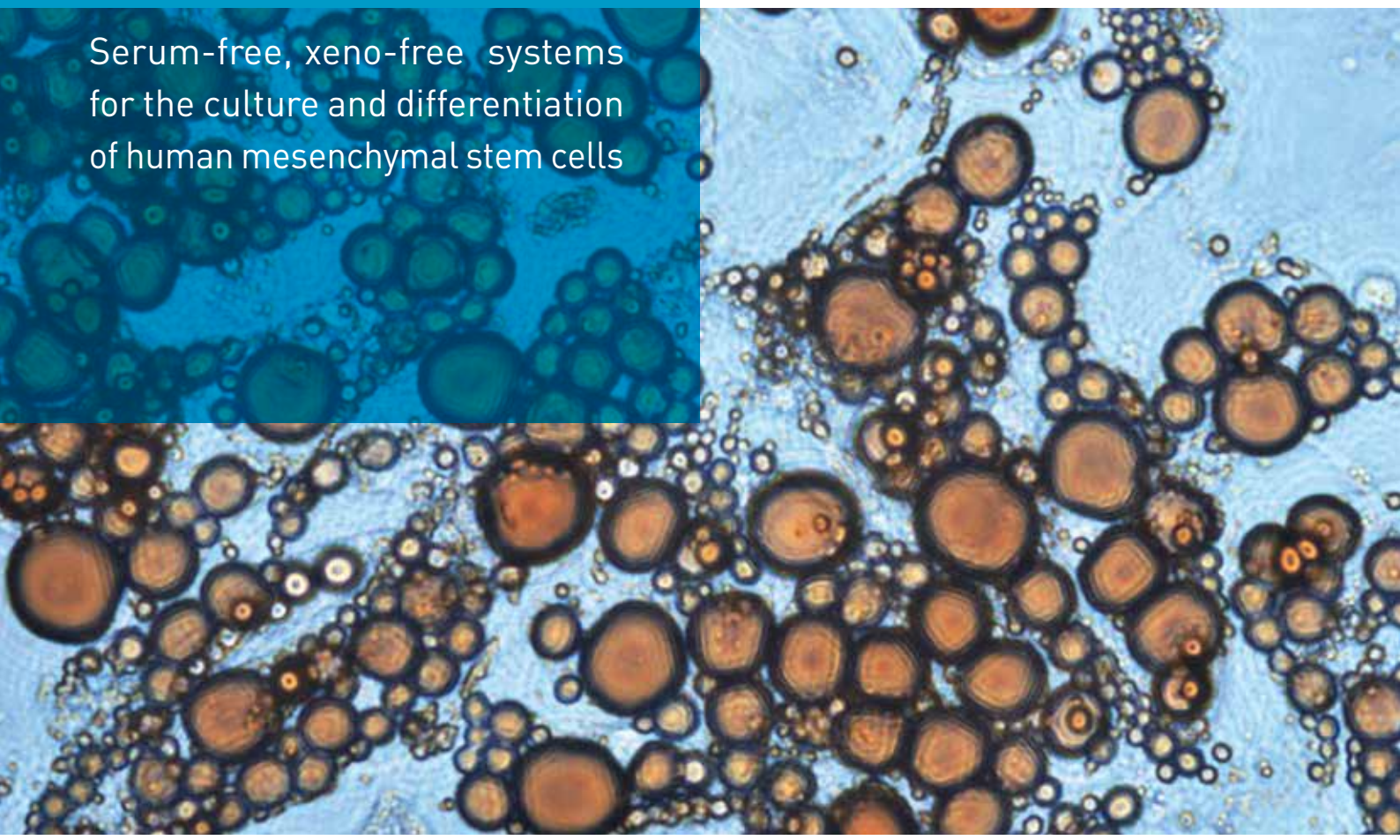
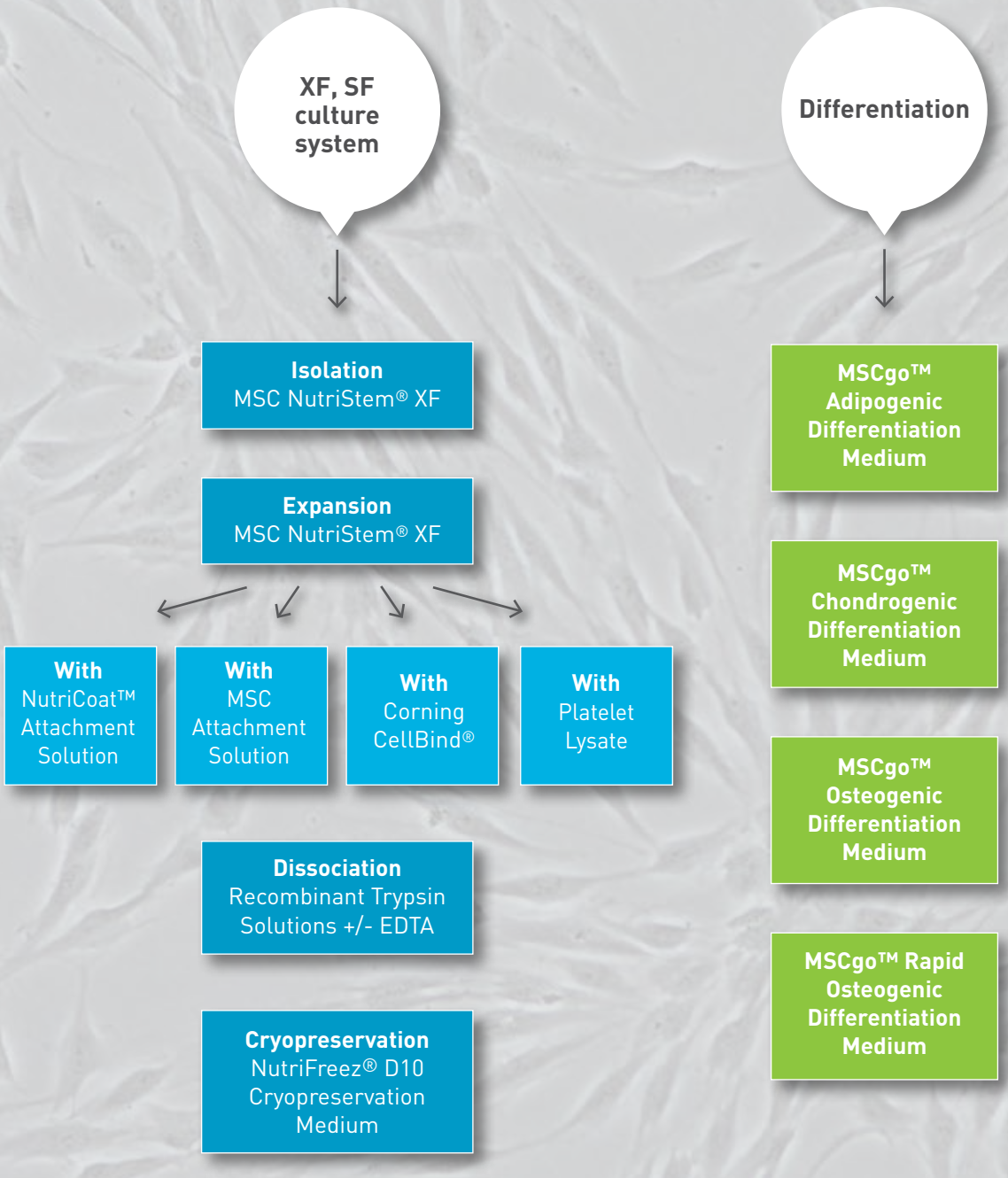
Human Mesenchymal Stem Cells

Serum-free, xeno-free systems for the culture and differentiation of human mesenchymal stem cells



BI
Biological Industries
Culture of Excellence

What works for you?



Seamless transition from research to the clinic

Human mesenchymal stem cells (hMSC) are multipotent adult stem cells present in a variety of tissue niches in the human body. hMSC have advantages over other stem cell types due to the broad variety of their tissue sources, for being immunoprivileged, and for their ability to specifically migrate to tumors and wounds *in vivo*.

Due to these traits hMSC have become desirable tools in tissue engineering and cell therapy. In most clinical applications hMSC are expanded *in vivo* before use. The quality of the culture medium and its performance are particularly crucial with regard to therapeutic applications, since hMSC properties can be significantly affected by medium components and culture conditions. A defined serum-free, xeno-free culture system optimized for hMSC isolation and expansion greatly facilitates the development of robust, clinically acceptable culture processes, reproducibility and generating quality-assured cells.

BI offers a novel serum-free (SF) and xeno-free (XF) culture system, which includes specially developed solutions for the attachment, dissociation and cryopreservation, as well as MSC NutriStem® media, which enable long-term growth of hMSC from various sources while retaining self-renewal and multi-lineage differentiation potential.

In addition to the culture system, BI offers serum-free, xeno-free media for the direct differentiation of hMSC from various sources into adipocytes, chondrocytes and osteocytes. The differentiation media contain all the growth factors and supplements necessary for the directed differentiation of hMSC.

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	None
Substrate required	MSC Attachment Solution (Human Fibronectin) / NutriCoat™ Attachment Solution (Human Fibrinogen)	None	None
Clinical-grade, cGMP	Yes	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		

MSC NutriStem® XF ,Xeno-Free, Serum-Free Culture System

Product Name	Cat. No.	Size	Storage
MSC NutriStem® XF Basal Medium	05-200-1A 05-200-1B	500ml 100ml	2-8°C
MSC NutriStem® XF Supplement Mix	05-201-1U 05-201-1-06	3ml 0.6ml	-20°C
MSC NutriStem XF PRF Phenol Red-Free Basal Medium	05-202-1A	500ml	2-8°C
NutriCoat™ Attachment Solution	05-760-1-15	1.5ml/vial	15 to 25°C
MSC Attachment Solution	05-752-1F 05-752-1H	1ml 5ml	2-8°C

Xeno-free, serum-free culture system, specially designed to support the growth of hMSC from various sources.

Advantages

Excellent performance

- → Superior isolation and cell growth
- → Superior maintenance of hMSC characteristics

Suitable for research and clinical applications

- → Produced under cGMP conditions
- → FDA drug master file available
- → Used in clinical trials worldwide

Defined, serum-free, xeno-free medium

- → Reproducible and consistent results throughout experiments
- → Batch-to-batch consistency
- → Save time and money: no need to prequalify FBS lots

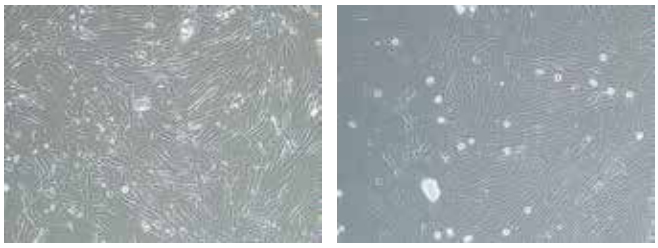
Flexible medium

- → Customization available
- → Suitable for various MSC sources (i.e bone marrow, adipose tissue, cord tissue, placenta, dental pulp)

Isolation

hMSC from various sources (hMSC-PL, hMSC-AT, hMSC-WJ, hMSC-BM) can be efficiently isolated using MSC NutriStem® XF on pre-coated dishes. Addition of 2-2.5% human AB serum may be required for certain tissues.
Using MSC NutriStem® XF for isolation of hMSC enhances purity of MSC populations in earlier passages and increases the number of hMSC in comparison to FBS-containing medium.

hMSC-PL



MSC NutriStem® XF **Serum-containg medium**

Figure 1: hMSC were isolated from frozen crude placenta under SF, XF culture conditions (MSC NutriStem® XF on pre-coated plates with MSC Attachment Solution, without supplementation of human AB serum) and in medium containing FBS. Representative images (x40) taken 11 days post initial isolation (P0).

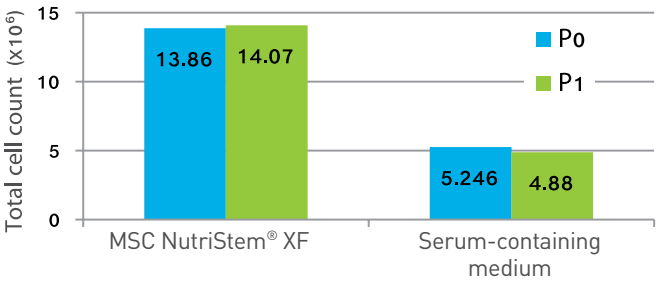
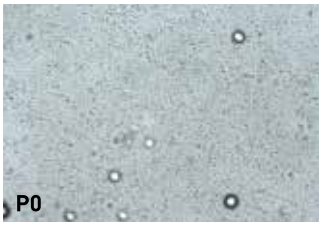


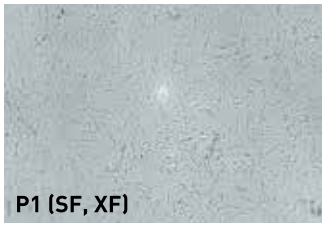
Figure 2: Comparison of hMSC-PL isolation from crude placenta 17 days post initial seeding (P0) in each medium. Quantity of viable cells, measured by trypan blue exclusion assay.

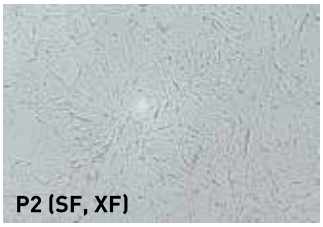
hMSC-AT

A



with human AB serum





without serum

B

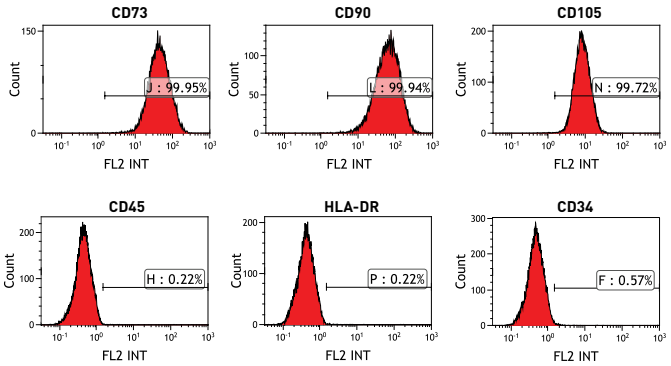
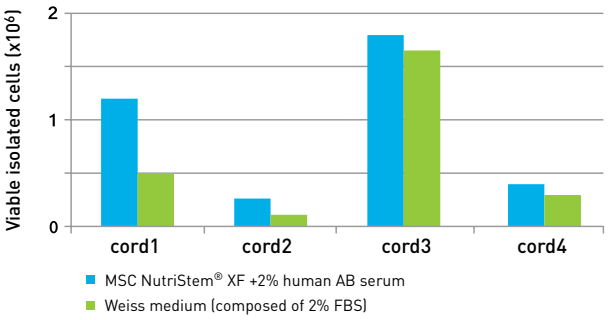


Figure 3: hMSC-AT were seeded in MSC NutriStem® XF supplemented with 2% human AB serum on pre-coated plates with MSC Attachment Solution for the initial isolation and expansion of hMSC-AT (P0).
The cells were cultured to 70-80% confluence before being sub-cultured. Further passages (P1-2) were done under SF, XF culture conditions, utilizing MSC NutriStem® XF culture medium on pre-coated dish.
A. Representative images taken 4 days post initial seeding (P0) and 3 days post P1 and P2.
B. Immunophenotyping results of hMSC-AT at passage 2 using FACS analysis.

hMSC-WJ

A



B

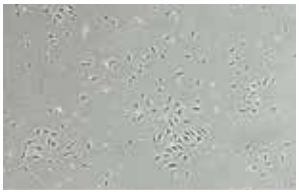
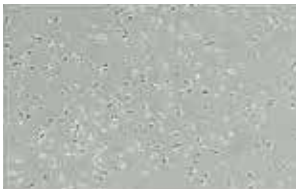
	Day 2 post initial isolation	Day 7 post initial isolation	
	Representative images	Total cell count Live	Dead
MSC NutriStem® XF (supplemented with 2% human AB serum)		395,000	15,000
Weiss medium (composed of 2% FBS)		295,000	75,000

Figure 4: hMSC were initially isolated from 4 independent human umbilical cords utilizing MSC NutriStem® XF supplemented with 2% human AB serum on pre-coated plates with MSC Attachment Solution in comparison to serum-containing medium.
A. Comparing the amount of viable cells – passage 0. Cell count was measured by trypan blue exclusion assay.
B. Representative images (x40) of cord 4 taken on day 2 post initial isolation in each medium, and cell count results of day 7 post initial isolation.

hMSC-BM

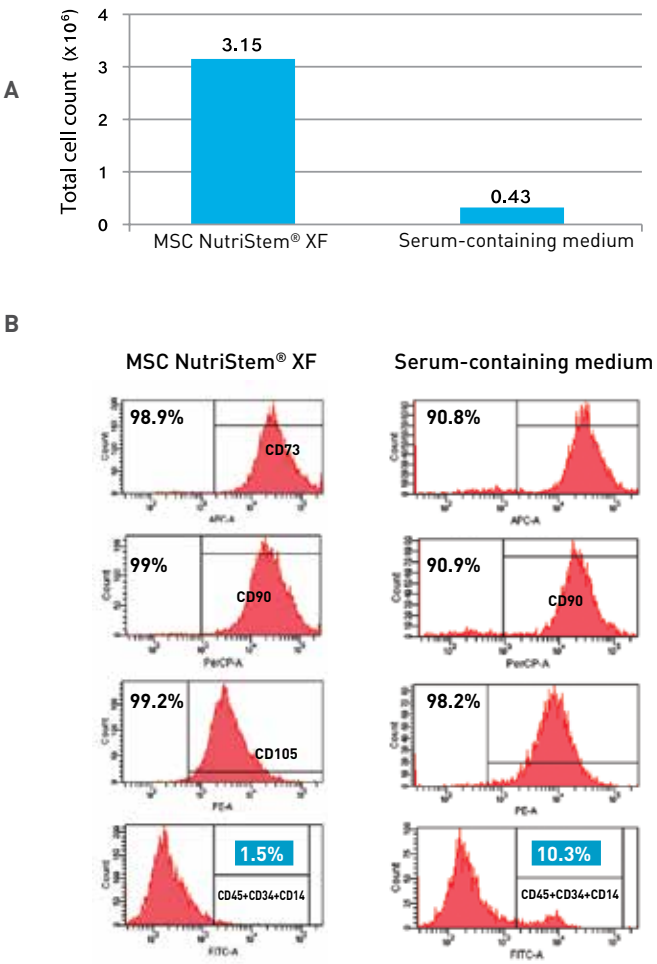


Figure 5: Comparison of hMSC-BM isolation from fresh BM utilizing MSC NutriStem® XF and serum-containing medium (11-day assay)
A. Cell count was measured by trypan blue exclusion assay.
B. Immunophenotype using FACS analysis.

Expansion

Superior proliferation of hMSC

hMSC cultured in MSC NutriStem® XF exhibit higher proliferation rate and long term growth in comparison to competitors' media.

hMSC-BM

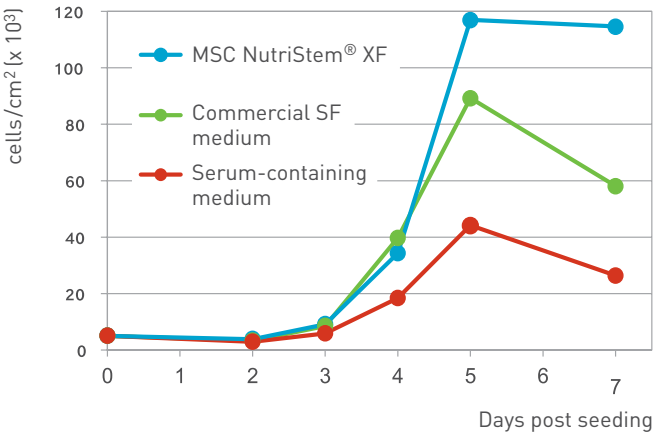
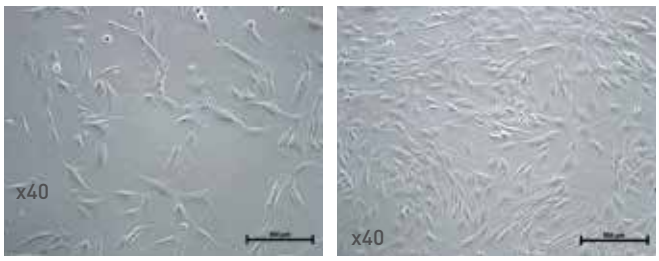


Figure 6: hMSC-BM were cultured in MSC NutriStem® XF in comparison to commercial SF and serum-containing media. Initial seeding was 5000 cells/cm² for each of the tested media (day 0). Cells were counted daily by trypan blue exclusion assay.



Serum-containing medium | MSC NutriStem® XF

Figure 7: Expansion of hMSC-BM in MSC NutriStem® XF and FBS-containing medium.
Initial seeding was 5000 cells/cm² for each of the tested media (day 0). Images were taken at day 3 post seeding.

Key References

- L. Berger et al. Tumor Specific Recruitment and Reprogramming of Mesenchymal Stem Cells in Tumor igenesis. STEM CELLS Volume 34, Issue 4, Version of Record online: 31 DEC 2015
- Cai, Zhen, et al. Chondrogenesis of Human Adipose-Derived Stem Cells by In Vivo Co-graft with Auricular Chondrocytes from Microtia. Aesthetic plastic surgery 39.3 (2015): 431-439.
- S.H. Mei, et al. Isolation and large-scale expansion of bone marrow-derived mesenchymal stem cells with serum-free media under GMP-compliance. Cytotherapy, Volume 16, Issue 4, Supplement , Page S111, April 2014
- Y. Lopez, M. Weiss, et al. Identification of Optimal Conditions for Generating MSCs for Preclinical Testing: Comparison of Three Commercial Serum-Free Media and Low-Serum Growth Medium. From 18th ISCT Annual Meeting, Seattle, USA, 2012.

hMSC-AT

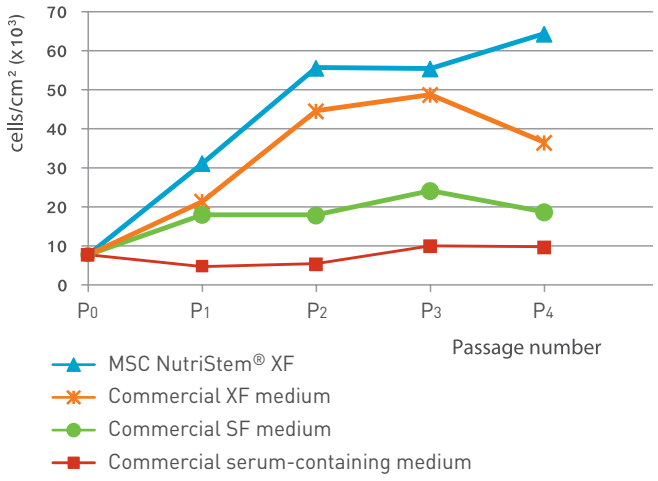
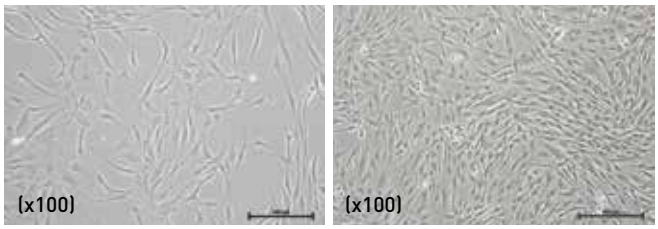


Figure 8: Expansion of hMSC-AT in MSC NutriStem® XF and commercially available XF, SF, and serum-containing media. Initial seeding was 5000 cells/cm² for each of the tested media (day 0). Cells were counted at day 3 in each passage.



Serum-containing medium | MSC NutriStem® XF medium

Figure 9: Expansion of hMSC-AT in MSC NutriStem® XF medium in comparison to serum-containing medium.
Initial seeding was 6000 cells/cm² for each of the tested media (day 0). Images were taken 3 days post initial culture.

hMSC-WJ

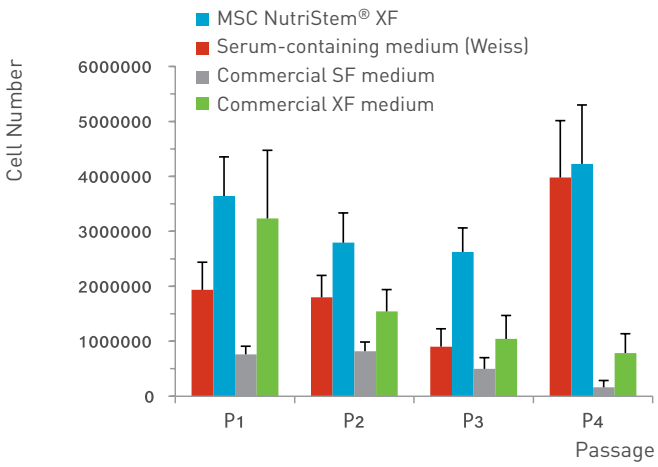
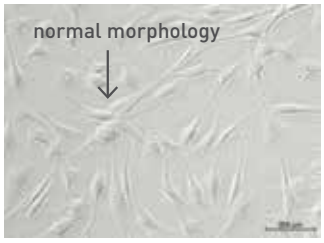


Figure 10: hMSC-WJ from 9 different donors expanded for 4 passages in MSC NutriStem® XF in comparison to serum-containing medium and commercial SF and XF media. Cell proliferation was assessed by cell count using a trypan blue exclusion assay.

Cell morphology

Typical fibroblast-like cells morphology was obtained when using MSC NutriStem® XF.

hMSC-AT



MSC NutriStem® XF
15x10⁴ cells/well

Commercial XF medium
11x10⁴ cells/well

Commercial SF medium
4x10⁴ cells/well

Figure 11: Expansion of hMSC-AT in MSC NutriStem® XF, competitor XF medium and competitor SF medium (day 0). Initial seeding was 5000 cells/cm² for each of the tested media. Images (x200) were taken 3 days post equal seeding (2 passages in each medium).

hMSC-BM

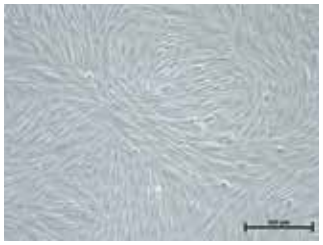


Figure 12: Expansion of hMSC-BM in MSC NutriStem® XF. Initial seeding was 5000 cells/cm² (day 0).
Image was taken 4 days post passage 1 (x100). Typical "shoal-like" pattern culture morphology is observed.

Self-renewal potential

hMSC cultured in MSC NutriStem® XF maintain their self-renewal potential.

hMSC-BM

hMSC-AT

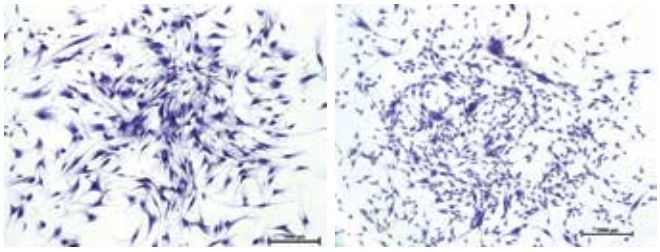


Figure 13: hMSC-BM and AT expanded in MSC NutriStem® XF for 3-5 passages prior to 14 day CFU-F assay. Representative images of colonies stained with 0.5% crystal violet (x100).

hMSC-WJ

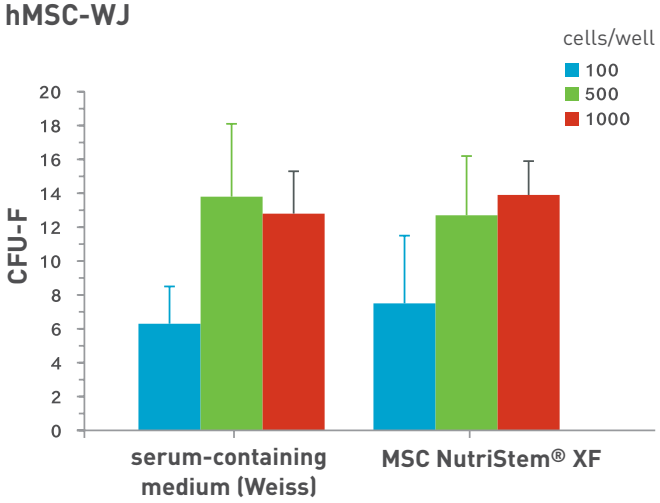


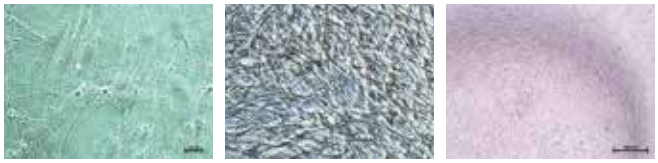
Figure 14: CFU-F assay of hMSC-WJ expanded for 5 passages in MSC NutriStem® XF and Weiss medium (2% FBS) in 3 different seeding concentrations.

Differentiation potential

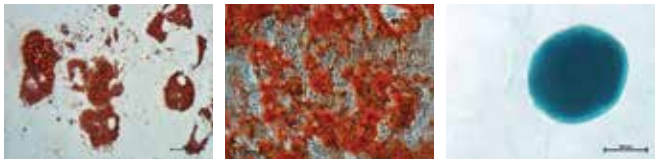
hMSC cultured in MSC NutriStem® XF maintain their trilineage differentiation potential.

hMSC-BM

Control



Differentiation

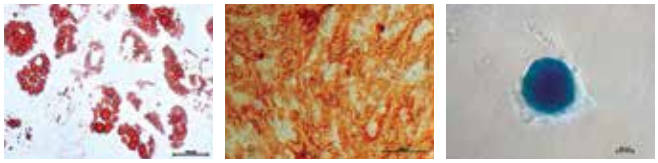


Adipocytes - Oil red O | Osteocytes - Alizarin red | Chondrocyte - Alcian blue

hMSC-AT

Control

Differentiation



Adipocytes - Oil red O | Osteocytes - Alizarin red | Chondrocyte - Alcian blue

Figure 15: hMSC-BM and hMSC-AT were expanded in MSC NutriStem® XF for 3-5 passages prior to differentiation. Representative images of stained Adipocytes (Oil Red O), Osteocytes (Alizarin red) and Chondrocytes (Alician blue).
The control images show cells which were cultured in MSC NutriStem® XF for the whole term. Staining was not obtained in the control cells.

Surface markers profile

hMSC expanded in MSC NutriStem® XF kept their classical profile of MSC markers; stained for MSC positive surface markers and did not stain for hematopoietic markers.

hMSC-PL

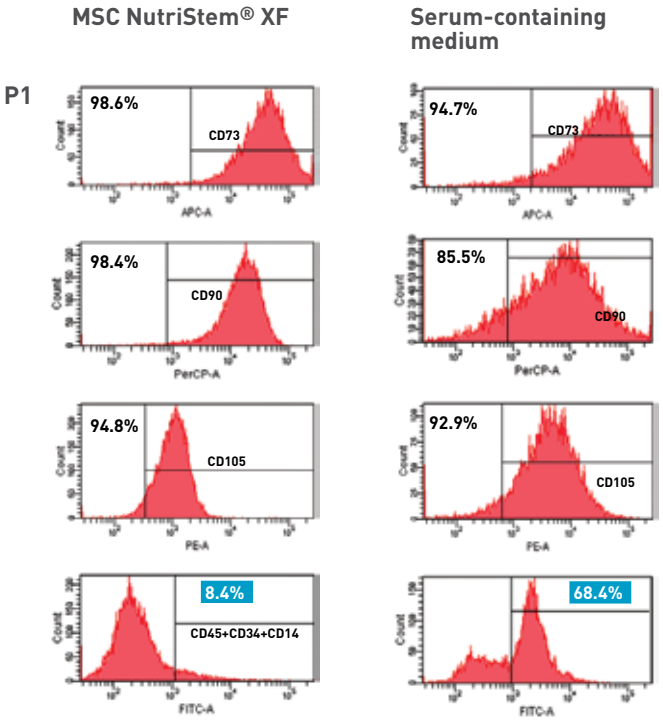
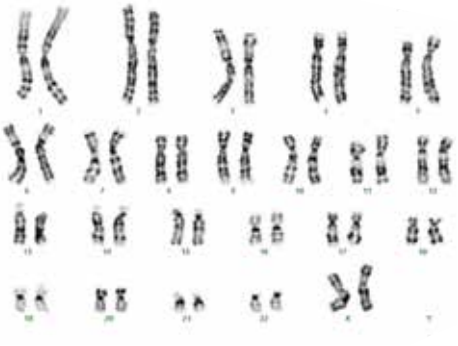


Figure 16: immunophenotype results of hMSC-PL after culturing in each medium. **Purer hMSC population is achieved using MSC NutriStem® XF.**

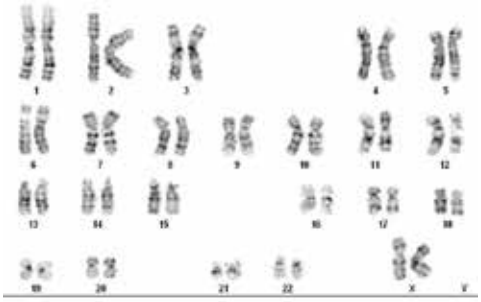
Karyotyping

Normal karyotypes of hMSC-BM (46, XY) hMSC-AT (46,XX) and hMSC-CT (46, XX) were observed after long term culturing in MSC NutriStem® XF.

hMSC-AT
P4 PD15
46, XX



hMSC-CT
P6 PD18
46, XX



hMSC-BM
P9 PD20
46, XY

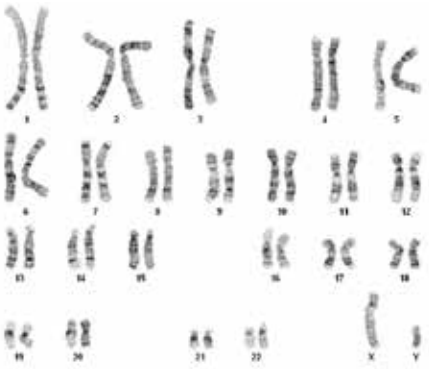


Figure 17: G-banding karyotyping analysis of hMSC from various sources expanded for 4-9 passages in MSC NutriStem® XF. hMSC cultured in MSC NutriStem® XF maintain genomic stability.

MSC NutriStem® XF Complete Medium Stability

The complete MSC NutriStem® XF is stable for 30 days at 2- 8°C. No significant differences of hMSC proliferation were observed between fresh and 30 days old complete medium.

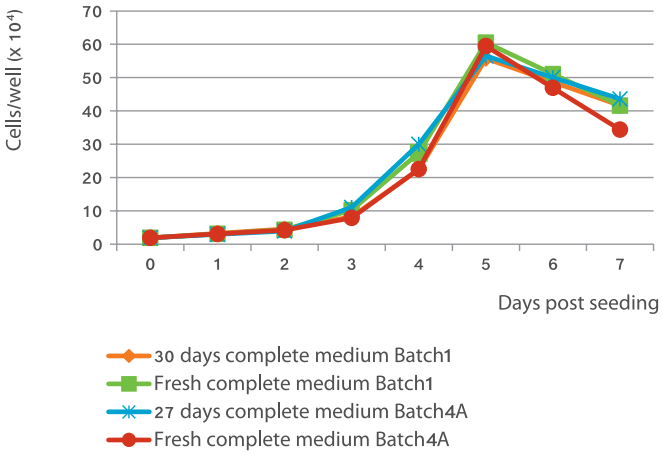
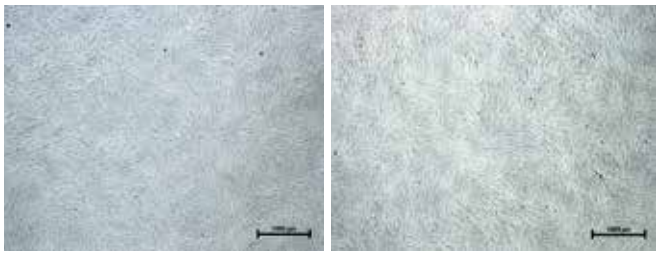


Figure 18: Growth curve of hMSC-BM cultured in MSC NutriStem® XF. Results were taken from 2 batches: batch No. 1: 7.5 months from production and batch 4A: 2.5 months from production. A complete medium was prepared 30 & 27 days before seeding (stored at 2-8°C) or freshly prepared. Initial seeding was 5000 cells/cm^2 for each of the tested media (day 0).
Cells were counted daily by trypan blue exclusion assay.

MSC NutriStem XF® complete medium



Fresh (x40)
40x10^3 cells/cm^2

30 Days (x40)
42x10^3 cells/cm^2

Figure 19: A complete medium was prepared freshly, or 30 days before seeding (stored at 2-8°C). Initial seeding was 5000 cells/cm^2 for each of the tested media (day 0).
Images were taken 4 days after equal split 1 (P2).

Key References

Clinical Trials

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2. 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

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

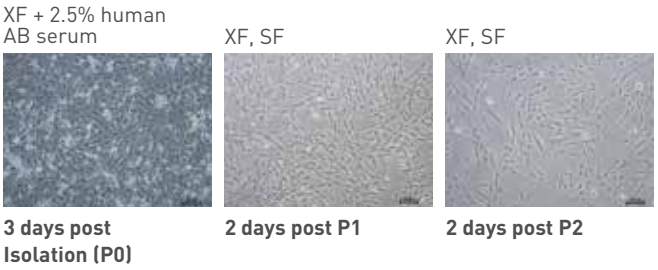
Coating-Free Options

MSC NutriStem® XF with CellBIND®

MSC MutriStem® XF medium shows superior performance in comparison to competitors media, using Corning CellBIND® surface with various tissues (no need for plate coating).

Isolation

A



B

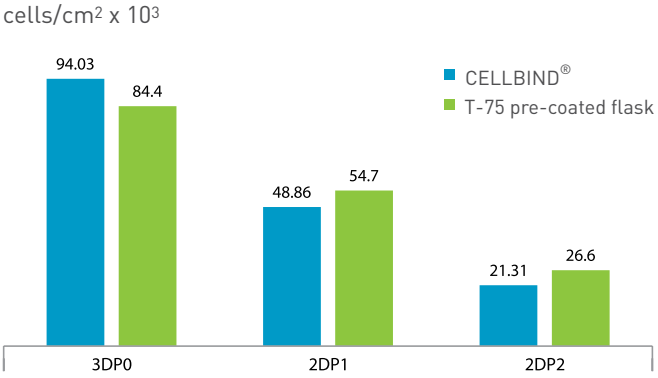


Figure 21: hMSC-AT isolation results using MSC NutriStem® XF and CellBIND®. 2.5% human AB serum was added only at P0. **A.** Representative images (x100) **B.** Quantity of viable cells.

Note: in comparison to the use of MSC NutriStem® XF with pre-coating procedure, similar proliferation rate is observed after seeding, however further passages using CellBIND® may lead to slightly reduced proliferation rate.

Expansion

Morphology and Proliferation

Superior morphology and higher proliferation of hMSC from various sources using MSC NutriStem® XF with CellBIND®.

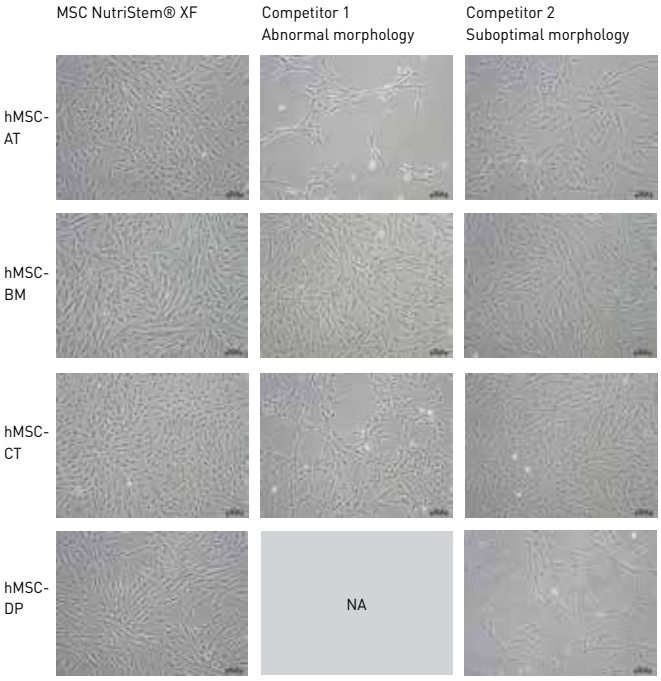


Figure 22: hMSC were cultured in MSC NutriStem® XF and in commercial xeno-free media using CellBIND®. Representative images (x100) 3 days post-split 1.

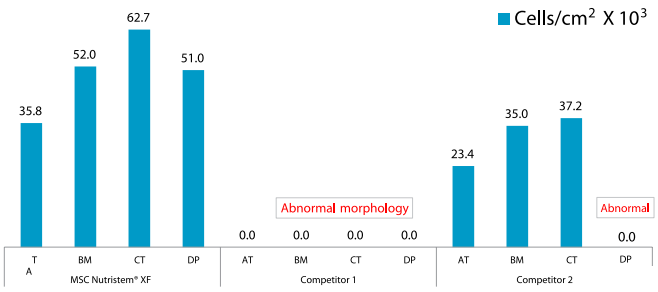
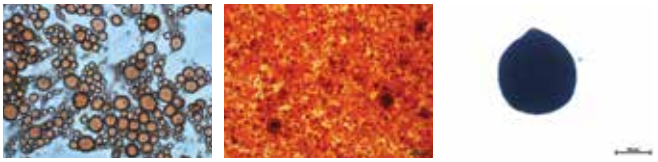


Figure 23: hMSC proliferation in MSC NutriStem® XF and in commercial xeno-free media using CellBIND®.

* CellBIND® is a registered trade mark of Corning.

Differentiation Potential

hMSC cultured in MSC NutriStem® XF using CellBIND® maintain their tri-lineage differentiation potential.



Adipocytes - Oil red O | Osteocytes – alizarin red | Chondrocytes – Alician blue

Figure 24: hMSC-AT were isolated on CellBIND® uncoated plate in MSC NutriStem® XF +2% human AB serum followed by 2 passages in MSC NutriStem® XF w/o AB serum. The differentiation assay was done using MSCgo™ adipogenesis XF, MSCgo™ Osteogenic XF using CellBIND® plate, and MSCgo™ Chondrogenic XF using uncoated U bottom 96w/p.

Marker Expression

hMSC cultured in MSC NutriStem® XF using CellBIND® kept their classical profile of MSC markers.

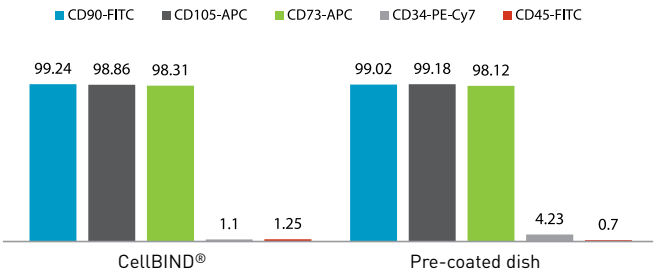


Figure 25: Flow cytometry analysis of hMSC-AT after 2P post isolation in MSC Nutristem® XF, using CellBIND® and pre-coated dish. % expression -CD90+105+34 1:250; CD73+45 1:500.

MSC NutriStem® XF with Human Platelet Lysate

MSC MutriStem® XF medium shows excellent performance in a xeno-free culture system with the addition of platelet lysate (no need for plate coating).

Morphology and Proliferation

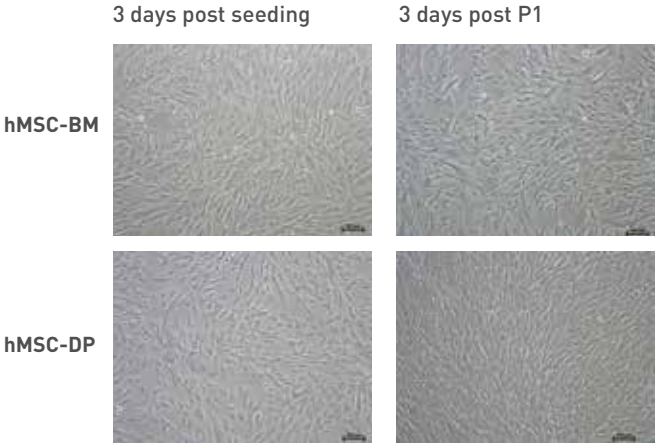


Figure 26: Representative images of hMSC cultured in MSC NutriStem® XF medium with 5% platelet lysate..

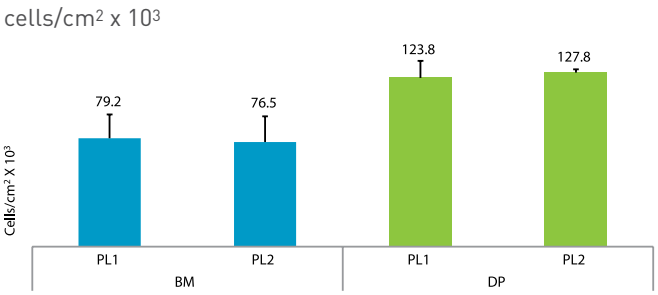


Figure 27: Average of hMSC proliferation during 2 passages cultured in MSC NutriStem® XF medium with 5% platelet lysate.

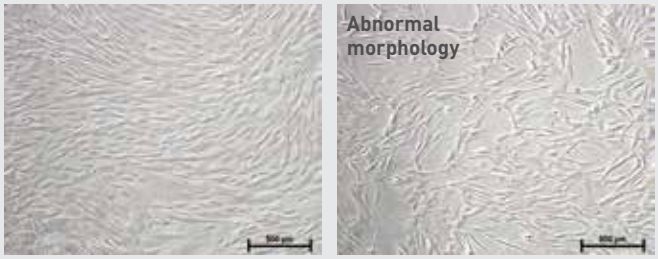
Dissociation

Product Name	Cat. No.	Size	Storage
Recombinant Trypsin Solution without EDTA	03-078-1A 03-078-1B	500ml 100ml	RT
Recombinant Trypsin Solution with EDTA	03-079-1A 03-079-1B	500ml 100ml	RT

Recombinant Trypsin Solution is an ACF cell dissociation solution, designed as an alternative to porcine/bovine trypsin.
The addition of EDTA usually accelerates the dissociation phase.
The solutions do not contain any chymotrypsin, carboxypeptidase A, or other protease contaminant.
Recombinant Trypsin Solution formulations were developed for efficient dissociation of adherent cell types from surfaces and tissues and were optimized for sensitive cells, such as hMSC.

Advantages:
- Ready-to-use
- Non-animal or human origin
- Optimized for hMSC (from a variety of sources), cultured in both SF and serum-containing systems
- Free from undesirable proteases such as carboxypeptidase A and chymotrypsin
- Eliminates contaminating activities found in bulk production of enzymes
- Storage: room temperature

Neutralization of Recombinant Trypsin is achieved with MSC NutriStem® XF or Soybean Trypsin Inhibitor (SBTI) Cat. No.: 03-048-1.
The use of recombinant trypsin, rather than crude trypsin, is often essential for successful, long term growth of cells under SF culture conditions.



Recombinant Trypsin Solution **Crude Trypsin EDTA Solution**

Figure 38: Recovery of hMSC-BM after dissociation with both Recombinant Trypsin Solution and the common Trypsin EDTA Solution (porcine) following re-seeding in MSC NutriStem® XF on pre-coated plates. Representative images were taken on day 5 post-dissociation (x100).

Cryopreservation

Product Name	Cat. No.	Size	Storage
NutriFreez® D10 Cryopreservation Medium	05-713-1A 05-713-1B 05-713-1C 05-713-1D 05-713-1E	500ml 100ml 20ml 10ml 50ml	2-8°C

NutriFreez® D10 Cryopreservation Medium is a chemically defined, animal component-free and protein-free formulation for the cryopreservation of animal cells. The medium shows excellent performance, high cell viability and cell recovery after thawing and is suitable for hMSC from various sources.

Advantages:
- A complete, ready-to-use solution (2-8°C)
- Protein-free
- Animal components-free
- Suitable for hMSC from various sources
- Suitable for cells cultured in both SF and serum-containing medium
- High cell viability and cell recovery after thawing

Cryopreservation of hMSC using NutriFreez® D10 Cryopreservation Medium led to high viability and high recovery rate after thawing.

	Total cells [cells/ml]	Nonviable cells [cells/ml]	Viable cells [cells/ml]	Viability [%]
Test 1	$9.36x10^5$	$3.97x10^4$	$8.96x10^5$	**95.8**
Test 2	$8.82x10^5$	$4.84x10^4$	$8.34x10^5$	**94.5**

hMSC-BM (2 individual tests) were thawed and expanded in MSC NutriStem® XF, 15 months post cryopreservation.

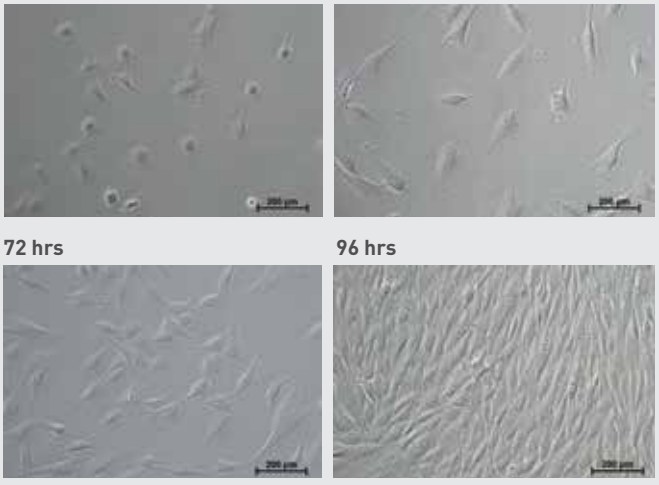


Figure 39: Recovery of hMSC-BM after thawing procedure. Cells were frozen using NutriFreez® D10 Cryopreservation Medium, thawed and re-seeded in MSC NutriStem® XF on pre-coated plates. Representative images were taken at the indicated time points post-thawing (x200).

Differentiation

MSCgo™ Differentiation Media

A unique line of serum-free and xeno-free differentiation media providing the ability to efficiently differentiate hMSC from various sources (hMSC-AT, hMSC-BM, hMSC-CT and hMSC-DP) into adipocytes, chondrocytes and osteocytes.

Advantages

Serum-free, xeno-free

→ Eliminating the drawbacks of unwanted background differentiation and interruption in cell metabolism

User friendly

→ All necessary ingredients are included

Suitable for various sources of hMSC

hMSC Differentiation

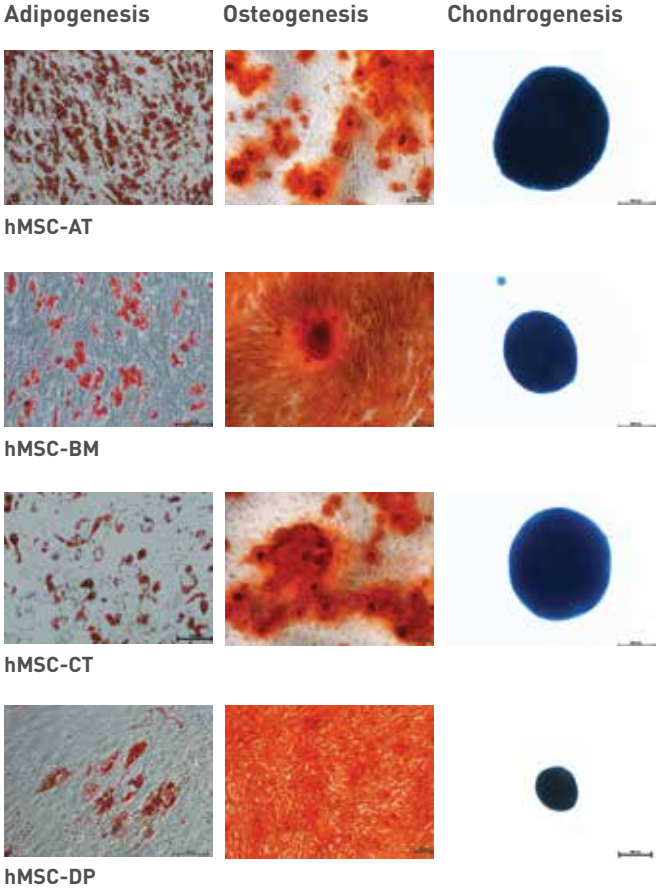


Figure 40: hMSC from various sources pre-cultured in MSC NutriStem® XF were reseeded into differentiation assays using each BI MSCgo™ differentiation medium respectively. Representative images of 16 days assay of Adipogenesis followed by Oil red O staining (X20), 11 days assay of osteogenesis followed by 2% ARS staining (X10) and 21 days assay of Chondrogenesis followed by Alcian blue staining(x4).

Chondrogenic Differentiation

An innovative serum-free, xeno-free medium for the initial differentiation of hMSC from various sources into chondrocytes.

Product Name	Cat. No.	Size	Storage
MSCgo™ Chondrogenic XF Basal Medium	05-220-1B	100ml	2-8°C
MSCgo™ Chondrogenic XF Supplement Mix	05-221-1D	10ml	-20°C

Chondrogenic evaluation

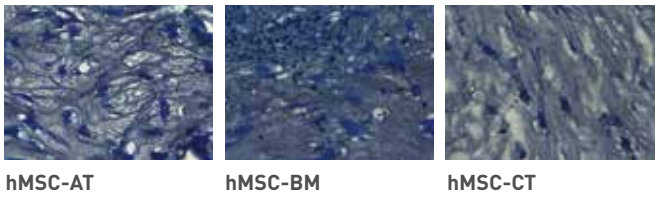


Figure 41: Representative histological images (x40) of differentiated samples stained with Toluidine blue. Mature differentiated cells (chondrocytes) surrounded by a cartilage matrix are observed in the 3 types of hMSC after a 21-day differentiation assay using MSCgo™ Chondrogenic XF.

Profile marker expression

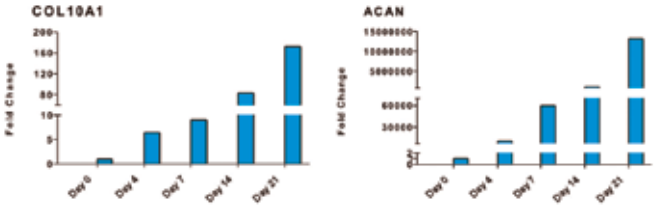


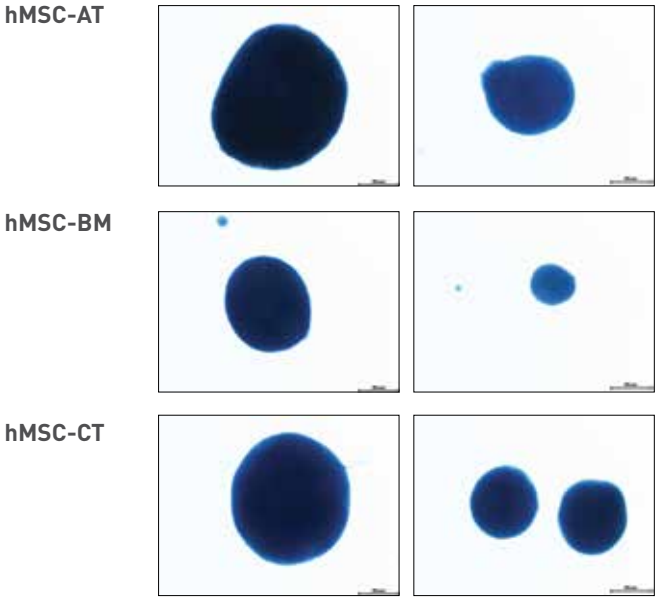
Figure 42: Relative expression (RT-PCR) of chondrocytes markers during 21 days of hMSC-AT differentiation assay using MSCgo™ Chondrogenic XF. Elevated expression of the chondrocyte-related genes, aggrecan (ACAN) and alpha chain of type X collagen (COL10A1), is observed.

MSCgo™ Chondrogenic XF in comparison to other serum-free and serum-supplemented media

Superior chondrogenesis is achieved using MSCgo™ Chondrogenic XF.

In all hMSC sources, MSCgo™ Chondrogenic XF exhibits larger cartilage spheroids with higher intensity of Alcian blue staining in comparison to other commercial SF medium.

A



B

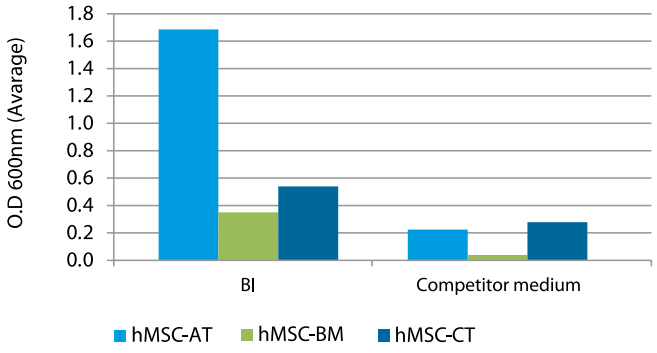


Figure 43: Cartilage differentiation results of hMSC from various sources after 21 day assay using MSCgo™ Chondrogenic XF vs. other commercial differentiation medium, followed by Alcian blue staining **(A)** and O/N elution with GuHCL (600nm) **(B)**. The results are average of absorbance read of each well with and without the cartilage.

Adipogenic Differentiation

An Innovative serum-free, xeno-free medium for the differentiation of hMSC into adipocytes.

Product Name	Cat. No.	Size	Storage
MSCgo™ Adipogenic XF Basal Medium	05-330-1B	100ml	2-8°C
MSCgo™ Adipogenic XF Supplement Mix I	05-331-1-01	0.1ml	-20°C
MSCgo™ Adipogenic XF Supplement Mix II	05-332-1-15	1.5ml	-20°C

Adipogenic evaluation

Figure 44: Typical expression of FABP4 is observed post 11 days adipogenesis of hMSC using MSCgo™ Adipogenic XF.

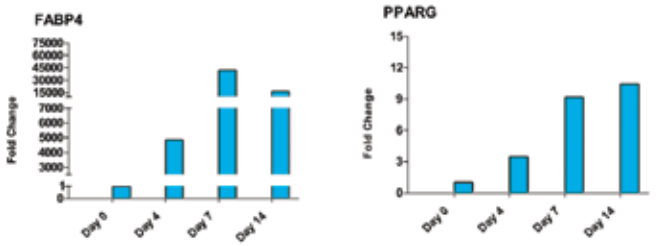
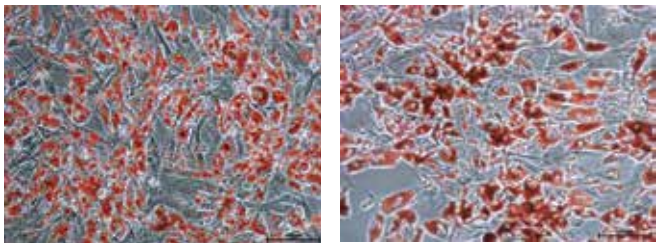


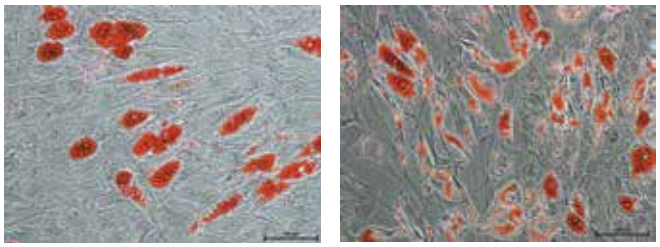
Figure 45: Elevate expression of the adipocyte-related genes, (FABP4) and alpha chain of type X collagen (PPARG), is observed during 14 days adipogenesis of hMSC using MSCgo™ Adipogenic XF.

MSCgo™ Adipogenic XF in comparison to other serum-free and serum-supplemented media

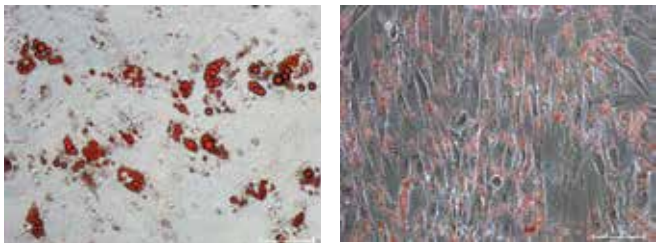
MSCgo™ Adipogenic XF **FBS-containing medium**



hMSC-AT



hMSC-BM



hMSC-CT

Figure 46: hMSC from various sources were differentiated into adipocytes using MSCgo™ Adipogenic XF followed by Oil red O staining.
MSCgo™ Adipogenic XF led to similar or superior (hMSC-CT) adipogenesis in comparison to commercial FBS-containing medium (11-17 day assay).

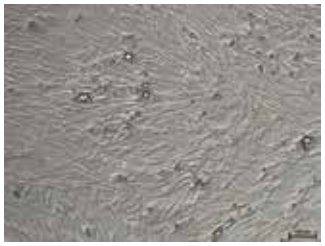
Osteogenic Differentiation

Complete, ready-to-use, xeno-free and serum-free media for the differentiation of hMSC from various sources into osteocytes.

Product Name	Cat. No.	Size	Storage
MSCgo™ Osteogenic XF	05-440-1B	100ml	2-8°C
MSCgo™ rapid Osteogenic XF	05-442-1B	100ml	2-8°C

MSCgo™ rapid Osteogenic XF will lead to faster osteogenesis (less than 10 days) in comparison to the MSCgo™ Osteogenic XF (10-21days).

Osteogenic evaluation



hMSC-BM

hMSC-AT

Figure 47: Calcified nodules observed using both hMSC-BM and hMSC-AT after a 10 day MSC differentiation assay using MSCgo™ Osteogenic XF.

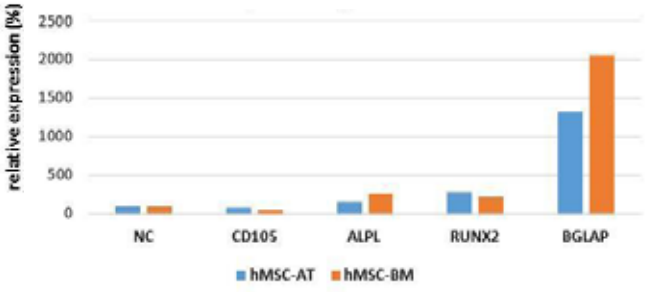
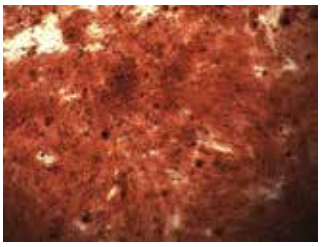


Figure 48: Relative expression (RT-PCR) of osteocyte markers after 10 days of osteogenesis of hMSC using MSCgo™ Osteogenic XF. Osteogenic markers were upregulated whereas an undifferentiated hMSC marker (CD-105) was downregulated. BGLAP represents a maturation state of osteogenesis.

Non-differentiated cells



Osteogenic differentiation

Figure 49: Positive Alizarin staining is observed, indicates of mature osteocytes after a 28 day differentiation assay of hMSC-AT using MSCgo™ Osteogenic XF medium.

Profile marker expression

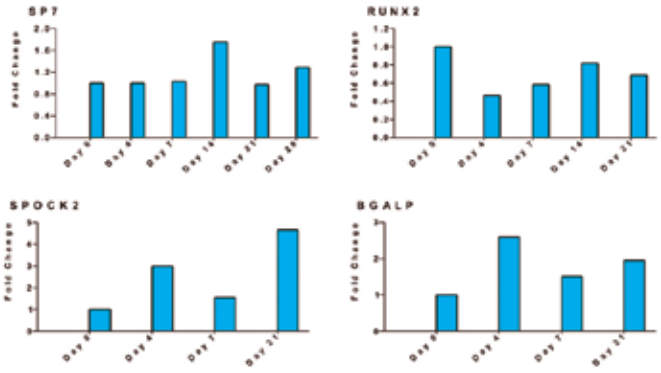


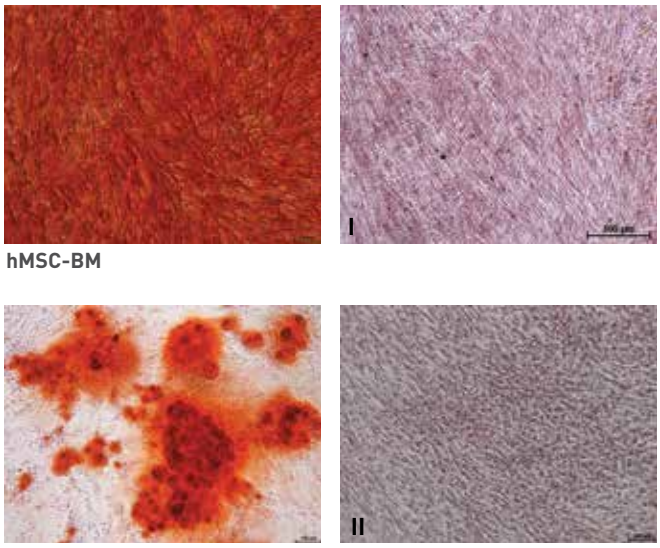
Figure 50: Profile marker expression after 28 days osteogenesis assay of hMSC using MSCgo™ Osteogenic XF. Relative typical expression of the osteocyte-related genes is observed.

MSCgo™ Osteogenic XF in comparison to other serum-free and serum-supplemented media

Superior osteogenesis is achieved using MSCgo™ Osteogenic XF. Commercial osteogenic media are not optimal for various sources of hMSC.

A

MSCgo™ Osteogenic XF | **FBS-containing media**



hMSC-BM

hMSC-CT

B

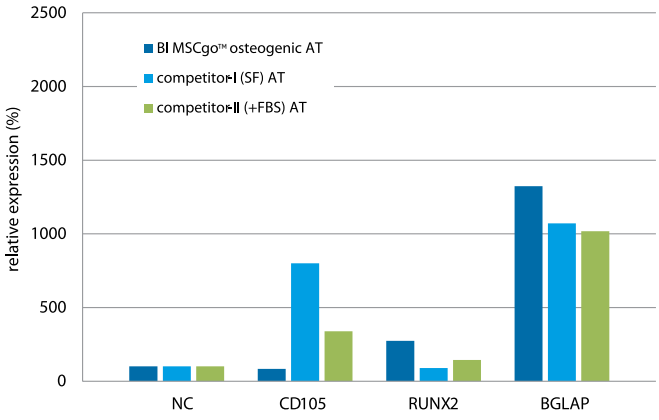


Figure 51: **A.** Positive Alizarin staining after a 10 day differentiation assay is observed only when using MSCgo™ Osteogenic XF.
B. MSCgo™ Osteogenic XF led to highest expression of osteogenic markers and lowest expression of un-differentiated hMSC marker (CD-105) in comparison to commercial media.
BGLAP represents a maturation state of osteogenesis.

Key References

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- L. Pu et. al. Compared to the amniotic membrane, Wharton's jelly may be a more suitable source of mesenchymal stem cells for cardiovascular tissue engineering and clinical regeneration, Stem Cell Research & Therapy20178:72
- M. Meng et al., Umbilical cord mesenchymal stem cell transplantation in the treatment of multiple sclerosis. American Journal of Translational Research, 2018;10(1):212-223

Ordering information

Product Name	Cat. No.	Size	Storage
MSC NutriStem® XF Basal Medium	05-200-1A 05-200-1B	500ml 100ml	2-8°C
MSC NutriStem® XF Supplement Mix	05-201-1U 05-201-1-06	3ml 0.6ml	-20°C
MSC NutriStem® XF Phenol Red-Free	05-202-1A	500ml	2-8°C
NutriCoat™ Attachment Solution	05-760-1-15	1.5ml/vial	15 to 25°C
MSC Attachment Solution	05-752-1F 05-752-1H	1ml 5ml	2-8°C 2-8°C
PLTMax® Human Platelet Lysate (Reserach Grade)	PLTMAX100R	100ml	-20°C
PLTMax® Human Platelet Lysate (Clinical Grade)	PLTMAX100GMP	100ml	
PLTGold® Human Platelet Lysate (Research Grade)	PLTGOLD100R	100 ml	-20°C
PLTGold® Human Platelet Lysate (Clinical Grade)	PLTGOLD100GMP		
Recombinant Trypsin Solution	03-078-1A 03-078-1B	500ml 100ml	RT
Recombinant Trypsin Solution with EDTA	03-079-1A 03-079-1B	500ml 100ml	RT
NutriFreez® D10 Cryopreservation Medium	05-713-1A 05-713-1B 05-713-1E 05-713-1C 05-713-1D	500ml 100ml 50ml 20ml 10ml	2-8°C
MSCgo™ Osteogenic XF	05-440-1A	500ml	2-8°C
MSCgo™ Rapid Osteogenic XF	05-442-1A 05-442-1B	500ml 100ml	2-8°C
MSCgo™ Chondrogenic XF	05-220-1A	500ml	2-8°C
MSCgo™ Chondrogenic XF Supplement Mix	05-221-1D	10ml	-20°C
MSCgo™ Adipogenic XF	05-330-1A	500ml	2-8°C
MSCgo™ Adipogenic XF Supplement Mix I	05-331-1-01	0.1ml	-20°C
MSCgo™ Adipogenic XF Supplement Mix II	05-332-1-15	1.5ml	-20°C

Biological Industries (BI) has been committed for over 30 years to provide optimal and innovative solutions for cell culture practice.
BI manufactures and supplies life science products to biopharmaceutical, academic and government research facilities, as well as to biopharma companies.

Our diverse portfolio of products and services includes all of the following:

- Liquid and powdered cell culture media
- Sterile sera (foetal bovine serum, newborn calf serum, donor horse, etc.)
- Novel serum-free and animal component-free media and supplements
- Products for stem cell research and cell-based therapies
- Products for cytogenetics
- Products for mycoplasma detection and treatment
- Disinfectants
- Products for molecular biology
- custom formulations and contract manufacturing services

All BI's products are manufactured via a quality management system ISO 9001:2015 and in regards of medical devices ISO 13485:2016. All aspects of the products life cycle fall under the QMS procedures. The set-up of clean zone and clean room facilities for manufacturing are following ISO 14644, whereas the production rooms are ISO 8, storage of sterile accessories ISO 7 and filling rooms ISO 5. Aseptic filling and validation is performed according to ISO 13408.

BI exports its products to more than 50 countries worldwide, via a network of exclusive distributors. Over the years we have established a reputation for fast delivery, and excellent technical support.
From the outset, the policy of BI has been based on the need to maintain an active Research and Development program in all facets of company activities. The company has its own in-house R&D department, and in addition, maintains active contact with science-based companies and research institutions in Israel and abroad, including know-how agreements with several such institutions. These ongoing efforts have led to the introduction of a series of serum-free medium products, as well as many other products for cell culture and molecular biology.

www.bioind.com

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