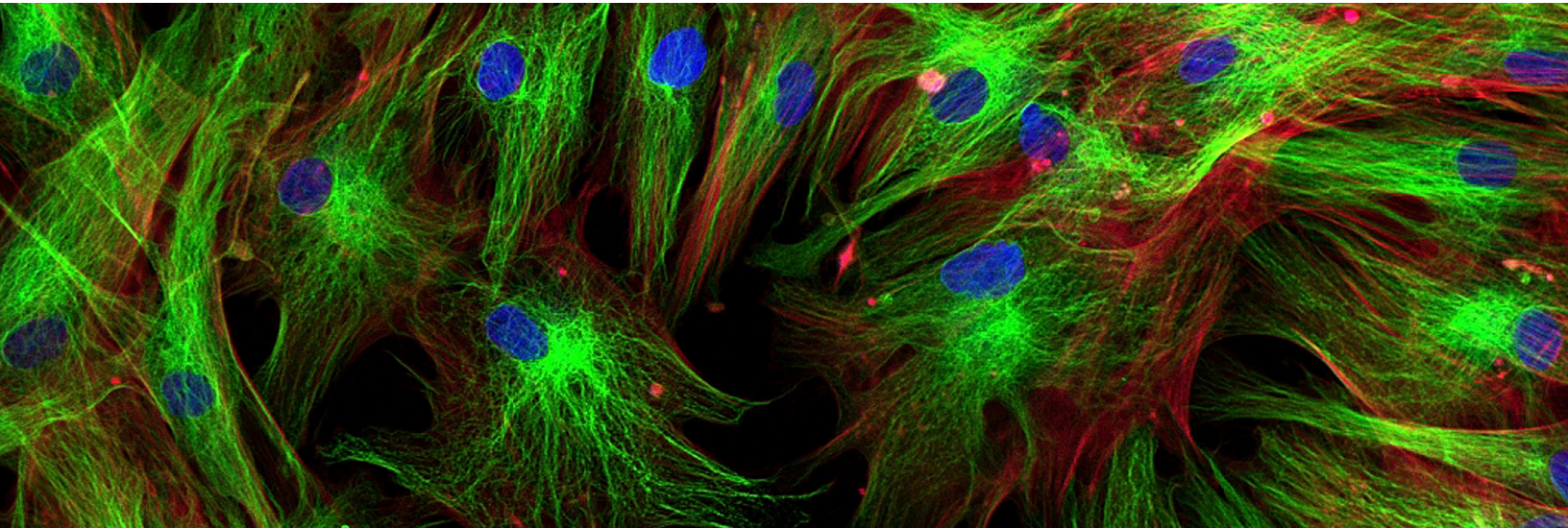


NutriStem® MSC XF Medium

A superior xeno-free, serum-free culture medium for MSCs



- Xeno-free, serum-free, defined medium
- Optimizable formulation
- Flexible culture systems
- Custom scale-up services
- cGMP-manufactured
- FDA Drug Master File
- Easily translate to the clinic

Accelerating regenerative medicine from research to clinical applications

NutriStem® MSC XF Medium is a defined, xeno-free, serum-free culture medium designed for optimal growth and expansion of human mesenchymal stem/stromal cells (hMSCs) derived from a variety of sources, including bone marrow (BM-MSC), adipose tissue (AT-MSC), umbilical cord tissue (UC-MSC), and dental pulp (DP-MSC). NutriStem® MSC XF Medium offers the ability to culture hMSCs in a reliable and consistent culture system that is of clinical quality, cGMP-produced, and supportive of healthy, long-term proliferation of high-quality cells.

NutriStem® MSC XF Medium allows for superior hMSC proliferation and self-renewal potential of hMSCs when compared to serum-containing media and other commercially available serum-free media. In addition, hMSCs cultured in NutriStem® MSC XF Medium maintain their proper cell morphology, tri-lineage differentiation potential, as well as demonstrate normal hMSC marker profiles and karyotypic stability over long-term culture.

NutriStem® MSC XF Medium can be used with or without human platelet lysate to create various systems for specific workflows, each of which having the ability to aid in the progress of hMSC-based applications such as exosome isolation or cell banking. Furthermore, NutriStem® MSC XF Medium has a complete FDA Drug Master File and is manufactured under cGMP, making it an ideal medium for both academic and clinical workflows.

NutriStem® MSC XF Medium Reference Guide

Product	NutriStem® MSC XF Medium		Fetal Bovine Serum
Cell type	hMSCs		
FDA DMF	Yes		No
Applications	Completely defined translational culture Exosome isolation	Translational culture Cell banking	Standard for basic research
Additional supplement(s)	None	Human Platelet Lysate (PLTGold®)	None
Substrate required	MSC Attachment Factor (Human Fibronectin)	None	None
Clinical-grade, cGMP	Yes		No
Lot-to-lot consistency	Yes	Yes	No
Protein-rich	No	Yes	Yes
Xeno-free	Yes	Yes	No
Dissociation reagent(s)	Recombinant Trypsin Solution	Recombinant Trypsin Solution	Recombinant Trypsin Solution
Freezing media	NutriFreez™ D10 Cryopreservation Medium		

References

Clinical Trials

- McIntyre, L.A., et al. Cellular Immunotherapy for Septic Shock. A Phase I Clinical Trial. Ameri. J. of Res. and Critical Care Medicine, Vol. 197, No. 3, 2018.
- Schlosser, K., et al. Effects of MSC Treatment on Systemic Cytokine Levels in a Phase 1 Dose Escalation Safety Trial of Septic Shock Patients. Critical Care Medicine. DOI 10.1097/CCM.0000000000003657

Publications

- Jonavice, U., et al. 2019. J. of Tissue Engine. and Regen. Med.
- Li, J.W., et al. 2019. European J. of Pharm.
- Zhu, Z., et al. 2018. <https://doi.org/10.1093/humrep/dey344>.
- Yamasaki, A., et al. 2018. J. of Orth. Res.
- N.B., Vu., et. al. 2018. Stem Cells in Clinical App. Spr. Cham.
- Ledwon, J.K., et al. 2018. Plas. and Recon. Surgery. 6(4S):116.
- Lisini, D., et al. Current Res. in Trans. Med. <https://doi.org/10.1016/j.retram.2018.06.002>.
- Peak, T.C., et al. 2019. 499. 4:1004-1010.
- Khan, S., et al. 2018. Cytotherapy. 20. 5: S42.
- Volz, A.C., et. al. 2018. 20. 4:576-588.
- Ceccaldi, C. et al. 2017. Macro. Bio., 2017
- Boruczkowski, D., et al. 2016. Turkish J. of Bio. 40:493-500.
- Jianxia, H., et al. 2016. Exper. and Therap. Med. 12 . 3.
- Bobis-Wozowicz, S., et al. 2016 J. of Mol. Med.
- Berger, L., et al. 2015. STEM CELLS. 34. 4:31 DEC.
- Tan, K.Y., et al. 2015. Cytotherapy.
- Zhen, C. et al. 2015. Aesth. 39.3: 431-439.
- Pokrywczynska, M., et al. 2015. Archi. Immun. Therap. Exper.
- Mei, S.H., et al. 2014. Cytotherapy. 16. 4:S111.
- McVey, M., et al. 2016 Ameri. J. of Phys. ajplung-00369.
- Lopez, Y., et al. 2012. ISCT Annual Meeting, Seattle, USA.
- Foster, R. D., et al. 2011. Tissue Eng Meth. Part C. 17:7.

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

Quickly translate into the clinic with BI-USA hMSC culture systems

Culture System Comparisons		System 1 NutriStem® MSC Medium on Human Fibronectin	System 2 NutriStem® MSC Medium + PLTGold® Human Platelet Lysate	FBS Classical Media + 10% FBS
First passage to ≥50 million cells	Fold Increase Per Passage	4	13	2.5
	Passage (time in culture)	P2 (12 days)	P1 (8 days)**	P4 (32 days)
	Actual cell yield at passage	5.4 x 10 ⁷	1.8 x 10 ⁸	8.5 x 10 ⁷
Calculated effort to reach 50 million cells	Total media required	1,932 mL	420 mL	5,040 mL
	Total T-175 flasks used	23	5	40
	Approximate media cost*	\$1,400	\$350	\$1,110

*Materials and costs are estimated based on 2018 USD list pricing.

Table 1: Expansion potential and cost comparison of NutriStem® MSC Medium culture systems and traditional classical media supplemented with 10% FBS. Using observed growth rates, the first passage to generate more than 50 million cells from an initial starting amount of 875,000 cells was calculated. This growth rate was then used to extrapolate the volume of media components required to generate 50 million cells.** Using System 2, an actual yield of 180 million cells could be achieved by Passage 2, therefore the time required to reach 50 million cells is less than 8 days. The defined NutriStem® MSC Medium on human fibronectin generates the same number of cells in about half the amount of time, materials, and reagents than media supplemented with FBS. Pairing NutriStem® MSC Medium with PLTGold® enables even more rapid cell proliferation, generating 50 million cells within one week, and only requiring 5 culture flasks.

**Culture parameters used to estimate media volumes and total costs: a seeding density of 5 x 10³ cells/cm², cultured in 175cm² flasks, with 42 mL complete media used per flask, and passaging (sub-culture) performed at time required to reach 70 to 80% confluency for each media condition (4 days for both NutriStem® MSC Medium culture systems and 7 days for traditional culture with FBS).

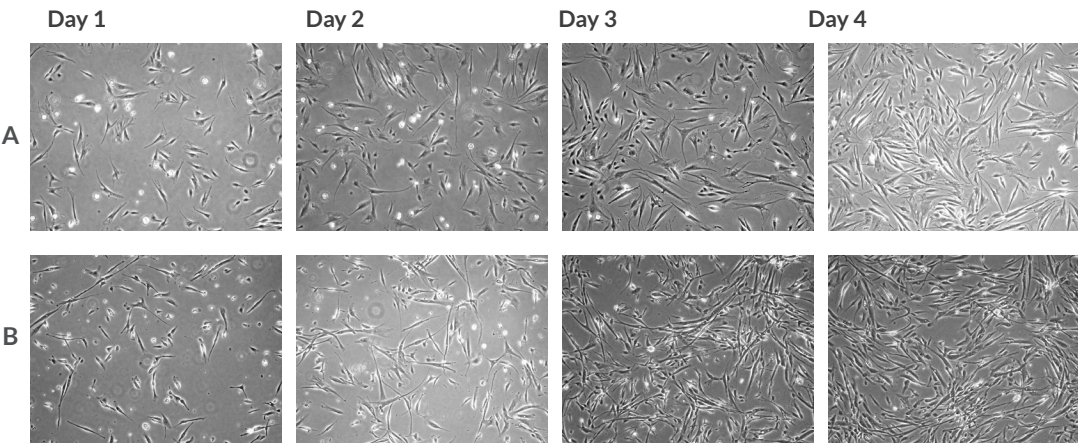


Figure 1: Later passage BM-MSCs (fourth passage post thaw) cultured with NutriStem® MSC XF Medium . **A.** on MSC attachment solution or **B.** supplemented with 5% PLTGold® Human Platelet Lysate show healthy cell proliferation over 4 consecutive days in culture and maintain normal cell morphology (5X). hMSCs cultured in both NutriStem® MSC XF Systems express proper amounts of the typical multipotent cell markers indicative of phenotype maintenance (data not shown).

Superior proliferation in consistent and reliable cultures

Xeno-free, serum-free culture in NutriStem® MSC XF Medium supports the generation of clinical-quality, healthy, and proliferative MSCs - outperforming cells cultured in traditional serum-containing media in terms of expansion and long-term growth.

MSCs cultured in NutriStem® MSC XF Medium with PLTGold® Human Platelet Lysate exhibit exceptional proliferation with significantly higher cellular fold increases than typical serum-containing cultures, ideal for cell-based applications requiring clinically-relevant numbers of high-quality and healthy MSCs.

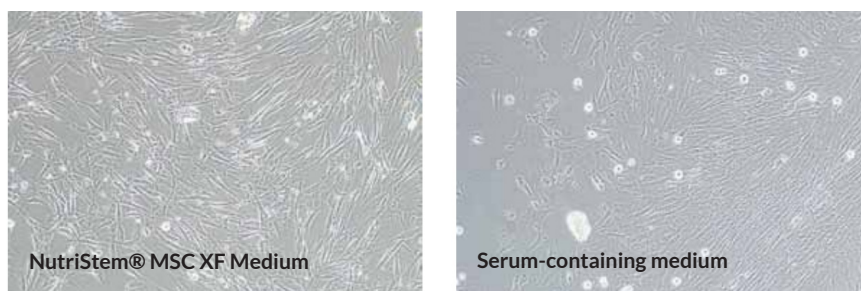


Figure 2: hMSCs were isolated from frozen crude placenta using NutriStem® MSC XF Medium on pre-coated plates with MSC Attachment Solution. Images taken 11 days post initial isolation (P0) exemplify higher confluence of hMSCs in NutriStem® MSC XF Medium when compared to cells cultured in serum-containing medium (40X).

ORDERING INFORMATION

PRODUCT	CAT. #	SIZE
NutriStem® MSC XF Medium*	05-200-1A-KT	500 mL
NutriStem® MSC XF Medium (without Phenol Red)	05-202-1A	500 mL
MSC Attachment Factor	05-752-1H	5 mL
PLTGold® Human Platelet Lysate (Research-grade)	PLTGOLD27R PLTGOLD100R PLTGOLD500R	27 mL 100 mL 500 mL
PLTGold® Human Platelet Lysate (Clinical-grade)	PLTGOLD27GMP PLTGOLD100GMP PLTGOLD500GMP	27 mL 100 mL 500 mL
NutriFreez™ D10 Cryopreservation Medium	05-713-1E 05-713-1B	50 mL 100 mL
Recombinant Trypsin Solution	03-078-1B	100 mL

*Includes basal media and supplement. Bulk orders, custom sizes and volume fills available upon request.

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

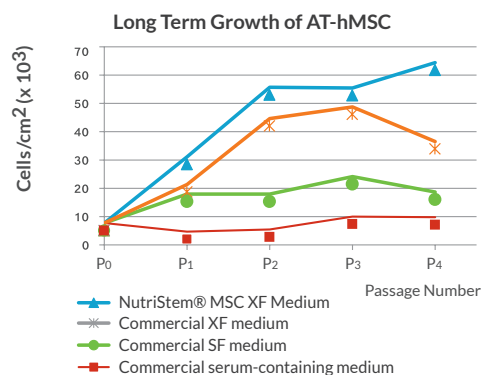
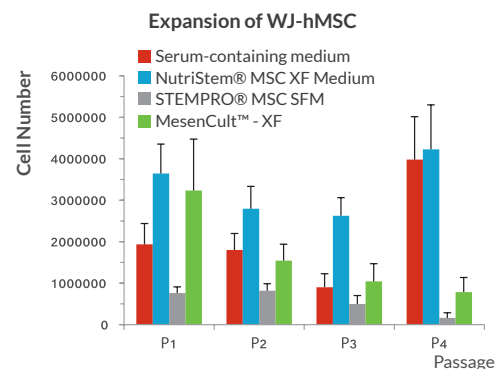
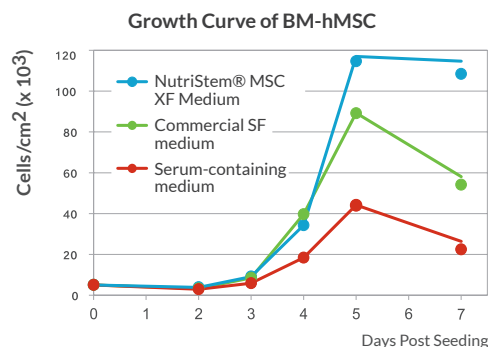


Figure 3: NutriStem® MSC XF Medium promotes superior proliferation and expansion of hMSCs over time as compared to other serum-free and serum-containing media.

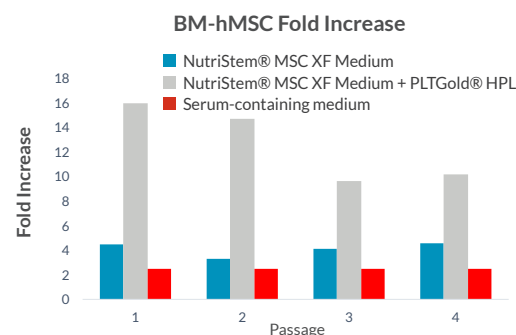


Figure 4: NutriStem® MSC XF Medium paired with PLTGold® Human Platelet Lysate allows for an average fold increase of 13, compared to average fold increases of 2.5 in serum-containing cultures.