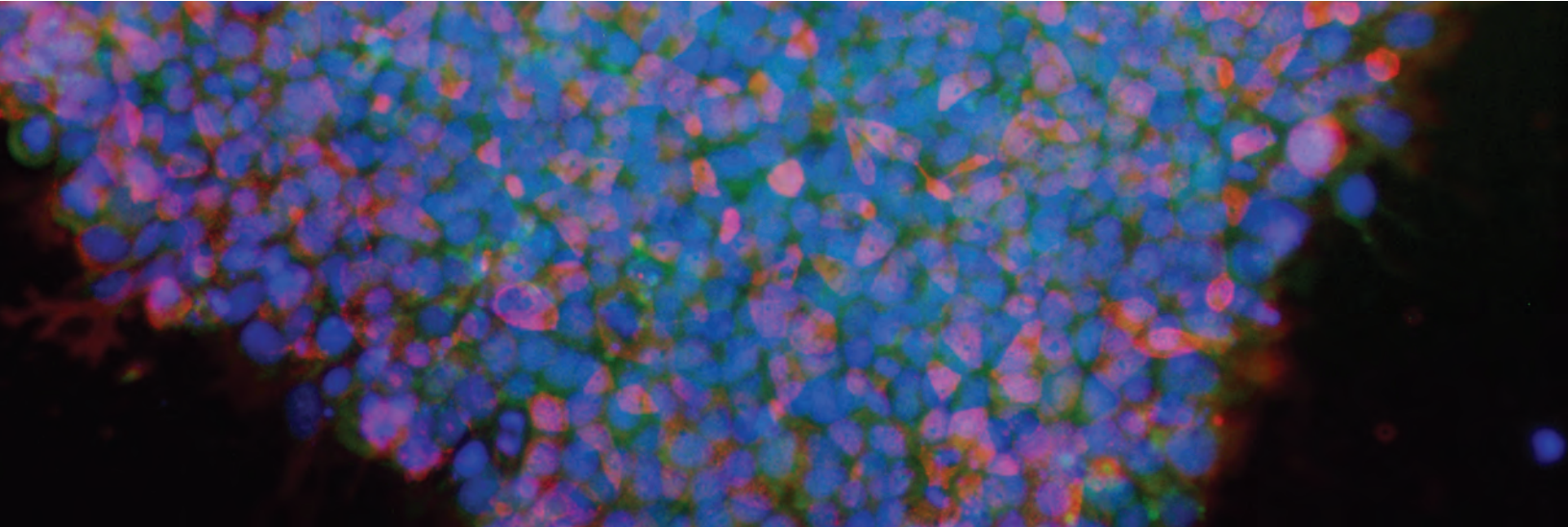


NutriStem® hPSC XF Medium

A superior xeno-free, serum-free culture medium for hES and hiPS cells



- Defined, serum-free, xeno-free medium
- Complete, ready-to-use formulation
- Flexible and compatible with multiple matrices
- Enhances clean cell growth
- Optimizable formulation
- FDA Drug Master File
- Easily translate to the clinic

Clinically-relevant medium designed for research and cell therapy applications

NutriStem® hPSC XF Medium is a defined, xeno-free, serum-free medium designed to support the growth and expansion of human induced pluripotent stem (hiPS) and human embryonic stem (hES) cells. NutriStem® hPSC XF Medium offers the ability to culture human pluripotent cells without the need for high levels of bFGF and other stimulatory growth factors or cytokines. The low-protein formulation contains only the most essential components required for maintenance of hES and hiPS cells, providing a simplified medium while maintaining the cells' full differentiation potential. This streamlined formulation is not only flexible and compatible with a multitude of culture systems, but also allows for extreme control over added components for specific applications.

The defined, xeno-free formulation of NutriStem® hPSC XF Medium provides consistent media performance and predictable cellular behavior, as well as increased reproducibility in long-term culture (over 50 passages). In addition, cells cultured in NutriStem® hPSC XF Medium show superior attachment and proliferation rates, making this medium optimal for high-throughput screening applications.

NutriStem® hPSC XF Medium has a Drug Master File and is manufactured under cGMP, making it an ideal medium for researchers working with both research and cell therapy applications.

NutriStem® hPSC XF Medium Reference Guide

Product	NutriStem® hPSC XF Medium				NutriStem® hPSC XF Medium, Growth Factor-Free	NutriStem® V9 XF Medium
Cell type	hPSCs (iPSCs, hESCs)					
Clinical	FDA Drug Master File				Reference FDA Drug Master File	n/a
Applications	Feeder-dependent culture	Feeder-free culture	Translational culture	Translational culture, single cell	Reprogramming	Cultures requiring vitronectin and higher amounts of growth factors
Additional supplement(s)	None, complete and ready-to-use formulation				bFGF (20 ng/mL+)	V9 supplement mix
Matrix	MEFs/HFFs	Matrigel® Cultrex® Geltrex® Other	Vitronectin Laminin-521 Laminin-511	Laminin-521	Matrigel® Laminin-521 Laminin-511	Vitronectin
Xeno-free	Possible (HFFs)	No	Yes	Yes	Yes	Yes
Weekend-free feeding*	No	Yes	Yes	Yes	n/a	Yes
Dissociation reagent(s)	Collagenase IV	Accutase Collagenase IV Dispase 0.5M EDTA	Accutase 0.5M EDTA	Accutase Recombinant Trypsin EDTA	Accutase Recombinant Trypsin EDTA	0.5M EDTA
Freezing media	NutriFreez™ D10 Cryopreservation Medium					

* Weekend-free feeding is possible, though with any hPSC culture, optimal growth is seen with daily feeding. It is not recommended to skip feedings on a routine or long-term basis.

References

Growing Methods of hESC and iPSC

Derivation, Expansion, Scaling up, and Suspensions

1. Yoda, K., et al. 2018. J. of Biotech. and Bioengin. 127. 3:381-387.
2. Gao, X., et al. 2018. Cellular Reprogramming. 20:5.
3. Teramura, T., et al. 2018. Bio. Res. Comm. 503. 4:3114-3120.
4. Lipsitz, Y.Y., et al. 2018. Biotech. and Bioengin. 1-6.
5. Altieri, F., et al. 2018. Stem Cell Res. 28:153-156.
6. Albalushi, H., et al. 2018. Stem Cells Intern. Art. ID: 7127042.
7. Russell, O.M., et al. 2018. Scientific Reports. Art. ID: 1799.
8. Rosati, J., et al. 2018. Stem Cell Res. 27:74-77.
9. Maroof M Adil, et al. 2017. Chem. Engine. 15:24-35.
10. Tateno, H., et al. 2016. Regen. Therapy, 6:1-8.
11. Baker, D., et al. 2016. Stem Cell Reports. 7. 5:998-1012.
12. Vega-Crespo, A., et al. 2016. Mol. Therapy. Art. ID: 16050.
13. Lipsitz, Y.Y., et al. 2015. BMC Proceedings, 9:O10.
14. Healy, L., et al. 2015. Atlas of hPSCs in Culture. 149-165.
15. Siqin, W., et al. 2014. Biomaterials 35.30: 8496-8502.

Differentiation of Pluripotent Stem Cells

1. Ji, SL, et al. 2019. Int J Ophthalmol. 12(1): 152-160.
2. Markus, A., et al. 2019. Exp. Eye Res. 180:29-38.
3. Shao, Z., et al. 2019. Nature Neuro. 22:229-242.
4. McPhie, D.L., et al. 2018. Trans. Psychiatry, 8: 230.
5. Ameri, J. et al. Cell Reports. 19.
6. De Santis, R., et al. 2018. Stem Cell Res. 29:189-196.
7. Welby, E., et al. 2017. Stem Cell Reports. <https://doi.org/10.1016/j.stemcr.2017.10.018>
8. R.A. Hazim, R.A., et al. 2017. Stem Cell Res. & Therapy.
9. Petrus-Reurer, S., et al. 2017. Retinal Cell Bio.
10. Lenzi, J., et al. 2016. Stem Cell Res. 17, 1:140-147.
11. Alessandri, K., et al. 2016. Lab on a Chip: 16(9).
12. Reyes, A., et al. 2015. Stem Cell Reports: 6, 1:9-17.
13. Schwab, A.J., et al. 2014. PLoS One. 9(7): e103112.
14. Nguyen, H.X. et al. 2014. J. of Com. Neur. 12:2767-2783.

Clinical Applications

Derivation and Expansion of hESC and iPSC

1. Gu, Q., et al. 2017. Stem Cell Reports. 9(1): 366-380.
2. de Oñate, L., et al. 2015. DOI: 10.5772/60902.
3. Menasché, P., et al. 2015. EU Heart J. 36:12:743-50.
4. Seki, T., et al. 2015. World J. of Stem Cells. 7. 1:116-125.
5. Luo, Y., et al. 2014. STEM CELLS Trans. Med. 3:7:821-35.
6. Durruthy-Durruthy, J., et al. 2014. PLoS ONE 9(4): e94231.
7. Tateno, H., et al. 2014. Sci. Reports, Art. ID: 4069.
8. Awe, J. P., et al. 2013. Stem Cell Res. & Therapy. 4:87.

Gene Editing

1. Supharattanasitthi, W., et al. 2019. CRISPR - Sci. Rep. 9:174.
2. Sweeney, CL, et al. 2017. Molecular Therapy.
3. Lenzi, J., et al. 2015. Disease Models & Mech. 8:755-766.
4. Cerbini, T., et al. 2015. JoVE PMID: 25741760.

The above reference guide only represents a sample of citations for these products.

Product	Size	Cat. #	References
NutriFreez™ D10 Cryopreservation Medium is a universal chemically defined, animal component-free, and protein-free freezing solution with high cell viability.	50 mL 100 mL 500 mL	05-713-1E 05-713-1B 05-713-1A	1. Gagliardi, G. et al. 2018. Stem Cell Reports. 11:665–680. 2. Reichman, S., et al. 2017. STEM CELLS 35.5:1176–1188.
Vitronectin XF™ is a recombinant fusion protein that contains the entire human vitronectin sequence and supports enzyme-free passaging and reproducible long-term hPSC culture.	2 mL / 500 µg	S2153-500UG	3. Masato, N., et al. 2015. PLOS One. https://doi.org/10.1371/journal.pone.0136350
Vitronectin ACF is a chemically-defined matrix which supports cell adhesion through binding to various integrins and proteoglycans.	200 µg	05-754-0002	4. Thomson, J. A., et al. 1998. Science 282 (5391): 1145–47. 5. Richards, M., et al. 2002. Nature Bio. 20 (9): 933–36.
LaminStem™ 521 promotes cellular survival and expansion of hPSCs after plating from single cell suspension also supports long-term self-renewal of hPSCs and neural stem cells.	1 mL	05-753-1F	6. Reyes, A., et al. 2016. Stem Cell Reports. 6. 1:9-17. 7. Rodin, S., et al. 2014. 5:3195.
Accutase Solution is an alternative solution to trypsin developed for gentle and effective detachment of adherent cells.	100 mL	03-073-1B	8. Bajpai, R., et al. 2008. Mol Reprod Dev. 75:818-827. 9. Zheng, K., et al. 2006. Cytotechnology. 52:209-218. 10. Wachs, F.P., et al. 2003. Lab Invest. 83:949-962.
Recombinant Trypsin-EDTA Solution is a pure and defined enzyme solution which maximizes the yield of viable cells from culture vessels, while preventing toxicity.	100 mL	03-079-1B	11. Rodin, S., et al. 2010. Nature Bio. 28. 6:611-15
0.5M EDTA Solution is an enzyme-free, chemically defined, animal component-free solution for the dissociation of human pluripotent stem cells.	100 mL	01-862-1B	12. Kleinman, H., et al. 1982. Ameri. Chem. Society. 6188–93.

Cardiomyocyte Differentiation

1. Chang, A.C.Y., et al. 2011. PNAS.
2. Rajasingh, S., et al. 2018. Acta Pharma. Sinica.
3. Ophir, R., et al. 2017. Ameri. J. of Res. and Critical Care Med.
4. Rajasingh, S., et al. 2015. PloS one 10.8, e0134093.
5. Jacquet, L., et al. 2015. PloS one 10.5.
6. Bellamy, V., et al. 2014. J. of Heart and Lung Transplan.
7. Di Pasquale, E., et al. 2013. JoVE 76: e50429-e50429.
8. Burridge, P.W., et al. 2013. Meth. in Mol. Bio. 997:149-161.

Organoids

1. Maliszewska-Olejniczak, K., et al. 2018. Cytotechnology. <https://doi.org/10.1007/s10616-018-0273-x>
2. Wilkinson, D.C., et al. 2017. Stem Cells Trans. Med. 6(2).
3. Tieng, V., et al. 2014. Stem Cells and Dev. 23(13): 1535-1547.
4. Maliszewska-Olejniczak, K., et al. Meth. in Mol. Bio. 1817.

Induction of Pluripotency of hESC and iPSC

1. Klein, T., et al. 2018. Stem Cell Res. 33:171-174.
2. Gao, X. et al. 2018. Stem Cell Res. 31:193-196.
3. Chandrabose, S.T., et al. 2018. Stem Cell Res. & The. 9:68.
4. Naaman, H. et al. 2018. Cell. Reprog. 20. 1:17–26.
5. Gao, X., et al. 2017. Stem Cell Res. 25:202-212.
6. Krivega, M.V., et al. 2015. Mol. Hum. 12:942-56.
7. Eminli-Meissner, S., et al. 2015. Hum Gene Ther. 11:751-66.
8. Brouwer, M., et al. 2015. Stem Cell Rev. 12. 1:54–72.
9. Warren, L., et al. 2010. Cell Stem Cell 7: 618-630.
10. Sugii, S., et al. 2010. PNAS 107. 8:3558-3563.

Proteins and Antibodies Expression and Isolation

1. DePalma, A. 2018. Genetic Engine. & Biotech. 38. 5:18-21.
2. Riordon, D.R., et al. 2018. Methods in Mol. Bio.1722.
3. Thakar, N.Y., et al. 2015. Mol. Bio. 26. 5:993-1006.

Versatility of Basement Membranes

1. Shafa, M. 2018. Vitronectin/Laminins. Front Med. 5:69.
2. Qin, Y., et al. 2017. Laminins. Cancer Bio. 45: 3-12.
3. Wu, S., et al. 2015. Silk. Cell. and Mol. Life Sci. 73. 7:1479-88.
4. Simonson, O. 2015. Laminins. Karolinska Institutet. 21.
5. Rodin, S. et al. 2014. Laminins. Nat. Prot. 9:2354–2368.

Drug Screening

1. Ye, Z., et al. 2013. Stem Cells. <http://dx.doi.org/10.1002/stem.154>.

Animal Models

1. Zhang, W., et al. 2016. PLOS ONE. <https://doi.org/10.1371/journal.pone.0158655>

Normal cell morphology and functional assessment of pluripotency

The formation of compact colonies of cells with a high nucleus-to-cytoplasm ratio, prominent nucleoli, and distinct colony borders are characteristic morphology traits of healthy undifferentiated hES and hiPS cells, and can be observed through a phase-contrast microscope (Figure 1). Human pluripotent stem cells hold the potential to differentiate into cell types of all three germ layers (endoderm, mesoderm, and ectoderm). This differentiation potential is assessed by the spontaneous differentiation within embryoid bodies cultured in vitro (Figure 2) and teratomas formed in vivo (Figure 3).

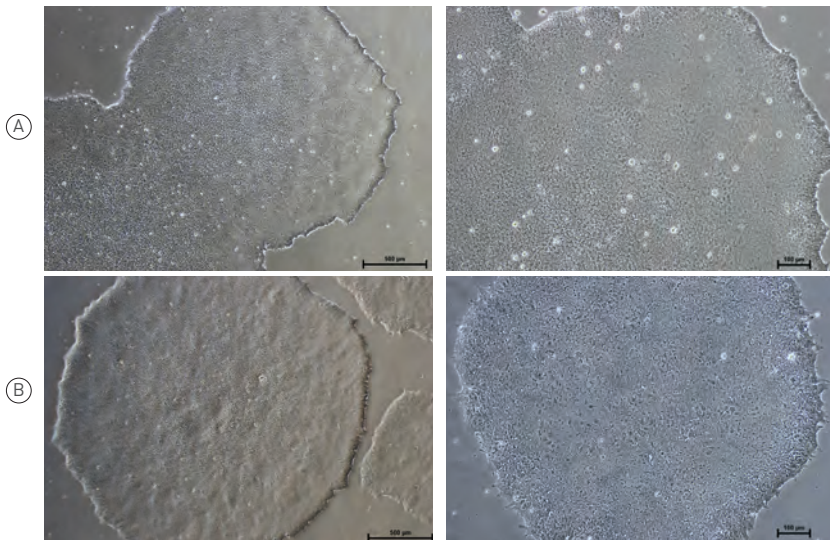


Figure 1: Normal Colony Morphology. H1 hES cells (panel A) and ACS-1014 hiPS cells (panel B) cultured in NutriStem® hPSC XF Medium on Matrigel-coated plates display colony morphologies typical of normal feeder-free hES and hiPS cell cultures, including a uniform colony of tightly compacted cells and distinct colony edges.

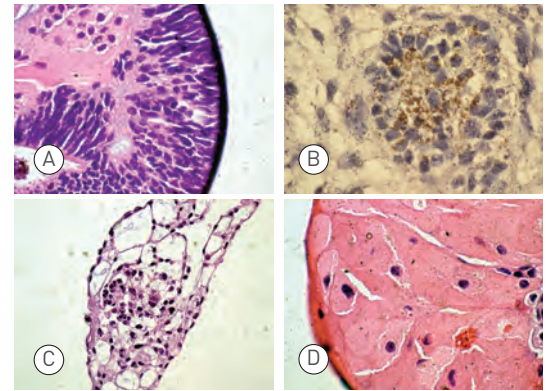


Figure 2: Embryoid Body Formation. Embryoid bodies (EBs) were generated from H9.2 hES cells cultured for 16 passages in NutriStem® hPSC XF Medium on Matrigel matrix as an evaluation of pluripotency. The pluripotent H9.2 cells were suspended in serum-supplemented medium, where they spontaneously formed EBs containing cells of embryonic germ layers. Examples of cell types that were identified by examination of the histological sections of 14-day-old EBs stained with H&E: (A) neural rosette (ectoderm), (B) neural rosette stained with Tubulin, (C) primitive blood vessels (mesoderm), and (D) megakaryocytes (mesoderm).

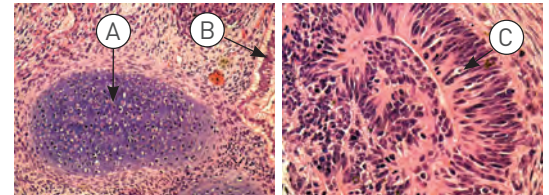


Figure 3: Teratoma Formation. H9.2 hES cells were cultured for 11 passages in NutriStem® hPSC XF Medium using a human foreskin fibroblast (HFF) feeder layer. The hES cells were subsequently injected into the hind leg muscle of SCID-beige mice for in vitro evaluation of pluripotency. The following tissues from all three germ layers were identified in H&E-stained histological sections of the teratoma 12 weeks post-injection: (A) cartilage (mesoderm), (B) epithelium (endoderm), and (C) neural rosette (ectoderm).

ORDERING INFORMATION

PRODUCT	CAT. #	SIZE
NutriStem® hPSC XF Medium	05-100-1A	500 mL
NutriStem® hPSC XF Medium (Growth Factor-Free)	06-5100-01-1A	500 mL
NutriStem® V9 XF Medium*	05-105-1A-KT	500 mL
LaminStem™ 521	05-753-1F	1 mL
Vitronectin XF™	S2153-500UG	2 mL / 500 µg
Vitronectin ACF	05-754-0002	200 µg
Bio-Pure™ Human Serum Albumin (HSA)	05-730-1E	50 mL

*Please note that NutriStem® V9 XF Medium is an optimized formulation with higher amounts of growth factors designed for applications using vitronectin. Bulk orders, custom sizes, packaging, and scale-up support is available upon request.

Biological Industries USA | T. 860.316.2702 F. 860.269.0596 | orders@bioindusa.com

©2019 Biological Industries USA, Inc. All rights reserved. The trademarks mentioned herein are the property of Biological Industries Israel Beit Haemek LTD. and/or its affiliates or their respective owners. BIUSA 0319A

Culture of Excellence

www.bioindusa.com