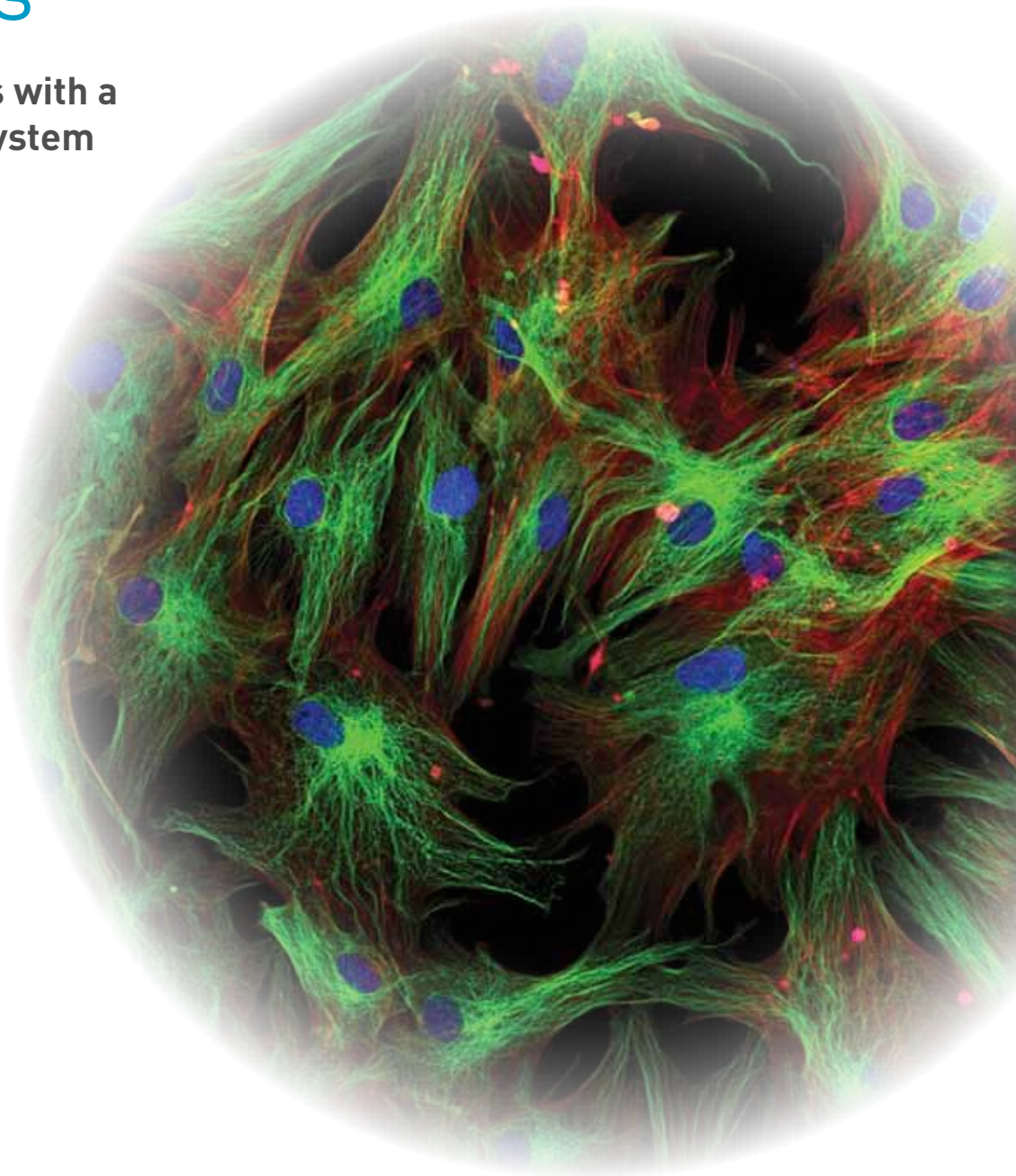
BI
Biological Industries
Culture of Excellence

Stem Cells and Cell Therapy Products

Expand your cells with a defined culture system



Culture of Excellence

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Pluripotent Stem Cells

Product Overview:

NutriStem® hPSC XF

Defined, xeno-free (XF), serum-free (SF) media for optimal growth and expansion of hESC and hiPSC

- Provides the ability to self-renew, by expansion in feeder-free culture conditions (Matrigel and Laminin), on human feeder layer or on mouse feeder cells
- Maintains pluripotency
- Supports hESC and hiPSC growth for >50 passages while preserving normal karyotypes
- Maintains differentiation capability after culturing
- Eliminates xeno-contamination during the in vitro derivation and propagation phases
- Complete, ready-to-use

Bio-Pure™ Human Serum Albumin (HSA)

Xeno-free supplement specially qualified for the growth of hESC and hiPSC, in both feeder-dependent and feeder-free conditions

LaminStem™ 521

Animal component-free recombinant protein designed as a substitute for Matrigel in feeder-free culture systems

CryoStem™

Animal component-free, protein-free and chemically defined freezing medium, for cryopreservation of hESC and hiPSC

Introduction

Human embryonic stem cells (hESC) and human induced pluripotent stem cells (hiPSC) research is one of the most dynamic fields in modern biology, but cell-based clinical applications are currently limited by xeno-contamination during the in-vitro derivation and propagation phases. Thus, bridging the gap between research models and clinical applications requires the design and implementation of qualified processes.

Xeno-free or animal component-free media are therefore an essential element in the development of regenerative stem cell therapies, where implantation in humans is the desired outcome.

Biological Industries and the Technion- Israel Institute of Technology have established a strategic collaboration to develop optimized cell culture environments for human embryonic stem cell research, including xeno-free defined media. Capitalizing on an outstanding pool of collective expertise, this collaboration will facilitate hESC and hiPSC research by developing innovative, reliable, high performance products.

The first products of this collaboration to be marketed are the proprietary serum-free NutriStem® hPSC XF formulations derived from xeno-free, defined components. NutriStem® hPSC XF was shown to support long-term (>50 passages) culture of undifferentiated hESC (i.e. H9.2, I6, I3.2, H1) as well as iPSC, while preserving normal karyotypes. Pluripotency was verified by testing the expression of multiple markers by Q-PCR, immunofluorescent staining, and FACS analysis, and by formation of embryoid bodies and teratomas.

Growth and Expansion

Defined, xeno-free, serum-free medium designed to support the growth and expansion of hESC and hiPSC

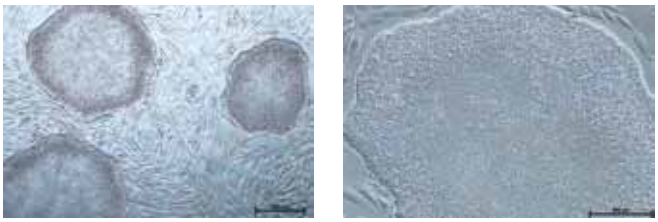
Product Name	Cat. No.	Size	Storage
NutriStem® hPSC XF	05-100-1A	500ml	-20°C
	05-100-1B	100ml	

Human Pluripotent Stem Cell Research

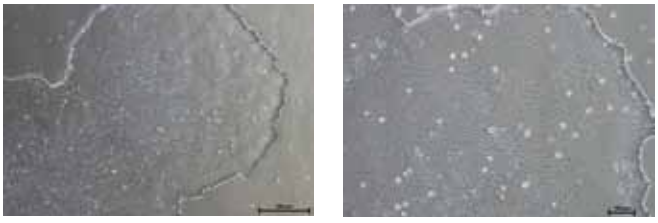
Formation of compact multicellular colonies of cells with a high nucleus-to-cytoplasm ratio, prominent nucleoli and distinct colony border are characteristic of undifferentiated hESC and hiPSC. Thus, when viewed under a phase contrast microscope, healthy hESC and hiPSC colonies tend to exhibit "phase-bright" centers.

Cell Morphology

H1 hESC cultured in NutriStem® hPSC XF on MEF feeder



H1 hESC cultured in NutriStem® hPSC XF on Matrigel™



ACS-1014 iPSC (ATCC) cultured in NutriStem® hPSC XF on Matrigel™

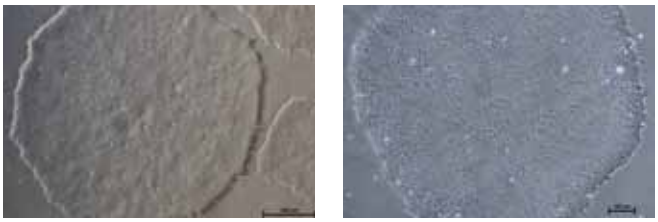


Figure 1: H1 hESC and ACS-1014 iPSC cultured in NutriStem® hPSC XF display compact colonies and distinct colony morphology typical of pluripotent hESC and hiPSC.

Proliferation

NutriStem® hPSC XF enables excellent proliferation of undifferentiated hESC and hiPSC

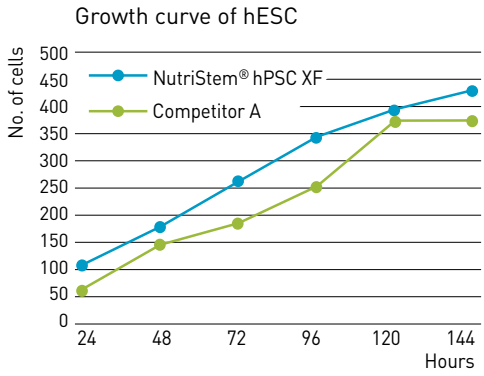


Figure 2: H1 cells (passage 6) were seeded in 96 well plates (Matrigel-coated) in the various media. Media were changed every 24 hours. The number of cells was determined using a CyQuant cell proliferation assay kit.

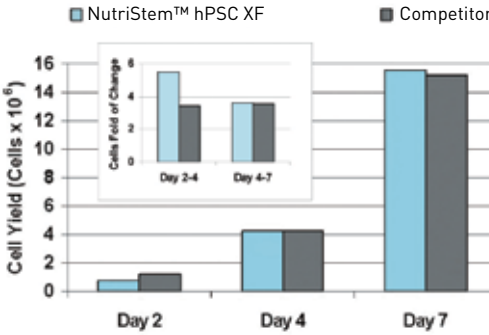


Figure 3: Evaluation of human embryonic stem cells (H9.2 cells) cultured in NutriStem® hPSC XF using Matrigel. Growth of hESCs cultured in NutriStem® hPSC XF was compared to growth using competitor A. Cell counts are reported for days 2, 4 and 7.

hESC and hiPSC Characteristics: Pluripotency and Differentiation Capabilities

Gene Expression Analysis

hESC and hiPSC are defined by their ability to proliferate indefinitely while remaining undifferentiated. Lack of differentiation is confirmed by monitoring the presence of specific cell surface markers (e.g. stage specific embryonic antigens SSEA-4), and the expression of certain transcription factors (e.g. Oct-4 and Nanog). Analysis by flow cytometry, Q-PCR and immunofluorescence of cells cultured in NutriStem® hPSC XF verified pluripotency is maintained.

Flow cytometry and gene expression analysis

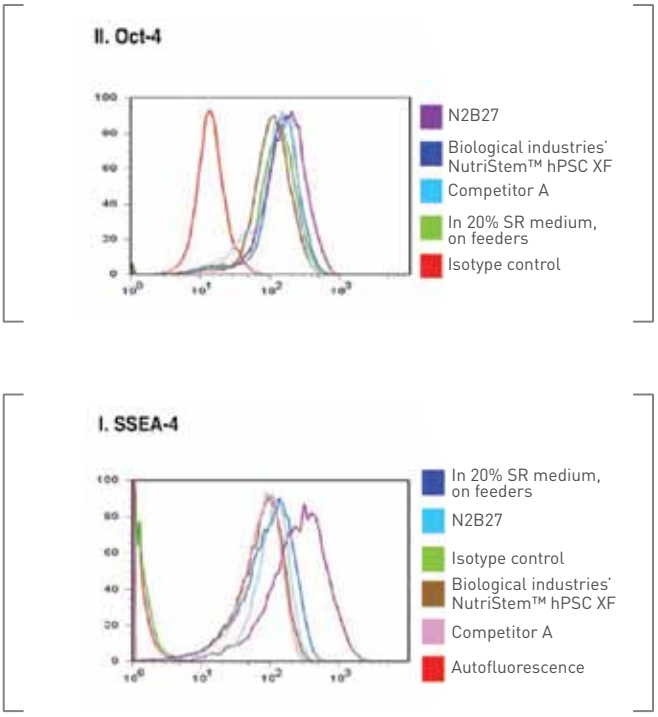


Figure 4: H1 cells cultured in different media for 6 passages were analyzed and compared.
Cells cultured in NutriStem® hPSC XF were found to be >90% positive for SSEA-4 and Oct-4.

Q-PCR

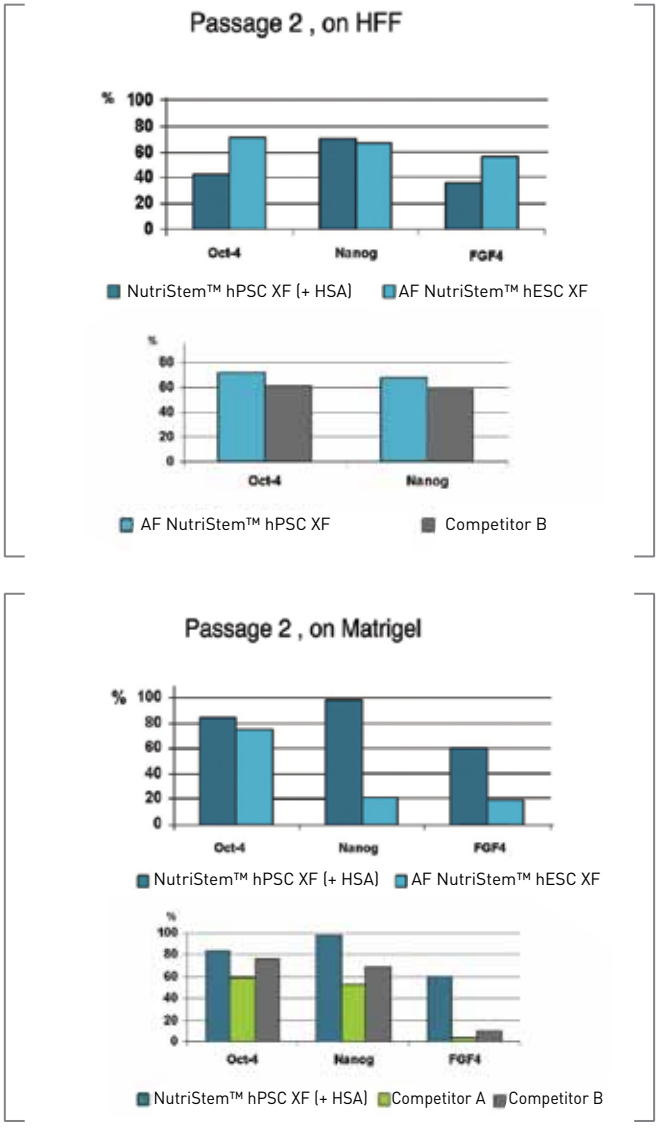


Figure 5: H1 cells cultured in different media for 2 passages were analyzed and compared.
Superior H9.2 cell expansion is achieved using NutriStem® hPSC XF medium.

Immunostaining

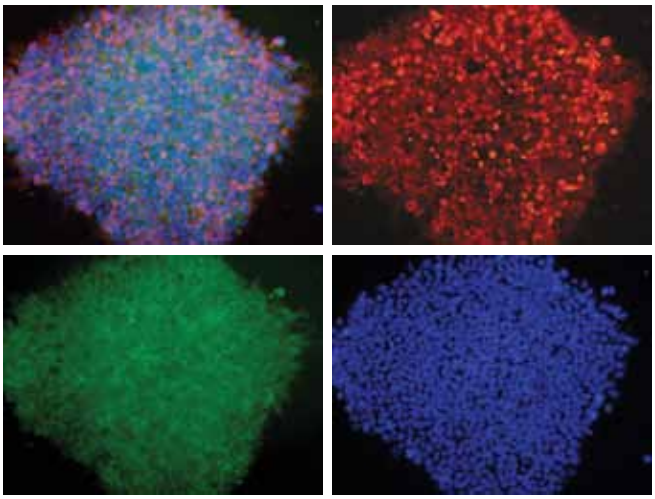


Figure 6: H1 cell morphology and immunofluorescence analysis of hESC markers red SSEA-4, green OCT4 and blue DAPI.
H1 cells stained positive for the expression of pluripotency markers.

Functional Assessment of Pluripotency

hESC and hiPSC differentiate into representatives of all three germ layers, i.e. endoderm, mesoderm and ectoderm.
This differentiation is defined by the formation of embryoid bodies in vitro and teratomas in vivo.
Teratomas form when embryonic stem cells are injected into severe combined immunodeficient (SCID) mice and tissue types found include gut epithelium, cartilage, bone and neural epithelium among others.

Teratoma formation

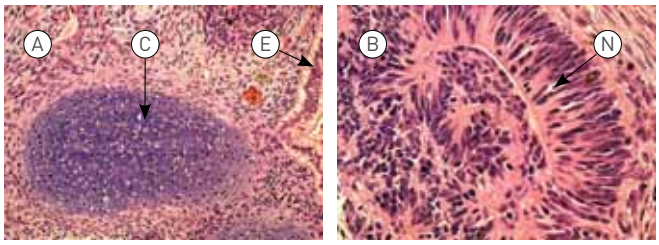


Figure 7: hESC from cell line H9.2 were cultured for 11 passages in NutriStem® hPSC XF using human foreskin fibroblasts (HFF) as supportive layer and subsequently tested in vivo for pluripotency by teratoma formation. Cells were injected into the hind leg muscle of SCID-Beigemice. 12 weeks post injection the following tissues from all three germ layers were identified by histological sections; (A) Cartilage (mesoderm, marked arrow C), endoderm columnar epithelium (endoderm, marked arrow E), (B) Neural rosette (ectoderm, marked arrow N). Stained with H&E.

Embryoid body (EB) formation

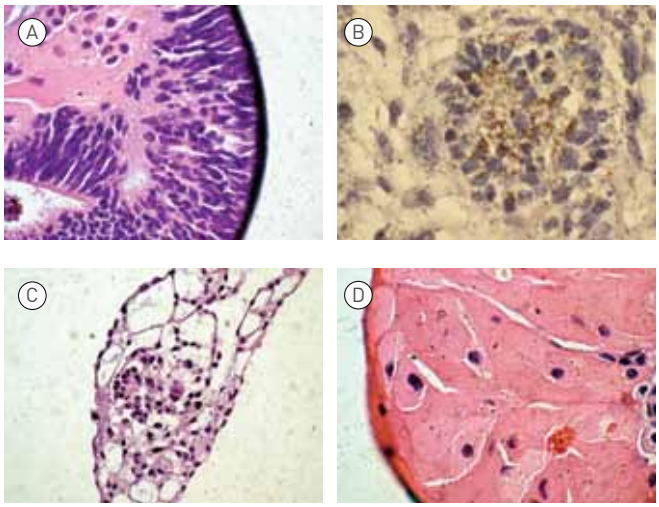


Figure 8: hESC from cell line H9.2 were cultured for 16 passages in NutriStem® hPSC XF using a Matrigel matrix and tested in vitro for pluripotency by EB formation.
After suspension in serum supplemented medium the cells spontaneously formed embryoid bodies containing embryonic germ layers. Examining the histological sections of 14-day-old EBs, the following cell types were identified; (A) Neural rosette (ectoderm), (B) Neural rosette stained with Tubulin, (C) Primitive blood vessels (mesoderm) and (D) Megakaryocytes (mesoderm).
Stained with H&E.

ACF Matrix

Chemically defined, animal component-free, xeno-free matrix for pluripotent stem cell culture. Superior alternative to Matrigel in feeder-free culture systems

Product Name	Cat. No.	Size	Storage
LaminStem™ 521	05-753-1F	1ml	-20°C

LaminStem™ 521 is composed of purified laminin-521, a cell-type specific basement membrane protein proven to support excellent attachment proliferation of hES and hiPS cells. LaminStem™ 521 with NutriStem® hPSC XF provide a superior culture environment for undifferentiated expansion and growth of hES and hiPS cells in a chemically defined, xeno-free, and feeder-free culture system while maintaining proper phenotype and genetic stability.

Recent studies have shown that efficient clonal derivation of hES cell lines is possible with the combined use of NutriStem® hPSC XF Medium and LaminStem™ 521 substrate, finding that the cells grew better in NutriStem® hPSC XF Medium than any other defined medium tested, and that hES cells can be passaged and maintained using a single-cell expansion protocol1, 2. In addition, effective differentiation methods have been published using human laminin-521 matrix with NutriStem® hPSC XF Media (with and without growth factors) 3.

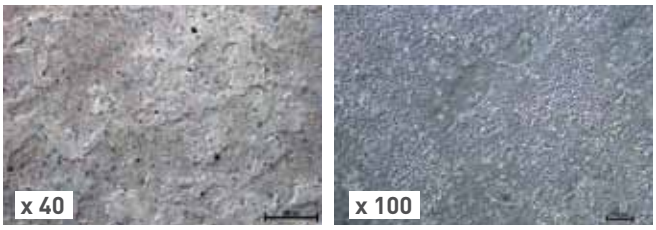


Figure 9: H1 hESC were cultured with LaminStem using NutriStem® hPSC (day 3).

Cryopreservation

Animal component-free formulation, designed for the cryopreservation of pluripotent stem cells

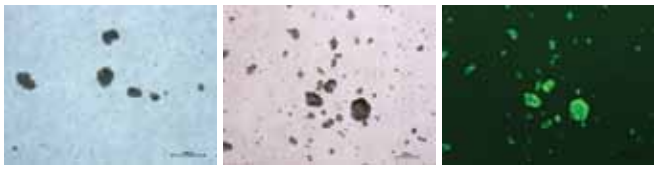
Product Name	Cat. No.	Size	Storage
CryoStem™	05-710-1D 05-710-1E	10ml 50ml	2-8°C

Features

- Chemically defined
- Animal component-free (ACF)
- Protein-free
- Suitable for freezing hESC and hiPSC cultured in both feeder and feeder-free conditions
- High recovery efficiency: maintains excellent attachment ability as well as growth performance
- Maintains hESC and hiPSC pluripotency
- Complete formulation; Ready-to-use at 2-8°C

H1 hESC

BG01V/hOG cells
(Variant hESC hOct4-GFP reporter cells)
Cat# R7799-105 Invitrogen



1h Post-thawing

Day 1 Post-thawing

Day 4 Post-thawing

Figure 10: hESC were frozen in CryoStem™ and were thawed into NutriStem® hPSC XF on Matrigel.

Customized Products

Customized NutriStem® hPSC XF for Reprogramming

Since the pioneering work done by Dr. Shinya Yamanaka describing the reprogramming of somatic cells to a pluripotent-like state by using retroviral vectors, the hiPSC has become an invaluable tool in regenerative medicine, disease modeling, drug discovery, and basic research.
The reprogramming of differentiated cells to pluripotency holds great promise that patient-specific induced pluripotent stem cells could be used to model disease or to generate clinically useful cell types for autologous cell therapies.
NutriStem® hPSC XF is a defined, xeno-free medium optimized for hESC and hiPSC. BI offers the possibility for special preparations of NutriStem® hPSC XF without growth factors and other components required to support mRNA-based cellular reprogramming of human cells. Clonal mRNA reprogrammed iPSC lines can be expanded and maintained in NutriStem® hPSC XF.

Customized Albumin-Free NutriStem® hPSC XF for Feeder culture

BI offers the possibility for special preparations of NutriStem® hPSC XF without albumin.
The albumin-free media is optimized for feeder culture and shows superior performance on HFF and MFF feeder layers.

Human Serum Albumin

Specially treated Human Serum Albumin, optimized for hESC and hiPSC culture

Product Name	Cat. No.	Size	Storage
Bio-Pure™ (HSA Solution, 10%), Optimized for hESC	05-720-1B	100ml	2-8°C

Xeno-free supplement specially qualified for the growth of undifferentiated pluripotent hESC and hiPSC, in both feeder-dependent and feeder-free conditions.
All individual plasma donations, as well as the plasma pool, are tested for Hepatitis B Surface Antigen (HBsAg), Anti (Human Immunodeficiency Virus) - HIV-I and II and anti-HCV and found to be negative.

References

Derivation and expansion of hESC and iPSC

L Healy, L Ruban, Derivation of Induced Pluripotent Stem Cells. Atlas of Human Pluripotent Stem Cells in Culture (2015)

T. Yokobori et al., Intestinal epithelial culture under an air liquid interface: a tool for studying human and mouse esophagi. Diseases of the Esophagus (2015)

Induction of early neural precursors & derivation of tripotent neural stem cells from hESC and iPSC

H.X. Nguyen et al., Induction of early neural precursors and derivation of tripotent neural stem cells from human pluripotent stem cells under xeno-free conditions. Journal of Comparative Neurology (2014)

iPSC derivation patents

M.F Yanik, M. Angel, Methods for Transfecting Cells with Nucleic Acids. US Patent 20,140,073,053 (2014)

C.E Buensuceso et al., Induced Pluripotent Stem Cells Prepared from Human Kidney-Derived Cells. US Patent 20,140,073,049 (2014)

Different basement matrix: (e.g., Laminin)

S. Rodin et al., Clonal culturing of human embryonic stem cells on laminin-521/E-cadherin matrix in defined and xeno-free environment. Nature Communications 5:3195 (2014)

S. Rodin et al., Monolayer culturing and cloning of human pluripotent stem cells on laminin-521–based matrices under xeno-free and chemically defined conditions. Nature Protocols 9, 2354–2368 (2014)

Immunocytochemistry/ Immunofluorescence

E. Moorefield, Immunocytochemistry / Immunofluorescence abreview for Anti-Oct4 antibody - ChIP Grade. www.abcam.com/ab19857/reviews/22928

Clinical applications- derivation and expansion of hESC and iPSC

Y. Luo et al., Stable Enhanced Green Fluorescent Protein Expression After Differentiation and Transplantation of Reporter Human Induced Pluripotent Stem Cells Generated by AAVS1 Transcription Activator-Like Effector Nucleases . Stem Cells Translational Medicine 3:1-5 (2014)

T. Seki, K. Fukuda, Methods of induced pluripotent stem cells for clinical application, World Journal of Stem Cells, 7(1): 116-125 (2015)

Patents

E. Zambidis, P Burridge. Compositions and Methods of Generating a Differentiated Mesodermal Cell. US Patent 20130136721 (2013)

Mesenchymal Stem Cells

Product Overview:

MSC NutriStem® XF

Xeno-free, serum-free cell culture medium, specifically designed to support the growth of hMSC

MSC NutriStem® XF PRF

Phenol red-free, xeno-free, serum-free medium, designed to support the growth of hMSC

MSC Attachment Solution

Xeno-free solution for attachment and spreading of hMSC cultured in serum free conditions

Recombinant Trypsin Solutions

Animal component-free solutions for efficient dissociation of adherent cell types from surfaces and tissues. Optimized for sensitive cells, such as hMSC

MSC Freezing Solution

Chemically defined, animal component-free and protein-free formulation for optimal cryopreservation of hMSC

MSCgo™ Osteogenic XF
MSCgo™ Rapid Osteogenic XF
MSCgo™ Chondrogenic XF
MSCgo™ Adipogenic XF

A unique line of serum-free and xeno-free hMSC differentiation media .

Introduction

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, they are immuno-privileged, 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 vitro 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.

To date, most of the common culture media for growth and expansion of hMSC, as well as auxiliary solutions (for attachment, dissociation, and cryopreservation), are typically supplemented with serum or other xenogenic compounds. A defined serum-free, xeno-free culture system optimized for hMSC isolation and expansion would greatly facilitate the development of robust, clinically acceptable culture process for reproducibly generating quality-assured cells.

BI has developed a novel SF and XF culture system optimized for the growth and expansion of hMSC from a variety of sources: placenta (hMSC-PL), adipose-tissue (hMSC-AT), Wharton jelly (hMSC-WJ) and bone marrow (hMSC-BM).

The SF, XF culture system includes specially developed solutions for the attachment, dissociation and cryopreservation, as well as MSC NutriStem® XF, which enables long-term growth of hMSC while retaining self-renewal and multi-lineage differentiation potential.

In addition to the culture system, BI now offers serum-free, xeno-free media for the direct differentiation of hMSC from various sources into adipocytes, chondrocytes and osteoblasts.

The differentiation media contain all the growth factors and supplements necessary for the directed differentiation of hMSC.

Isolation and Expansion

Xeno-free, serum-free cell culture medium, specifically designed to support the growth of hMSC

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 medium	05-202-1A	500ml	2-8°C

Advantages

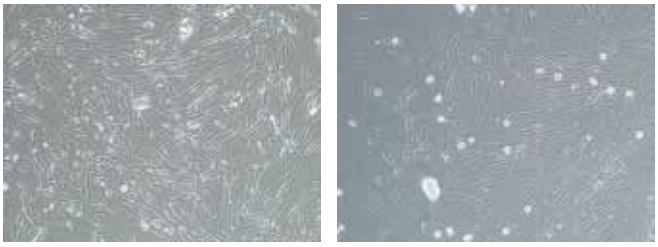
- Superior proliferation rate in comparison to serum-containing media and to competitors SF, XF media.
- Supports long-term growth of hMSC cells from various tissues.
- Superior maintenance of hMSC characteristics:
  - Typically fibroblast-like, spindle shape cell morphology.
  - Self-renewal potential.
  - Tri-lineage differentiation potential.
  - Normal profile of hMSC markers.
  - Karyotype stability.

Initial 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

Isolation of hMSC-PL using MSC NutriStem® XF and serum-containing medium



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). **Higher confluence is observed utilizing MSC NutriStem® XF without the requirement of human AB serum supplementation.**

Superior isolation of hMSC-PL using MSC NutriStem® XF vs. medium containing FBS.

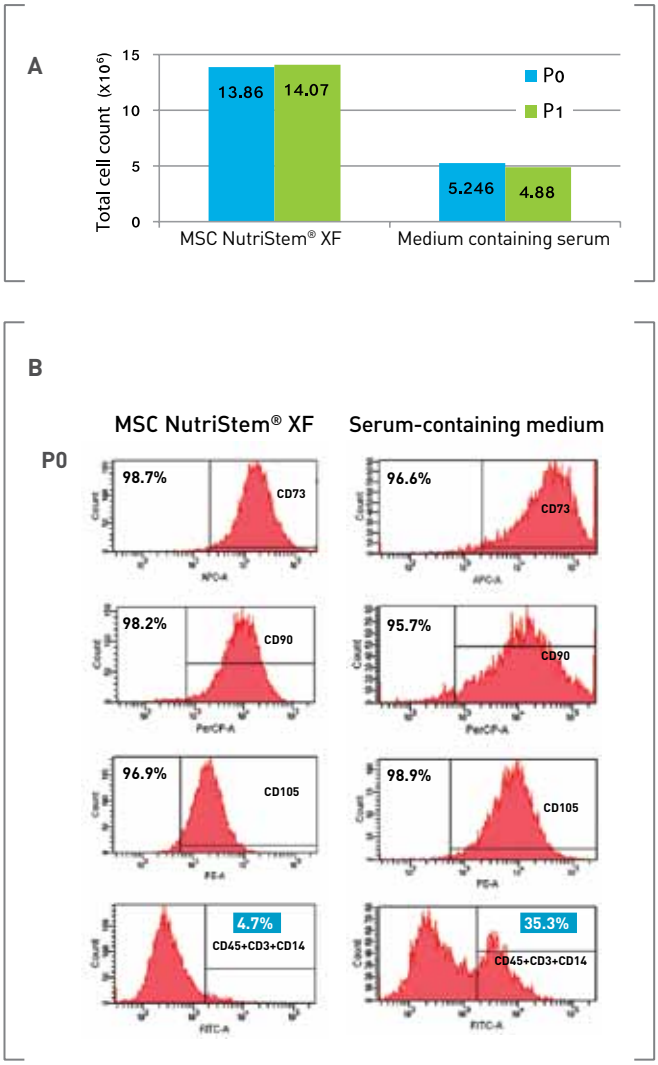


Figure 2: Comparison of hMSC-PL isolation from crude placenta 17 days post initial seeding (P0) in each medium.
A. Quantity of viable cells, measured by trypan blue exclusion assay.
B. Immunophenotype results using FACS analysis.

Initial isolation of hMSC–PL under SF, XF culture system using MSC NutriStem® XF (without supplementation of human AB serum) achieves a higher number of purer and viable cells that maintain a normal profile of MSC markers.

hMSC-AT

Evaluation of hMSC-AT isolation using MSC NutriStem® XF on pre-coated plates (MSC Attachment Solution).

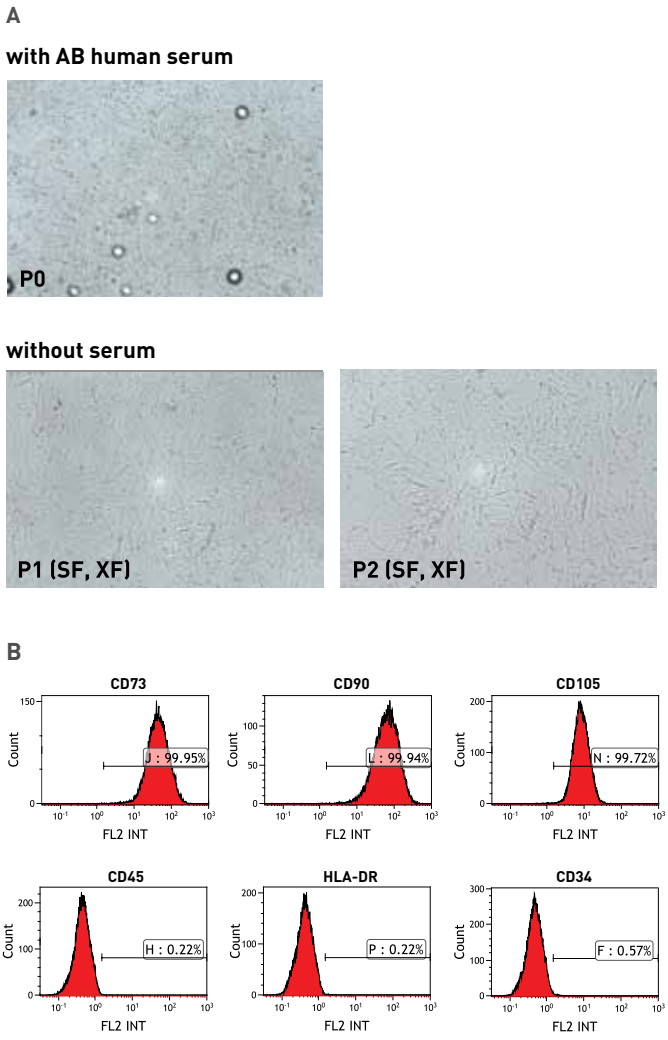
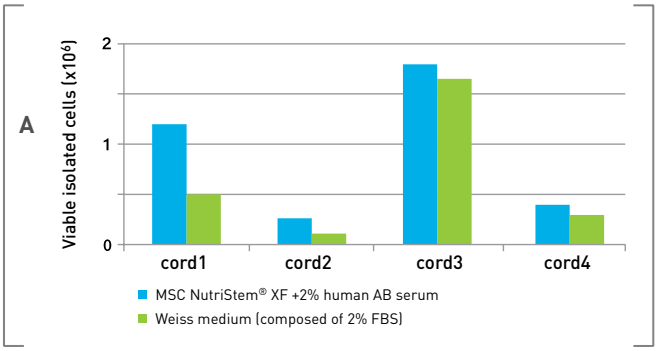


Figure 3: hMSC-AT were seeded in MSC NutriStem® XF supplemented with 2% human AB serum on pre-coated plates with MSC Attachment Solution for the initial isolation and expansion of hMSC-AT (P0).
The cells were cultured to 70-80% confluence before being sub-cultured. Further passages (P1-2) were done under 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.

Successful isolation of hMSC-AT that maintains a classical profile of MSC markers was achieved under XF conditions, utilizing MSC NutriStem® XF.

hMSC-WJ

Superior isolation of hMSC-WJ utilizing MSC NutriStem® XF vs. serum-containing medium.



B

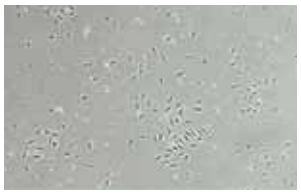
	Day 2 post initial isolation	Day 7 post initial isolation	
	Representative images	Total cell count Live	Dead
MSC NutriStem® XF (supplemented with 2% human AB serum)		395,000	15,000
Weiss medium (composed of 2% FBS)		295,000	75,000

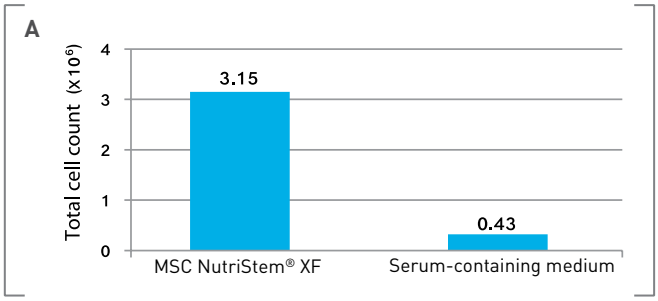
Figure 4: hMSC were initially isolated from 4 independent human cords utilizing MSC NutriStem® XF supplemented with 2% human AB serum on pre-coated plates with MSC Attachment Solution in comparison to serum-containing medium.
A. Comparing the amount of viable cells – passage 0. Cell count was measured 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, respectively.

Superior isolation of hMSC-WJ utilizing MSC NutriStem® XF vs. serum-containing medium.

Initial isolation of hMSC–WJ under XF culture system achieves higher number of viable cells.

hMSC-BM

Superior isolation of hMSC-BM using MSC NutriStem® XF vs. FBS containing medium.



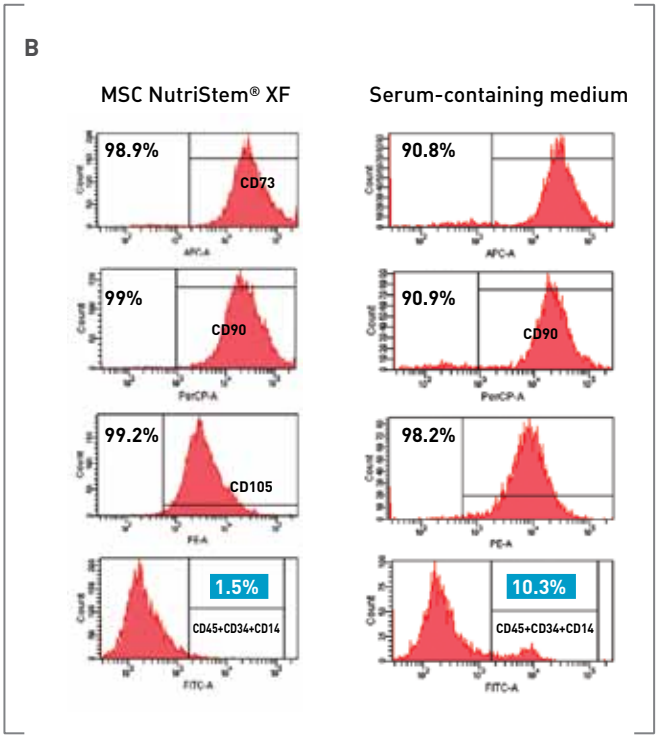


Figure 5: Comparison of hMSC-BM isolation from fresh BM utilizing MSC NutriStem® XF and serum-containing medium (11-day assay)
A. Cell count was measured by trypan blue exclusion assay.
B. Immunophenotype using FACS analysis.

Initial isolation of hMSC-BM using MSC NutriStem® XF achieves MSC populations with a higher number of viable cells and higher levels of purity that maintain a classical profile of MSC markers.

Expansion

Superior proliferation of hMSC from various sources is achieved using MSC NutriStem® XF

MSC NutriStem® XF in comparison to competitors' media: serum-containing and SF, XF

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

hMSC-BM

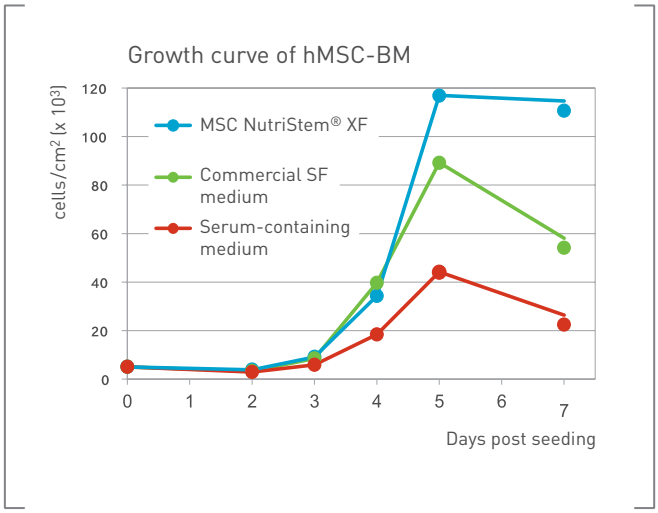
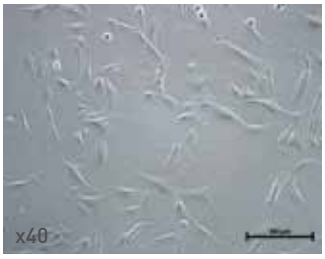
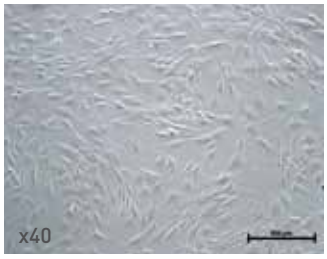


Figure 6: hMSC-BM were cultured in MSC NutriStem® XF in comparison to commercial SF (I) and serum-containing medium (P).
Initial seeding was 5000 cells/cm² for each of the tested media (Day 0). Cells were counted daily by trypan blue exclusion assay.



serum-containing medium



MSC NutriStem® XF

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

hMSC-AT

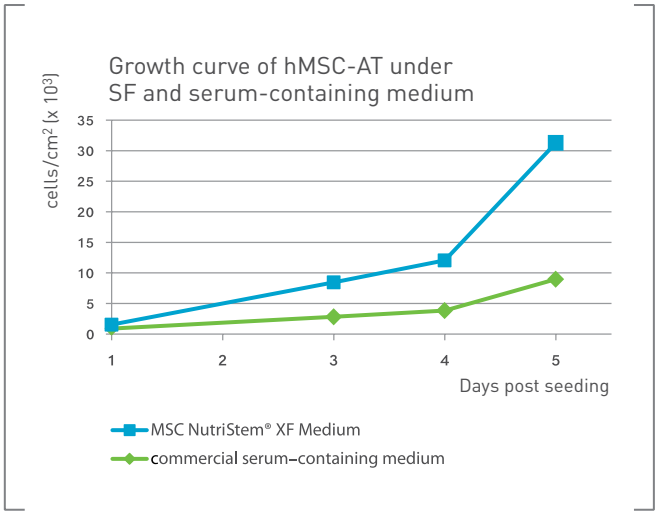
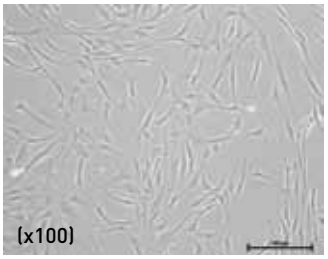
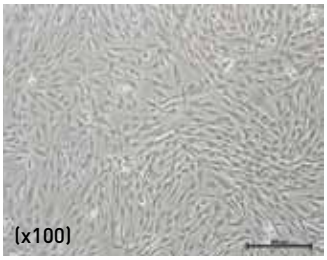


Figure 8: Expansion of hMSC-AT in MSC NutriStem® XF medium and commercial serum-containing medium (P).
Initial seeding was 5000 cells/cm² for each of the tested media (Day 0). Cells were counted daily by trypan blue exclusion assay.



Serum-containing medium



MSC NutriStem® XF medium

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

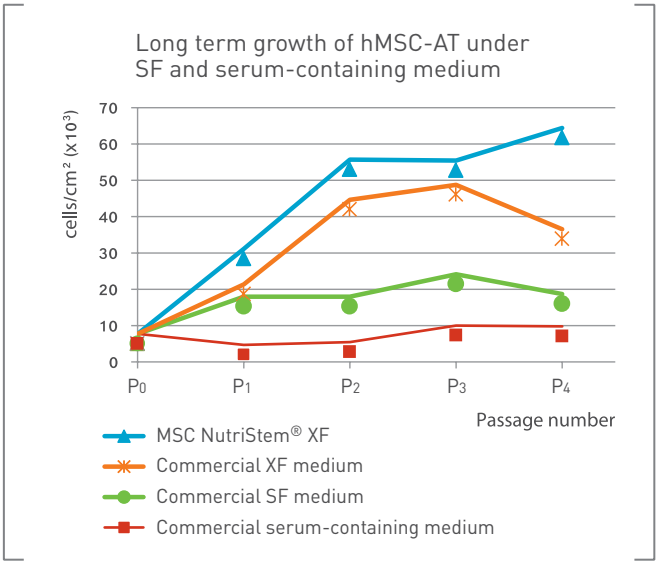


Figure 10: Expansion of hMSC-AT in MSC NutriStem® XF and commercial competitors XF, SF, and serum-containing media. Cells were cultured in plates, pre-coated with MSC Attachment Solution. Initial seeding was 5000 cells/cm² for each of the tested media (Day 0).
Cells were counted at day 3 in each passage.

hMSC-WJ

MSC NutriStem® XF produces the best overall expansion of hMSC-WJ

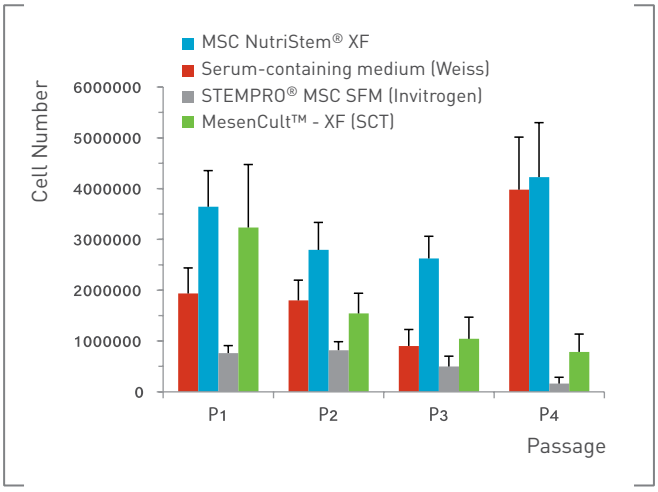


Figure 11: hMSC-WJ from 9 different donors expanded for 4 passages in MSC NutriStem® XF in comparison to serum-containing medium and commercial SF and XF media. Cell proliferation was assessed by cell count using a trypan blue exclusion assay.

MSC NutriStem® XF is optimized for hMSC from various sources

MSC NutriStem® XF promotes proliferation of hMSC from a variety of sources while maintaining normal fibroblast-like, spindle shape cell morphology.

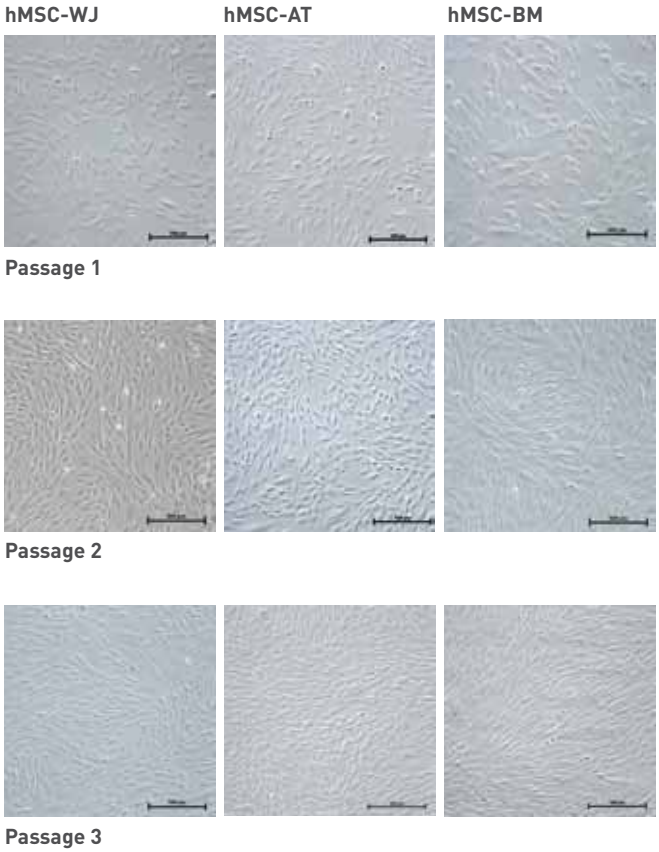


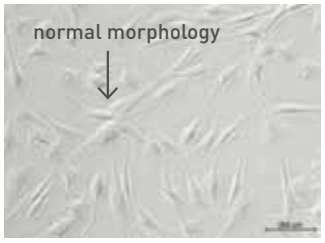
Figure 12: hMSC derived from a variety of sources: WJ, AT and BM were cultured for 3 passages In MSC NutriStem® XF. Images were taken at days 2, 3 or 4 post seeding.

hMSC Characterization

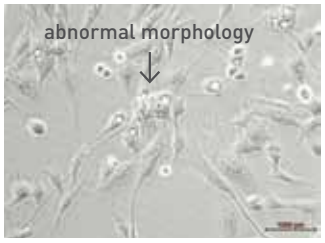
Cell morphology

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

hMSC-AT



MSC NutriStem® XF
15x10^4 cells/well



Competitor (S)
11x10^4 cells/well

Competitor (I)
4x10^4 cells/well

Figure 13: Expansion of hMSC-AT in MSC NutriStem® XF, competitor XF medium (S) and competitor SF medium (I). Initial seeding was 5000 cells/cm^2 for each of the tested media (Day 0).
Images (x200) were taken 3 days post equal seeding (2 passages in each medium).

hMSC-BM

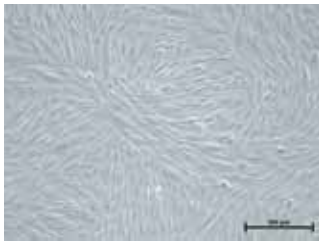


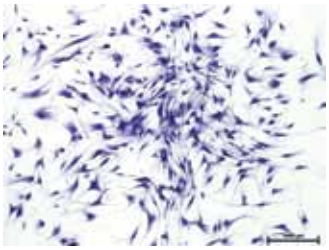
Figure 14: Expansion of hMSC-BM in MSC NutriStem® XF. Initial seeding was 5000 cells/cm^2 (Day 0).
Image was taken 2 days post seeding (x100).

Typically culture morphology of adherent hMSC-BM, shoal-like pattern is observed.

Self-renewal potential

hMSC cultured in **MSC NutriStem® XF** maintain their self-renewal potential.
MSC Colony Forming Unit-Fibroblast (CFU-F) assay was used to evaluate the self renewal potential.

hMSC-BM



hMSC-AT

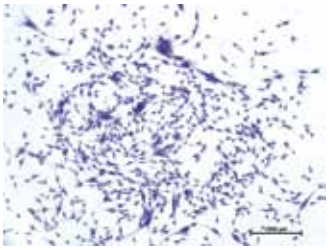


Figure 15: hMSC-BM and AT expanded in MSC NutriStem® XF for 3-5 passages prior to 14 day CFU-F assay. Representative images of colonies stained with 0.5% crystal violet (x100).

hMSC-WJ

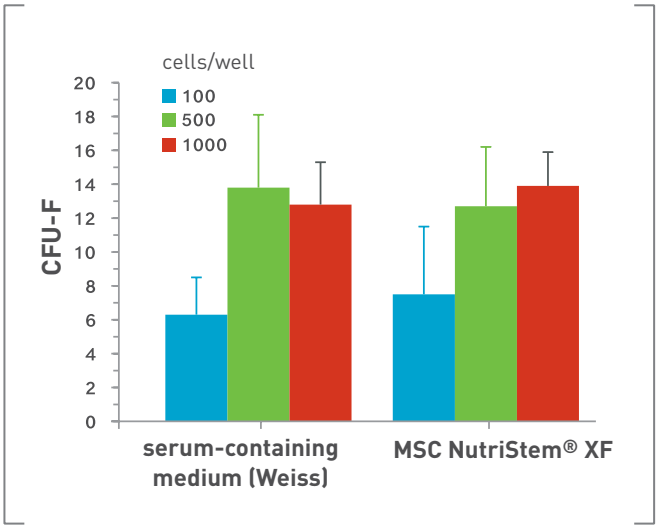


Figure 16: CFU-F assay of hMSC-WJ expanded for 5 passages in MSC NutriStem® XF and Weiss medium (2% FBS) in 3 different seeding concentrations.

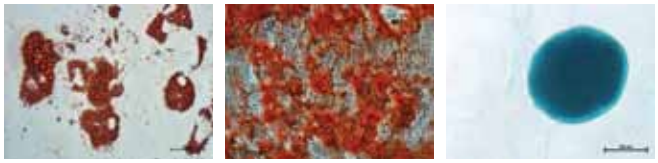
Differentiation potential

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

hMSC-BM

Control

Differentiation

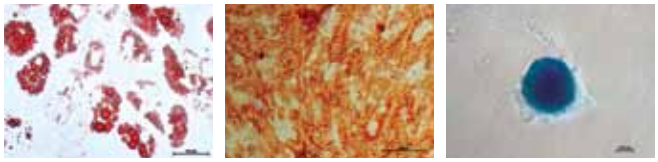


Adipocytes - Oil red O | Osteocytes - Alizarin red | Chondrocyte - Alcian blue

hMSC-AT

Control

Differentiation



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

Figure 17: 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. Stain 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

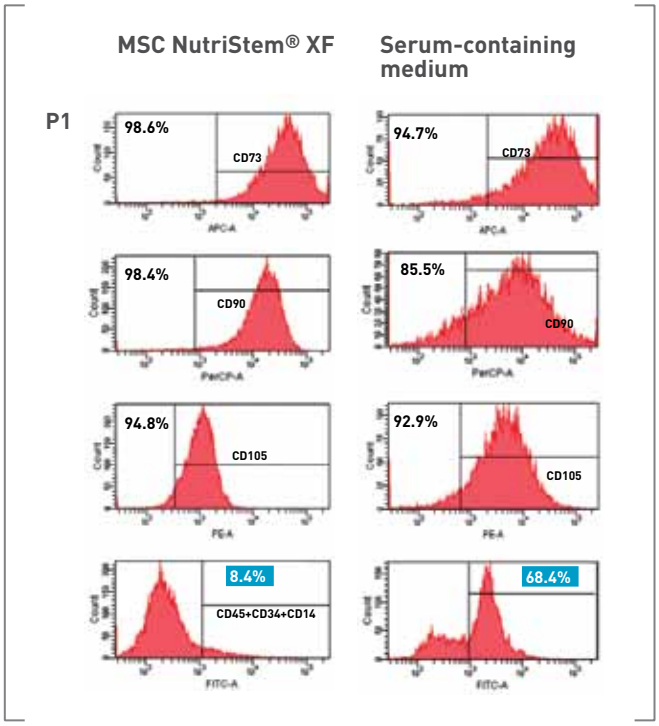


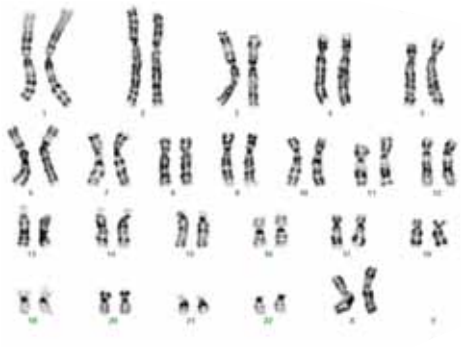
Figure 18: immunophenotype results of hMSC-PL after culturing in each medium.

Purer hMSC population is achieved using MSC NutriStem® XF.

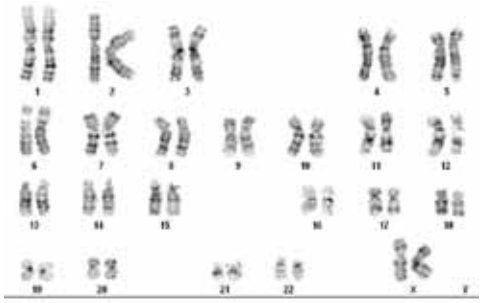
Karyotyping

Normal karyotyping 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

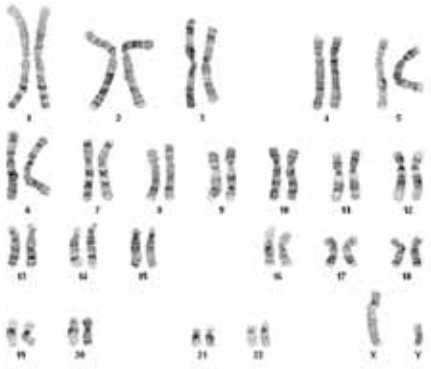


Figure 19: G-banding karyotyping analysis of hMSC from various sources expanded for 4-9 passages in MSC NutriStem® XF. hMSC cultured in MSC NutriStem® XF maintain genomic stability.

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.

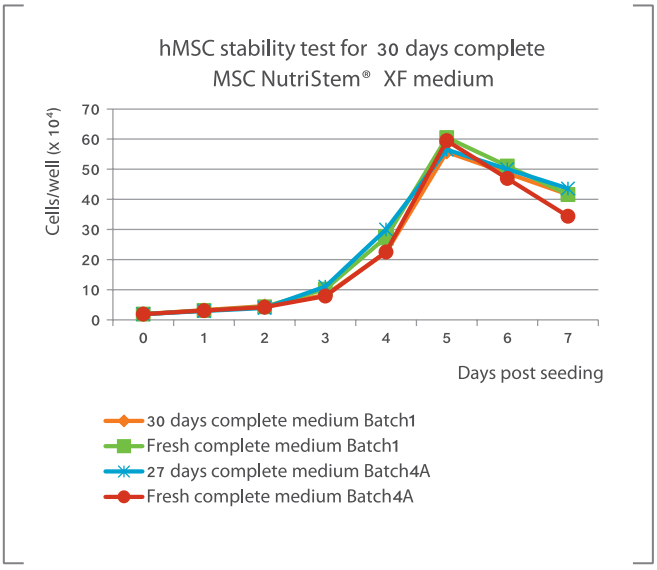
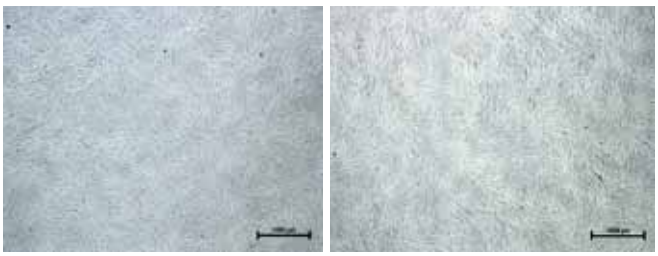


Figure 20: Growth curve of hMSC-BM cultured in MSC NutriStem® XF.
Results were taken from 2 batches: batch No. 1: 7.5 months from production and batch 4A: 2.5 months from production.
A complete medium was prepared 30 & 27 days before seeding (stored at 2-8°C) or freshly prepared.
Cells were cultured in pre-coated plate with MSC Attachment Solution. 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)
16x10^4 cells/well

30 Days (x40)
17x10^4 cells/well

Figure 21: A complete medium was prepared freshly, or 30 days before seeding (stored at 2-8°C). hMSC-BM were cultured in plate, pre-coated with MSC Attachment Solution. 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).

Attachment

Under a SF, XF culture system, a pre-coating procedure is required for the attachment and spreading of hMSC

Product Name	Cat. No.	Size	Storage
MSC Attachment Solution	05-752-1F 05-752-1H	1ml 5ml	2-8°C

- Ready-to-use (concentrated x100) solution (2-8°C).
- Without xenogenic components (XF).
- Suitable for hMSC from various sources.
- Human fibronectin (hFN) based solution.
- Suitable for both hMSC proliferation and differentiation assays.

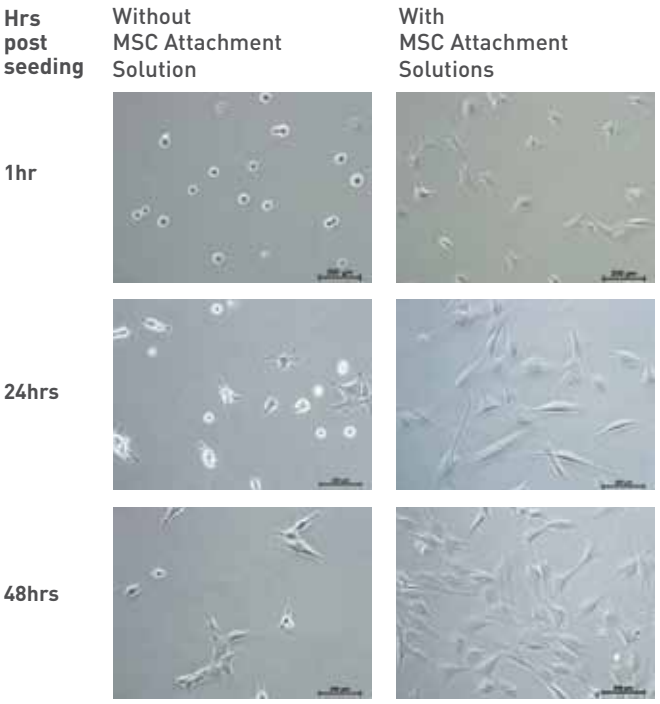


Figure 22: hMSC-BM cultured in MSC NutriStem® XF on pre-coated plates with MSC Attachment Solution and without. Representative images were taken at the indicated time points post-seeding (x200).

Dissociation

Under SF, XF culture the use of chemicaly defined dissociation solution is required.

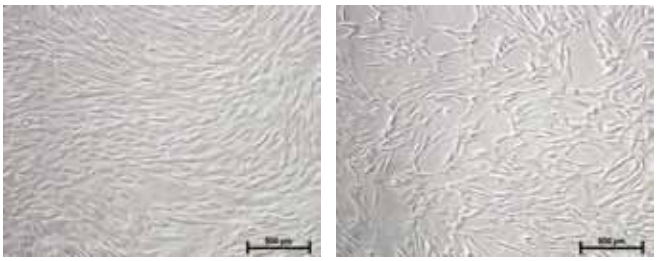
Product Name	Cat. No.	Size	Storage
Recombinant Trypsin Solution without EDTA	03-078-1B 03-078-1C	100ml 20ml	-20°C
Recombinant Trypsin Solution with EDTA	03-079-1B 03-079-1C	100ml 20ml	-20°C

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.
- After initial thawing, Recombinant Trypsin Solution may be stored at RT for at least 6 months.

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 **Trypsin EDTA Solution**

Figure 23: 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

A chemically defined, animal component-free and protein-free formulation for optimal cryopreservation of hMSC

Product Name	Cat. No.	Size	Storage
MSC Freezing Solution	05-712-1D 05-712-1E	10ml 50ml	2-8°C

- 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 MSC Freezing Solution 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.

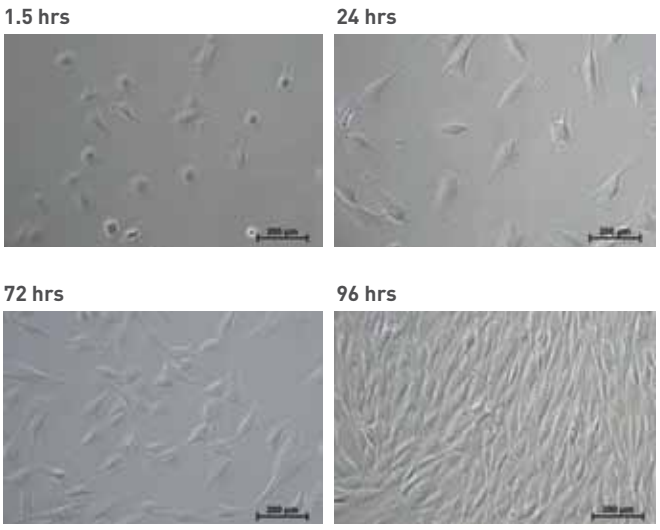


Figure 24: Recovery of hMSC-BM after thawing procedure. Cells were frozen using MSC Freezing Solution, thawed and re-seeded in MSC NutriStem® XF on pre-coated plates. Representative images were taken at the indicated time points post-thawing (x200).

Differentiation

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 and hMSC-CT) into adipocytes, chondrocytes and osteocytes.

Features and 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.

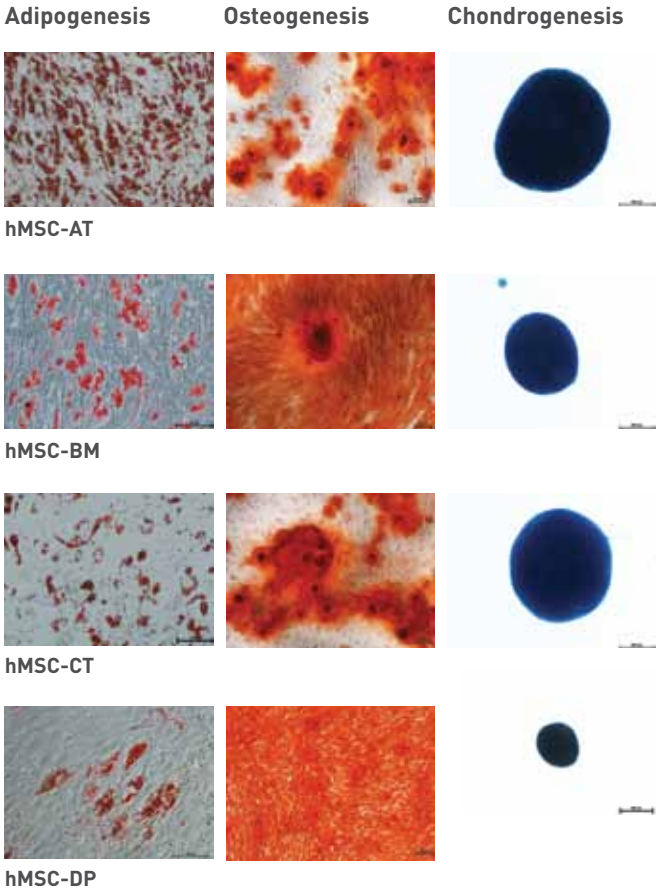


Figure 25: hMSC from various sources pre-cultured in MSC NutriStem® XF were reseeded into differentiation assays using each BI MSCgo™ differentiation media respectively.
Representative images of 16 days assay of Adipogenesis following Oil red O staining (X20), 11 days assay of osteogenesis following 2% ARS staining (X10) and 21 days assay of Chondrogenesis following Alcian blue staining(x4).

Efficient differentiation of variety sources of hMSC into mature adipocytes, osteocytes and chondrocytes is achieved under complete SF,XF culture condition using the BI novel MSCgo™ media.

Osteogenic Differentiation

Complete, ready-to-use, xeno-free and serum-free media for the initial 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 (14-21days).

Osteogenic evaluation

hMSC-BM hMSC-AT

Figure 26: Calcified nodules observed in both hMSC-BM and hMSC-AT after a 10 day MSC differentiation assay using MSCgo™ Osteogenic XF.

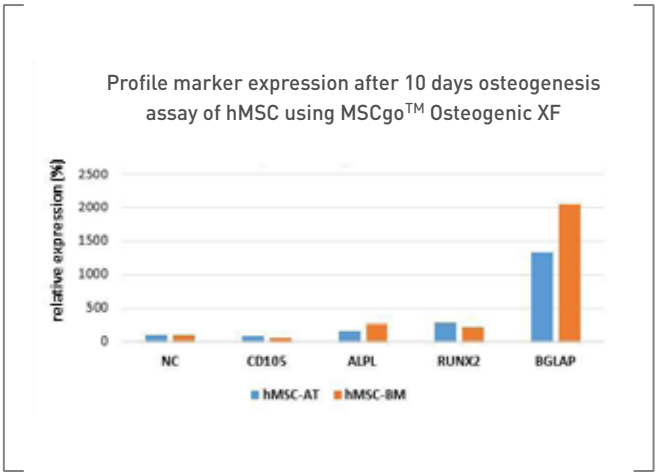


Figure 27: Relative expression (RT-PCR) of osteocyte markers after 10 days of osteogenesis of hMSC using MSCgo™ Osteogenic XF. Osteogenic markers were upregulated whereas an undifferentiated hMSC marker (CD-105) was downregulated. BGLAP represents a maturation state of osteogenesis.

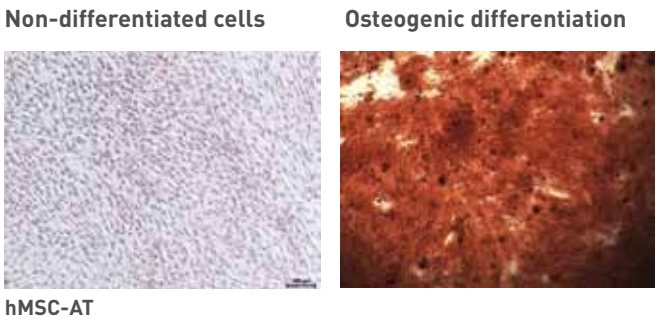


Figure 28: Positive Alizarin staining is observed, indicates of mature osteocytes after a 28 day differentiation assay of hMSC-AT using MSCgo™ Osteogenic XF medium

Profile marker expression

Profile marker expression after 21 days osteogenesis assay of hMSC usnig MSCgo™ Osteogenic XF

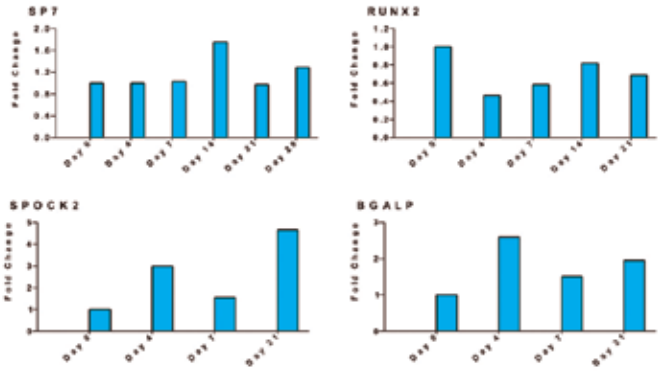


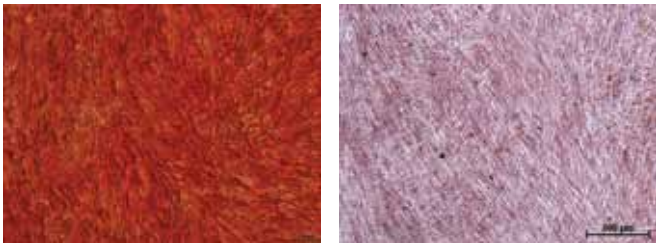
Figure 29: Relative typical expression of the osteocyte-related genes is observed during osteogenesis of hMSC using MSCgo™ Osteogenic XF.

MSCgo™ Osteogenic XF in comparison to competitor media

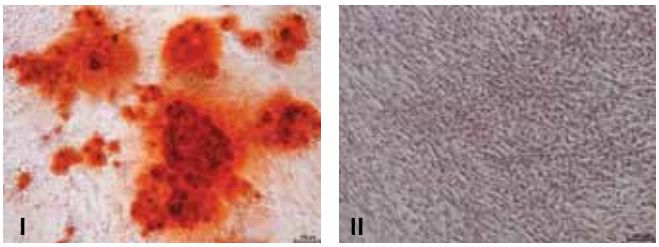
Superior osteogenesis is achieved using MSCgo™ Osteogenic XF.

A

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



hMSC-BM



hMSC-CT

B

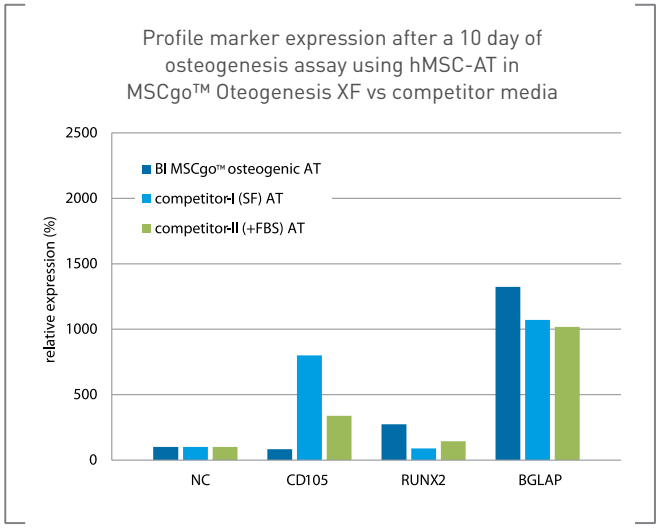


Figure 30: **A.** Positive Alizarin staining after a 10 day differentiation assay is observed only when using MSCgo™ Osteogenic XF.
B. MSCgo™ Osteogenic XF led to highest expression of osteogenic markers and lowest expression of un-differentiated hMSC marker (CD-105) in comparison to commercial media.
BGLAP represents a maturation state of osteogenesis.

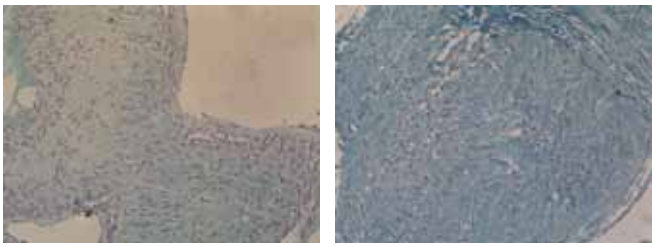
Chondrogenic Differentiation

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

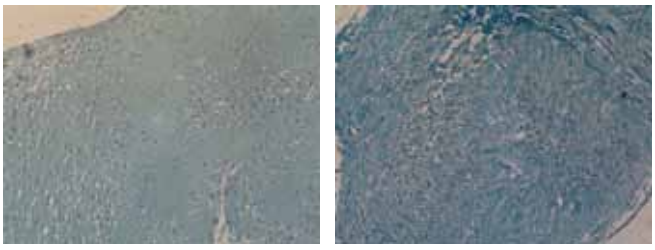
Product Name	Cat. No.	Size	Storage
MSCgo™ Chondrogenic XF Basal Medium	05-220-1B	100ml	2-8°C
MSCgo™ Chondrogenic XF Supplement Mix	05-221-1D	10ml	-20°C

Chondrogenic evaluation

Non-differentiated cells **Chondrogenic differentiation**



14 day assay



21 day assay

Figure 31: Histopathological evaluation (Toluidine blue staining) of cartilage maturation in vitro. Well differentiated hMSC-AT into mature chondrocytes are observed using MSCgo™ Osteogenic XF compare with non-differentiated cells.

Profile marker expression

Profile marker expression after 21 days chondrogenesis assay of hMSC using MSCgo™ Chondrogenic XF

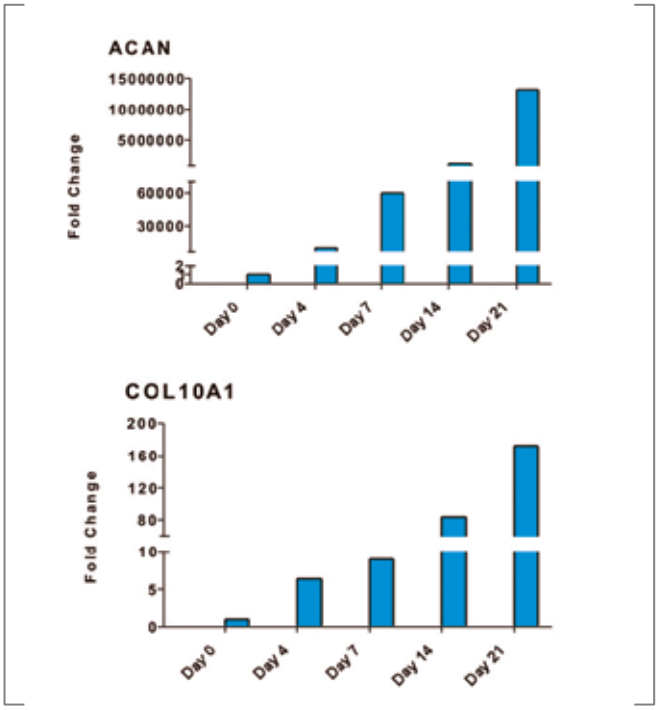


Figure 32: Relative expression (RT-PCR) of chondrocytes markers during 21 days of hMSC-AT differentiation assay using MSCgo™ Chondrogenic XF. Elevated expression of the chondrocyte-related genes, aggrecan (ACAN) and alpha chain of type X collagen (COL10A1), is observed.

hMSC-AT hMSC-BM hMSC-CT

Figure 33: Representative histological images (x40) of differentiated samples stained with Toluidine blue.

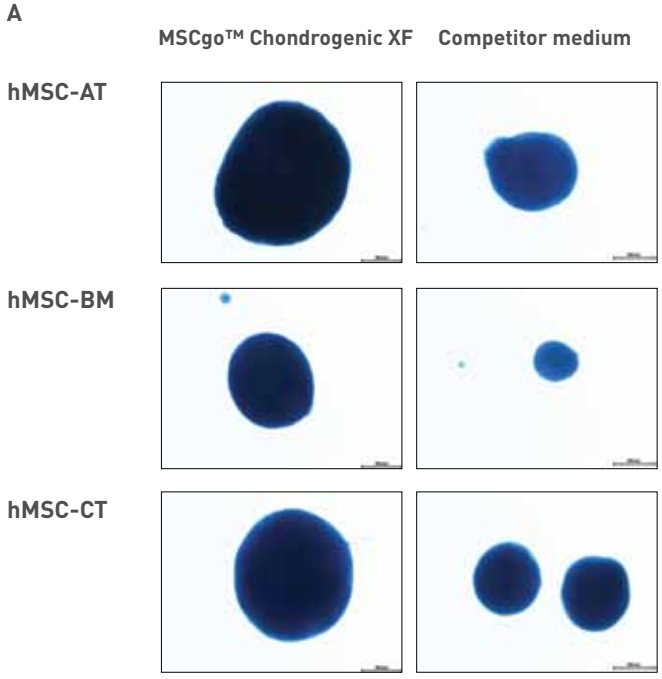
Mature differentiated cells (chondrocytes) surrounded by a cartilage matrix are observed in the 3 types of hMSC after a 21-day differentiation assay using MSCgo™ Chondrogenic XF.

MSCgo™ Chondrogenic XF in comparison to competitor medium

Superior chondrogenesis is achieved using MSCgo™ Chondrogenic XF.

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

A



B

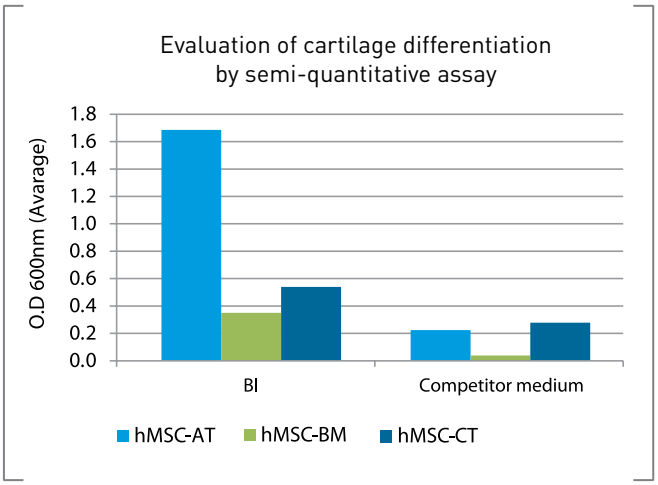


Figure 34: Cartilage differentiation results of hMSC from various sources after 21 day assay using MSCgo™ Chondrogenic XF vs. commercial differentiation medium, following Alcian blue staining **(A)** and O/N elution with GuHCL (600nm) **(B)**.
The results are average of absorbance read of each well with and without the cartilage.

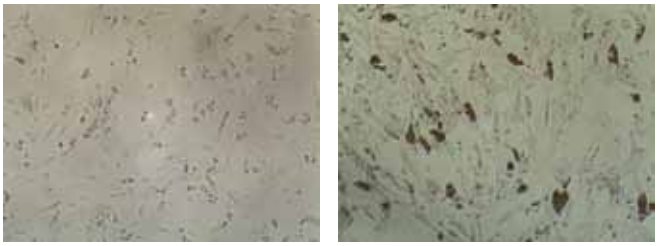
Adipogenic Differentiation

Innovative serum-free, xeno-free medium for the initial 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

Non-differentiated cells **Adipo-differentiated cells**



hMSC-AT

Figure 35: Possitive Oil red O staining is observed, indicates of mature adipocytes after a 14 day differentiation assay of hMSC-AT using MSCgo™ Adipogenic XF.

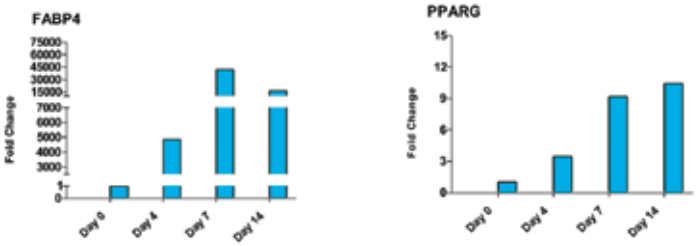


Figure 36: Elevate expression of the adipocyte-related genes, (FABP4) and alpha chain of type X collagen (PPARG), is observed during 14 days adipogenesis of hMSC using MSCgo™ Adipogenic XF.

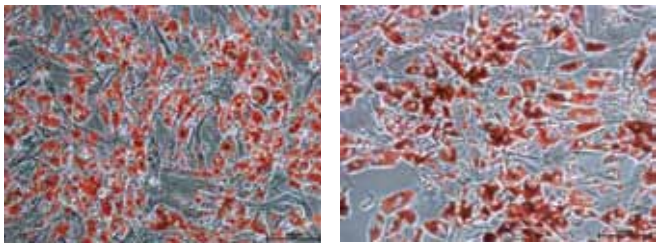
Light **FABP4** **Merged (Dapi)**

hMSC-BM

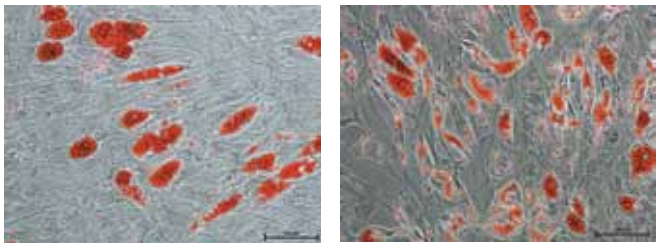
Figure 37: Typical expression of FABP4 is observed post 11 days adipogenesis of hMSC using MSCgo™ Adipogenic XF.

MSCgo™ Adipogenic XF in comparison to competitor media

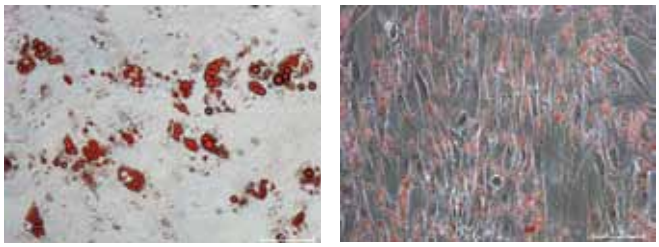
MSCgo™ Adipogenic XF **FBS-containing medium**



hMSC-AT



hMSC-BM



hMSC-CT

Figure 38: hMSC from various sources were differentiated into adipocytes using MSCgo™ Adipogenic XF following 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).

Summary

Biological Industries has developed a novel culture system to enable xeno-free and serum-free culture of hMSC, while maintaining hMSC typically characterizations.

This system has the quality and consistency needed to optimize hMSC culture for research, cell therapy and tissue engineering.

MSC NutriStem® XF and the necessary auxiliary solutions support initial isolation, and exhibit superior proliferation and long-term growth compared with serum-containing media and other commercially-available SF media.

MSCgo™ differentiation media led to superior adipogenesis, osteogenesis and chondrogenesis of hMSC from various sources.

Acknowledgment

We would like to thank Professor Mark L. Weiss, Kansas State University, Department of Anatomy and Physiology, Manhattan, KS, for his invaluable contribution to the MSC NutriStem® XF evaluation using WJ-hMSC.

References

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2. U Pivoraité et. al., Exosomes from Human Dental Pulp Stem Cells Suppress Carrageenan-Induced Acute Inflammation in Mice. Inflammation, April 2015
3. Allen Kuan-Liang Chen et al. Application of human mesenchymal and pluripotent stem cell microcarrier cultures in cellular therapy: Achievements and future direction. Biotechnology Advances, Volume 31, Issue 7, 15 November 2013, Pages 1032–1046
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5. 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
6. Mark L. 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. Poster: ISCT 2012

Endothelial Cells (EC)

EndoGo™ XF NEW

A novel xeno-free culture medium specially designed for in vitro long-term expansion of large and small vessels EC from various sources.

Abbreviations:

EC	Endothelial Cells
hMEC	Human Microvascular Endothelial Cells
HAMEC	Human Adipose Microvascular Endothelial Cells
HBdMEC	Human Bladder Microvascular Endothelial Cells
HDBEC	Human Dermal Blood Microvascular Endothelial Cells
HDLEC	Human Dermal Lymph Microvascular Endothelial Cells
HDMEC	Human Dermal Microvascular Endothelial Cells
HPMEC	Human Pulmonary Microvascular Endothelial Cells

Introduction

Endothelial cells (EC) form the inner lining of a blood vessel, termed endothelium. They provide a selective permeability barrier and an anticoagulant barrier between the vessel wall and blood.
Their unique location in the interface between the blood and surrounding tissue allows EC to detect local changes and blood-borne signals, and react by producing a wide range of vasoactive substances that regulate vascular tone, cellular adhesion, thromboresistance, smooth muscle cell proliferation, and vessel wall inflammation. Additionally, EC are pivotal in cancer research, angiogenesis and vasculogenesis. Consequently, EC have become a key element in tissue engineering and cell therapy, to improve graft implantation.

Growth and Expansion

Product Name	Cat. No.	Size	Storage
EndoGo™ XF	05-400-1A	500ml	2-8°C
EndoGo™ XF Supplement Mix	05-400-1-25	2.5ml	-20°C

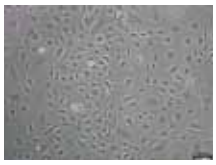
EndoGo™ XF is a novel xeno-free culture medium specially designed for in vitro long-term expansion of large and small vessels EC from various sources.
Before use, supplementation with 2-5% of human AB serum off the clot (OTC) is required. It does not contain any non-human origin ingredients e.g., Bovian Brain Extract (BBE).
The medium provides an optimally balanced nutritional environment that selectively promotes in vitro proliferation of normal human EC, while maintaining typical cobblestone-like cell morphology, phenotypic surface marker profile, and angiogenic differentiation potential (tube formation assay).
EndoGo™ XF supports microvascular endothelial cells (MVEC) from blood and lymph vessel as well as EC derived from: dermal, cardiac, lung, bladder, and adipose tissues.
In addition, EndoGo™ XF supports EC from large vessels, i.e., arteries and veins (e.g., HUVEC).

Cell Morphology

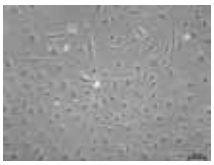
EndoGo™ XF promotes proliferation of both micro and macro EC from a variety of sources while maintaining classical EC morphology.

Macrovascular EC classical morphology

HUVEC
at day 4 post P4



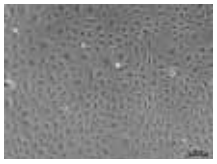
HPAEC
at day 3 post P3



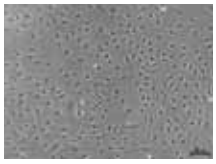
HCAEC
at day 3 post P3

Figure 1: Cells were seeded on hFN-coated dishes and cultured in EndoGo™ XF for several sequential passages with equal seeding during passages.

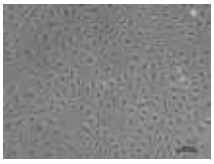
Microvascular EC classical morphology



HDMEC
at day 4 post P2

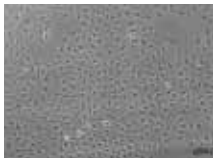


HDLEC
at day 4 post P3

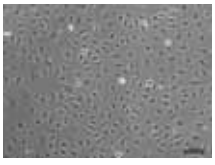


HDBEC
at Day 3 post P5

HAMEC
at day 4 post P2



HPMEC
at day 4 post P2



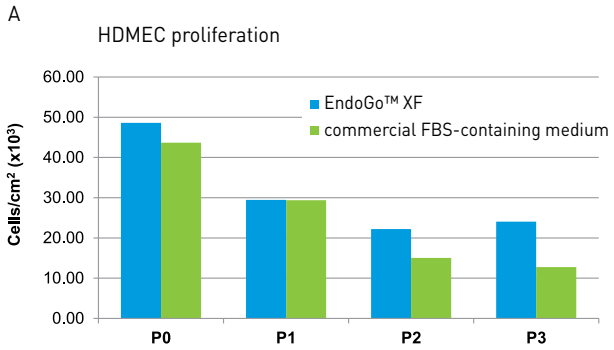
HBdMEC
at day 3 post P2

Figure 2: Cells were seeded on hFN pre-coated dishes and cultured in EndoGo™ XF +2% OTC human AB serum for several sequential passages with equal seeding (6000 cells/cm^2).

Cell Proliferation

Superior cell number and population doubling level (PDL) of human microvascular endothelial cells in EndoGo™ XF.

A



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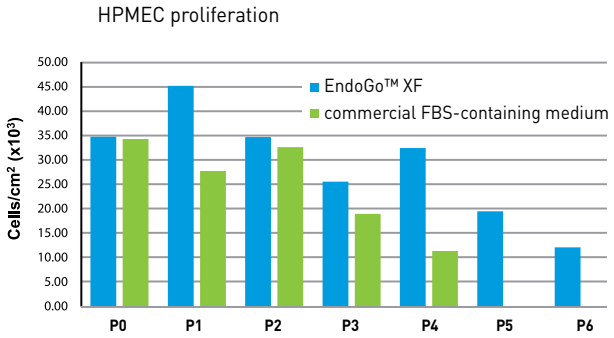


C

	P0	P1	P2	P3	PDL
EndoGo™ XF	2.07	2.56	2.15	2.26	9.04
Commercial FBS-containing medium	1.42	2.07	1.59	1.35	6.43

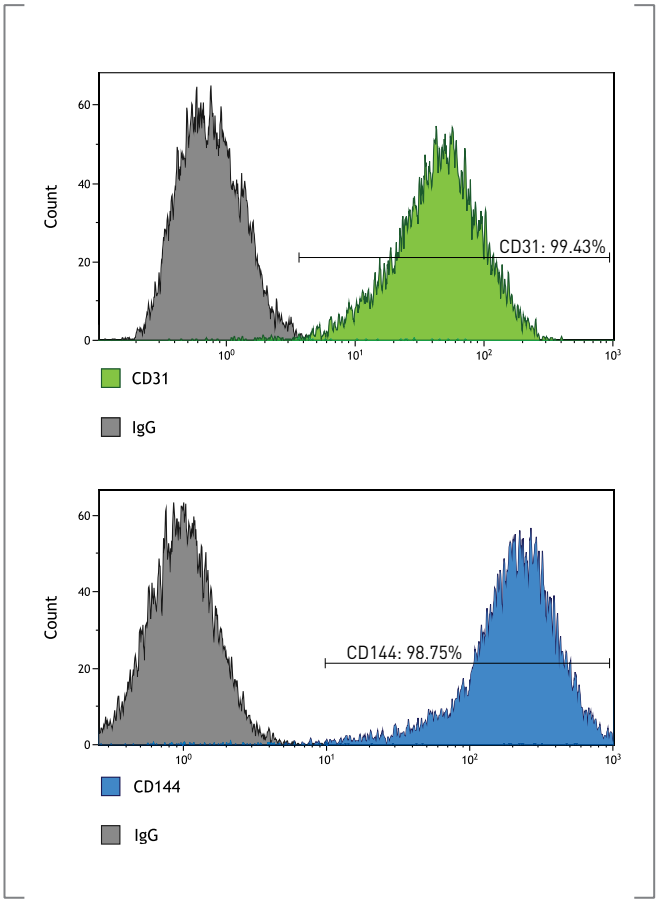
Figure 3: Cell counts and population doubling level of HDMEC **(A and C)**, HPMEC **(B)** expanded for several passages in EndoGo™ XF in comparison to commercial FBS-containing medium. Viable cells were counted using ChemoMetec Viability and Cell Count Assay.
*HPMEC did not survive P5 in the FBS-containing medium.

Cell Characteristics

Immunophenotyping

Microvascular EC cultured in EndoGo™ XF maintain a classical profile of EC markers (>98%).

Immunophenotyping of HDLEC after 6 passages in EndoGo™ XF.



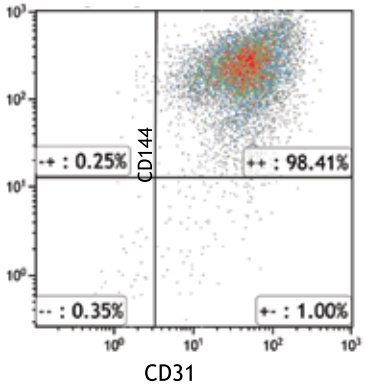


Figure 4: Cells were cultured on hFN pre- coated dishes (equal seeding of 6000 cells/cm²) in EndoGo™ XF +2% OTC human AB serum. Cells were labeled with antibodies against CD31 and CD144, and analyzed by FACS.

Gene expression

Microvascular EC cultured in EndoGo™ XF maintain a similar gene expression profile pattern of EC during passages.

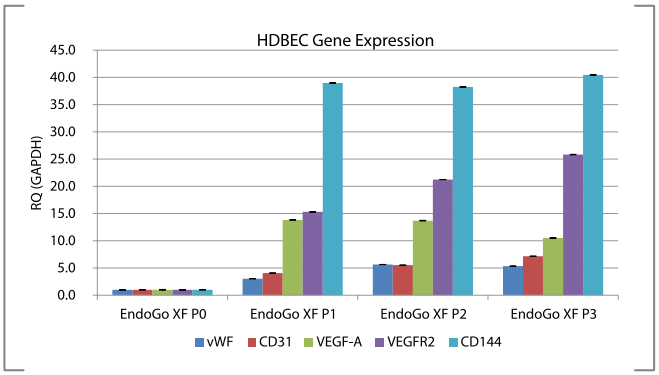


Figure 5: Real-time results of HDBEC post P1, P2, and P3 in EndoGo™ XF analyzed in comparison to P0 (original cell pellet w/o proliferation).

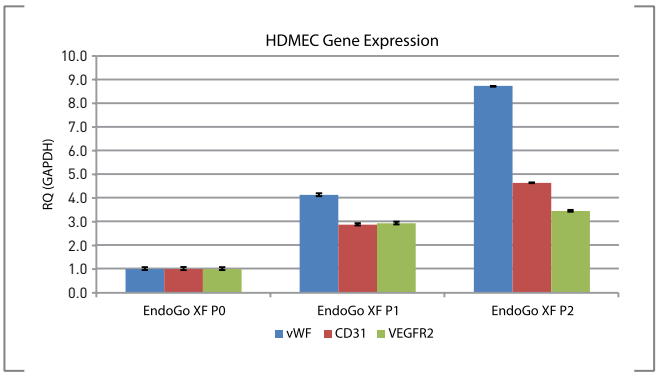
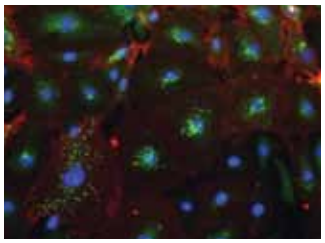


Figure 6: Real-time results of HDMEC post P1 and P2 in EndoGo™ XF analyzed in comparison to P0 (original cell pellet w/o proliferation).

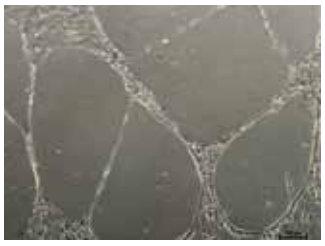
Angiogenic features

Endothelial cells expanded in EndoGo™ XF preserved endothelial cell features (markers expression and angiogenic potential to form capillary-like tubes).

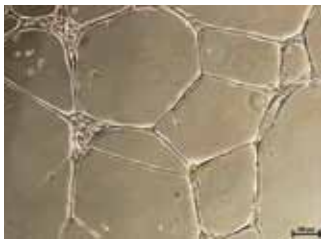


HDBEC

Figure 7: Immunofluorescence staining of HDBEC after expansion for 5 passages in EndoGo™ XF. Cells stained for the classical endothelial cells markers: CD31 (PECAM) (red) and Von-Wilibrant factor (vWF) (green), and counterstained with DAPI (blue).



A- HDBEC



B- HUVEC

Figure 8: Angiogenic potential. Tube formation assay (TFA) of cells after cultivation in EndoGo™ XF. Cells were seeded on Matrigel™ in EndoGo™ XF + 5% OTC human AB serum (50000 cells/well of 48wp). Representative image of: HDBEC from P2 after 18h **(A)** HUVEC from P5 after 21h. **(B)**

Auxiliary Products

BI offers auxiliary products for a complete XF culture system for endothelial cells.

Attachment

Product Name	Cat. No.	Size	Storage
Human Fibronectin Solution	05-750-1F 05-750-1H	1ml 5ml	2-8°C

Fibronectin is an attachment factor that facilitates the attachment and cytoplasmic spreading of all types of anchorage-dependent cells.
BI's human Fibronectin Solution (hFN) is obtained by affinity purification on gelatine-sepharose from human plasma.
The solution is complete, ready-to-use, and performance tested.

Dissociation

Product Name	Cat. No.	Size	Storage
Recombinant Trypsin EDTA Solution	03-079-1B 03-079-1C	100ml 20ml	-20°C

Recombinant Trypsin EDTA is an animal component-free cell dissociation solution, developed for efficient dissociation of adherent cells from surfaces and tissues and optimized for sensitive cells.
The solution was developed as an alternative to porcine trypsin, and does not contain any chymotrypsin, carboxypeptidase A, or other protease contaminant.

Neutralization

Product Name	Cat. No.	Size	Storage
Soybean Trypsin Inhibitor	03-048-1C	20ml	-20°C

Soybean trypsin inhibitor is a single polypeptide that forms a stable, stoichiometric, enzymically inactive complex with trypsin, thereby reducing the availability of trypsin by somewhat binding chymotrypsin.
With BI's Soybean Trypsin Inhibitor Solution, any excess trypsin activity may be completely neutralized, thereby avoiding use of serum for this purpose. The cells can then be successfully re-suspended in a suitable growth medium.

Freezing Medium

Product Name	Cat. No.	Size	Storage
SF Cell Freezing Medium	05-065-1A 05-065-1C	500ml 20ml	2-8°C

An animal component-free, serum-free and protein-free freezing medium.
BI's SF Cell Freezing Medium has been demonstrated to result in high rates of cell viability, proliferation, adherence (in relevant lines), and bioactivity/ expression following freezing and thawing.
Superior results were obtained both in comparison with serum-containing freezing media as well as competing serum-free products, making this an ideal product for both serum-containing and serum-free applications.

Ordering Information

Product Name	Cat. No.	Size	Storage
NutriStem® hESC XF	05-100-1A 05-100-1B	500ml 100ml	-20°C
Bio-Pure™ Human Serum Albumin	05-720-1B	100ml	2-8°C
LaminStem™ 521	05-753-1F	1ml	-20°C
CryoStem™	05-710-1D 05-7110-1E	10ml 50ml	2-8°C
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	05-202-1A	500ml	2-8°C
MSC Attachment Solution	05-752-1F 05-752-1H	1ml 5ml	2-8°C
Recombinant Trypsin Solution without EDTA	03-078-1B 03-078-1C	100ml 20ml	-20°C
Recombinant Trypsin Solution with EDTA	03-079-1B 03-079-1C	100ml 20ml	-20°C
MSC Freezing Solution	05-712-1D 05-712-1E	10ml 50ml	2-8°C

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™ Chondrogenic XF Basal Medium	05-220-1B	100ml	2-8°C
MSCgo™ Chondrogenic XF Supplement Mix	05-221-1D	10ml	-20°C
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
EndoGo™ XF EndoGo™ XF Supplement Mix	05-400-1 05-410-1		2-8°C -20°C
Human Fibronectin Solution	05-750-1F 05-750-1H	1ml 5ml	2-8°C
Soybean Trypsin Inhibitor	03-048-1C	20ml	-20°C
SF Cell Freezing Medium	05-065-1A 05-065-1C	500ml 20ml	2-8°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 culture
- Products for cytogenetics
- Products for mycoplasma detection and treatment
- Disinfectants
- ECM-coated plastic ware
- Products for molecular biology
- Contract manufacturing and custom formulations

All BI's products are manufactured via a quality management system ISO 9001:2008 and in regards of medical devices ISO 13485:2003. 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 6. 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.

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Biological Industries Israel Beit Haemek Ltd.
Kibbutz Beit Haemek 2511500, Israel
T.+972.4.9960595 F.+972.4.9968896
Email: info@bioind.com

Biological Industries USA
100 Sebethe Drive . Cromwell, CT, 06416-1073
T. 860-316-2702 F. 860-269-0596
E-mail: orders-usa@bioind.com