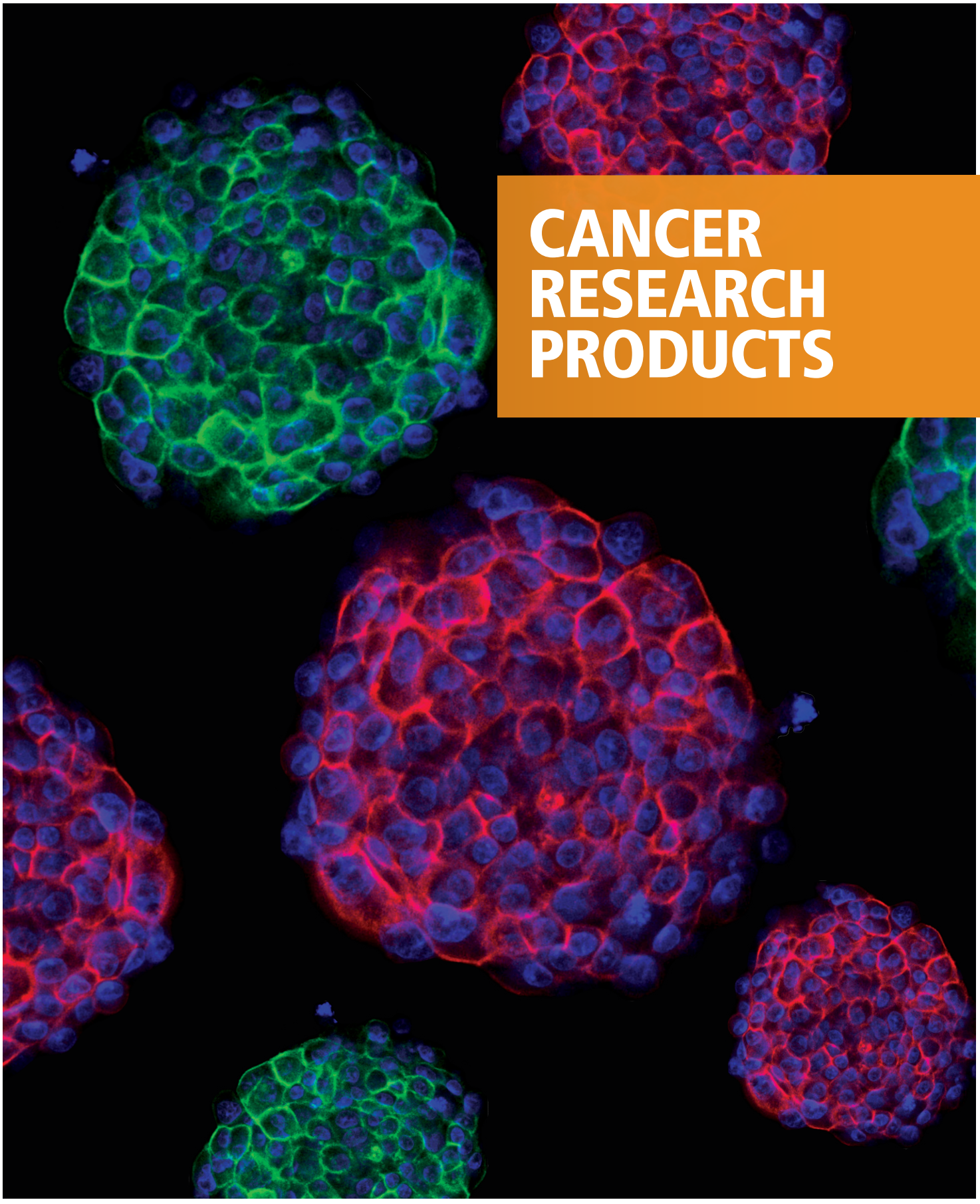


CANCER RESEARCH PRODUCTS

STEMCELL™ TECHNOLOGIES

Scientists Helping Scientists™ | WWW.STEMCELL.COM

TABLE OF CONTENTS

Cancer Spheroids

3D Cell Culture

Three dimensional (3D) cell culture is more physiologically relevant than traditional adherent or single cell culture methods. It provides a better representation of the in vivo microenvironment and is widely thought to be more predictive of disease state and drug response.

3D culture systems can be used for many applications, including disease modeling,[1,2] drug screening,[3] cell signaling and differentiation studies,[4] and 3D tissue engineering.[5]

3D Spheroids with AggreWell™

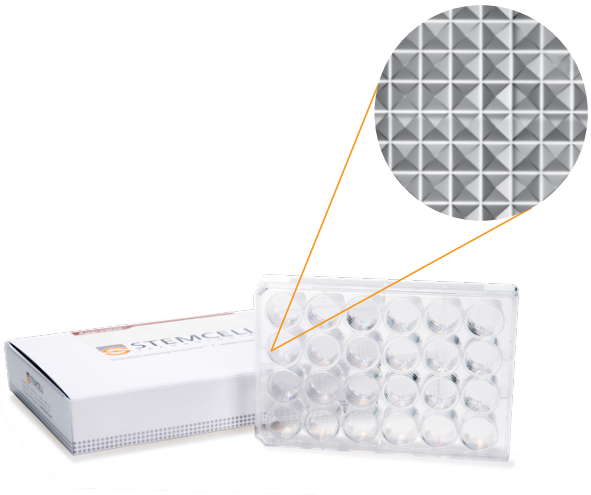
Easily generate large numbers of uniform 3D cancer spheroids with AggreWell™ plates. Each well contains a standardized array of microwells, allowing the production of highly uniform spheroids in just 24-48 hours. Spheroid size can be easily controlled by adjusting the cell seeding concentration.

AggreWell™ plates are compatible with a variety of cell types, including breast cancer,[6] prostate cancer,[7] colon cancer,[7] liver cancer[3,8,9] glioblastoma cell lines[10] and more.

AggreWell™ plates are available in 2 sizes of microwells and multiple plate formats to fit your research needs.

AggreWell™ Products for Spheroid Production

PRODUCT	SIZE OF MICOWELL	PLATE FORMAT	CATALOG #
AggreWell™400	400 µm	24-well plate	34411/34415
		6-well plate	34421/34425
AggreWell™800	800 µm	24-well plate	34811/34815
		6-well plate	34821/34825
Anti-Adherence Rinsing Solution	Required for use with AggreWell™ plates to ensure optimal performance.		07010



AggreWell™ Plate with Microwells.

Why Use AggreWell™?

- High yield of spheroids
- Uniform spheroids with consistant size & shape
- Low cost-per-spheroid
- Easy to use
- Reproducible
- Compatible with a variety of cell types

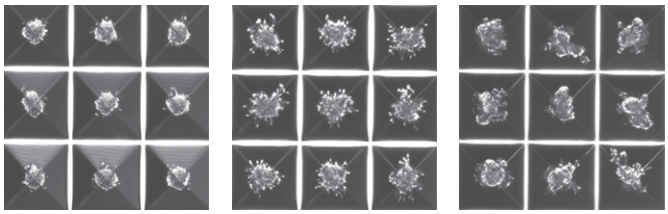


Figure 1. Cancer Spheroids Generated in AggreWell™

Cancer cell lines form uniform spheroids in AggreWell™. Shown are DU145 (prostate), A549 (lung) and MCF7 (breast) cancer cell lines, 500 cells per microwell in AggreWell™400.

For more information about AggreWell™, please visit us at **www.stemcell.com/Aggrewell** or email us at **aggrewell@stemcell.com**.

Cancer Stem Cell Research

ALDEFLUOR™ and ALDH^{br} Cells

The ALDEFLUOR™ fluorescent reagent system (Catalog #01700) has supported more than 2000 publications by detecting Aldehyde Dehydrogenase-bright (ALDH^{br}) cells in over 80 distinct cell types.

ALDEFLUOR™ was originally designed to identify a unique population of human stem and progenitor hematopoietic cells that exhibit elevated levels of ALDH expression. ALDEFLUOR™ is a non-immunological reagent system that enables identification, quantification and isolation of viable cells based on intracellular ALDH activity levels, rather than on cell surface phenotype. The utility of ALDH activity as a marker to identify multipotential hematopoeitic stem and progenitor cells has subsequently been extended to other applications, where it has been recognised as a useful marker for putative stem and progenitor cells in a variety of healthy and cancerous tissues.

A selected list of publications using ALDEFLUOR™ for cancer research is available at **www.stemcell.com/ALDreferences**.

ALDEFLUOR™ in Cancer Research

While not a universal marker for cancer stem cells in any tissue, ALDH activity has proven a useful marker for both normal and malignant cells with stem-like properties in a great variety of tissues. Increased ALDH expression has been found in multiple myeloma and acute myeloid leukemia (AML),[11-13] prostate,[14] colon,[15,16] head and neck,[17,18] thyroid gland,[19] breast,[20-22] liver,[23] ovarian,[24] cervical,[25] bladder,[26] brain[27] and lung[28] cancers. Studies have also shown a correlation between the ALDH phenotype and poor prognosis in various cancers.[24, 29,30]

REFERENCES
Selected Cancer References
www.stemcell.com/ALDreferences

VIDEO
The Basic FACS About ALDEFLUOR™
www.stemcell.com/BasicFACS

Why Use ALDEFLUOR™?

- No antibodies required
- Can be used with multiple species and cell types
- Compatible with immunophenotyping
- Compatible with standard cell sorters or analyzers
- Has supported 2000+ publications
- Highly reproducible results

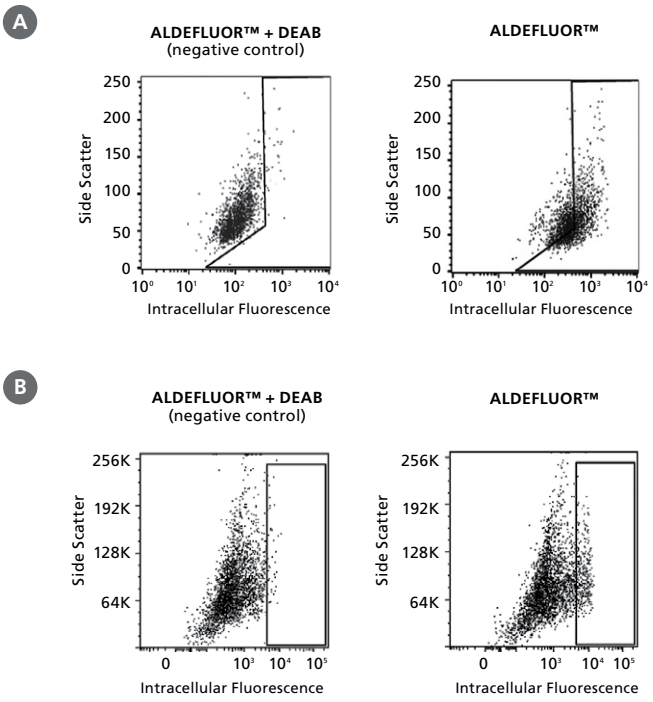


Figure 2. ALDEFLUOR™ is compatible with a variety of cell types.

ALDEFLUOR™ is used to detect ALDH activity in many cell types, including cancer cell lines and primary tissue samples. (A) SKBR3 breast cancer cells stained with ALDEFLUOR™. (B) Primary normal human mammary epithelial samples stained with ALDEFLUOR™.

Genome Editing

CRISPR-Cas9, an RNA-guided genome editing technology, is revolutionizing cell biology due to the ease and efficiency by which it enables genetic manipulation of mammalian cells. Through targeted modification of specific genes or regulatory regions, researchers can now rapidly generate precise genetic models to study normal and diseased cell physiology. Beyond genetic manipulation for research purposes, CRISPR-Cas9 genome editing also holds great potential for therapeutic applications, including immunotherapy and regenerative medicine.

Why Use ArciTect™?

CUSTOMIZABLE. Design crRNA to target your sequence of interest.

FLEXIBLE. Multiple variations of Cas9 to suit your specific genome editing needs.

RAPID. No need for transcription and translation.

REDUCED OFF-TARGET EFFECTS. Timely degradation of the RNP complex to minimize potential off-target cutting.

ArciTect™

ArciTect™ is a ribonucleoprotein (RNP)-based Cas9 genome editing system, which provides a rapid, flexible, and precise method of genome editing. Unlike previous CRISPR technologies which use plasmid or mRNA-based systems, the ArciTect™ system results in timely degradation of the RNP complex, minimizing cleavage of off-target regions.

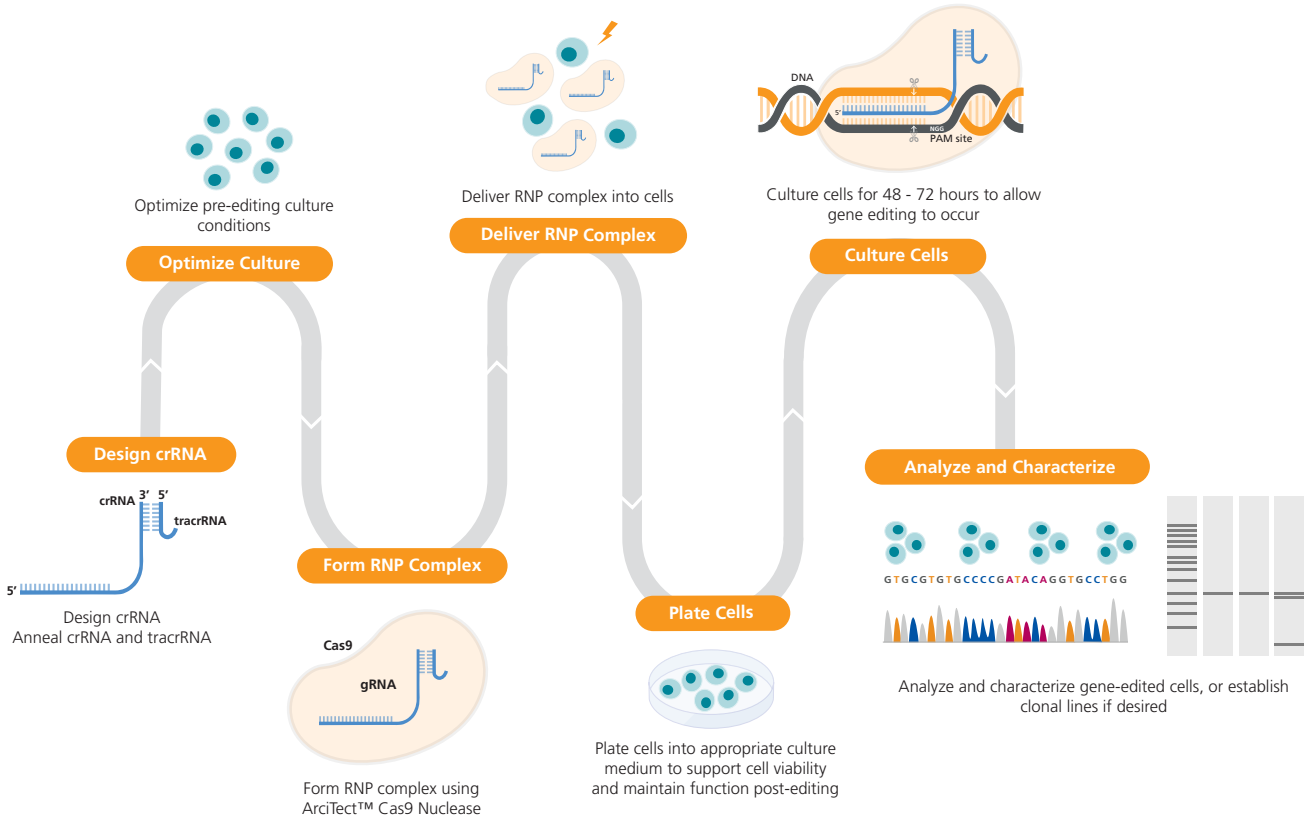


Figure 3. Genome Editing Workflow.

The guide RNA (gRNA) complex, consisting of a crRNA and tracrRNA, can be customized to target the genomic region of interest. Cells should be cultured in conditions optimized for cell quality, in preparation for genome editing. The ArciTect™ CRISPR-Cas9 RNP is then prepared and delivered into the cells, and cells are cultured for 48 - 72 hours to allow editing to occur. Following editing, clonal cell lines can be established and cells can be characterized for downstream applications.

Genome Editing for Immunotherapy Research

With improved expression and delivery methods, CRISPR-Cas9 genome editing is now rapidly being incorporated into the development of next-generation immunotherapies, such as chimeric antigen receptor (CAR) T cell therapy, wherein CRISPR-Cas9 enables generation of allogeneic immune effector cells that are compatible for patient infusion.[31] The ribonucleoprotein (RNP)-based ArciTect™ CRISPR-Cas9 system is designed to fully support genome editing of difficult-to-edit cell types such as human primary T cells.

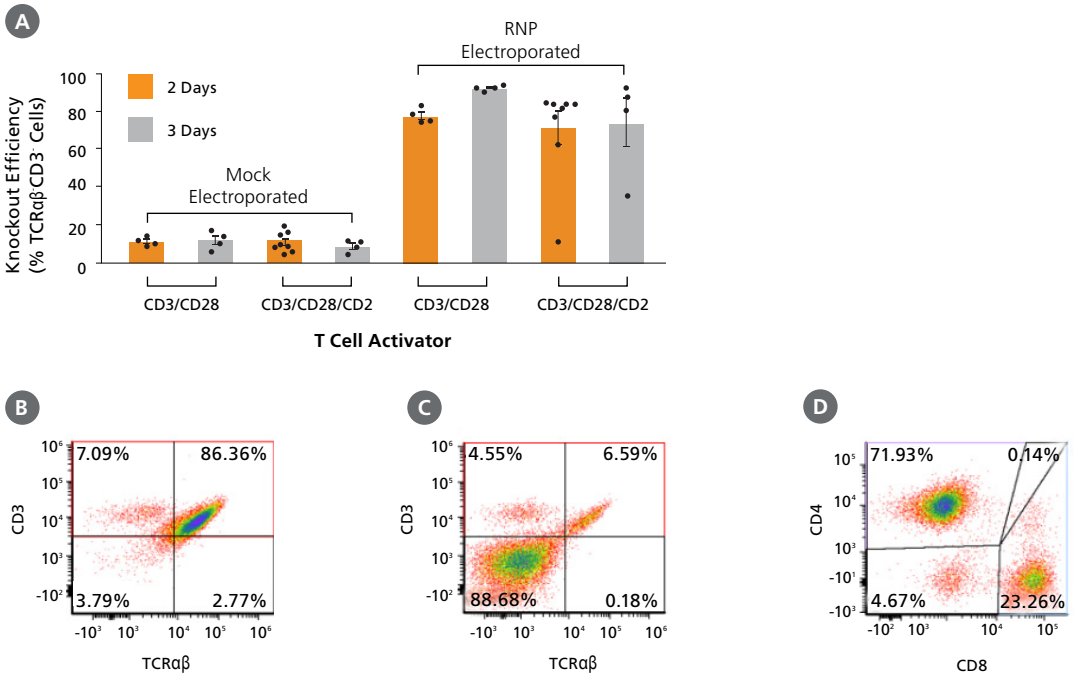


Figure 4. High Efficiency TRAC Knockout Across Activation Conditions and Dynamics, using ArciTect™.

Human T cells were activated with ImmunoCult™ Human CD2/CD28 or CD3/CD28/CD2 T Cell Activators for 2 or 3 days and the cells were electroporated with ArciTect™ RNP-complexes to knockout the T cell receptor (TCR) alpha constant (TRAC) locus. Knockout efficiency was assessed 2 days after electroporation by flow cytometry analysis of TCRαβ and CD3 expression, and 3 day activation with ImmunoCult™ Human CD2/CD28 T Cell Activator showed highest editing efficiency (A). Representative flow cytometry plots of control (mock electroporated, B) and edited T cells (RNP electroporated, C). Edited T cells retained expression of CD4 and CD8 (D).

Products for Genome Editing

PRODUCT	SIZE	CATALOG #
ArciTect™ crRNA	2 nmol 10 nmol 20 nmol	76010 76011 76012
ArciTect™ Cas9 Nuclease	100 µg 300 µg	76002 76004
ArciTect™ T7 Endonuclease I Kit	25 Reactions 125 Reactions	76021 76022

PRODUCT	SIZE	CATALOG #
ArciTect™ Human HPRT Positive Control Kit	1 Kit	76013
ArciTect™ tracrRNA Kit	5 nmol Kit 10 nmol Kit 20 nmol Kit	76016 76017 76018
ArciTect™ Annealing Buffer (5X)	1 mL	76020
ArciTect™ High-Fidelity DNA Polymerase Kit	500 Reactions	76026

For more information about Immunotherapy Research and STEMCELL's complete suite of product offerings to isolate, activate, expand, and edit T cells, please see page 13. Learn more at **https://www.stemcell.com/Arcitect**.

Organoids For Cancer Research

Tumor-derived organoids are adding new depth to cancer research by providing a biologically relevant model for studying cancer biology and disease progression. Organoids closely mimic the cellular heterogeneity, morphology, and tissue architecture of the originating cancer sample.[32-36] As such, organoids are proving to be invaluable tools for studying cancer biology, developing and screening novel cancer therapeutics, and predicting therapeutic response on a patient-by-patient basis.[37-39]

Intestinal Organoids

IntestiCult™ organoid media are complete media that support efficient establishment and long-term maintenance of intestinal organoids from mouse or human cells.

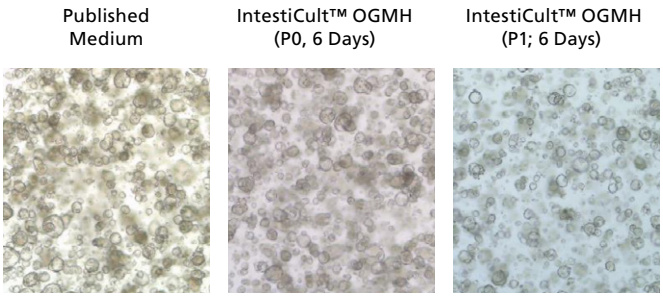


Figure 5. Growth of Cancer-Derived Organoids in IntestiCult™ Organoid Growth Medium (Human).

Organoids were established from colorectal cancer biopsies in published medium,[33] then switched to IntestiCult™ (P0). Cancer-derived organoids demonstrated efficient growth both after establishment in IntestiCult™, as well as after passaging. Data used with permission from Hubrecht Organoid Technology.

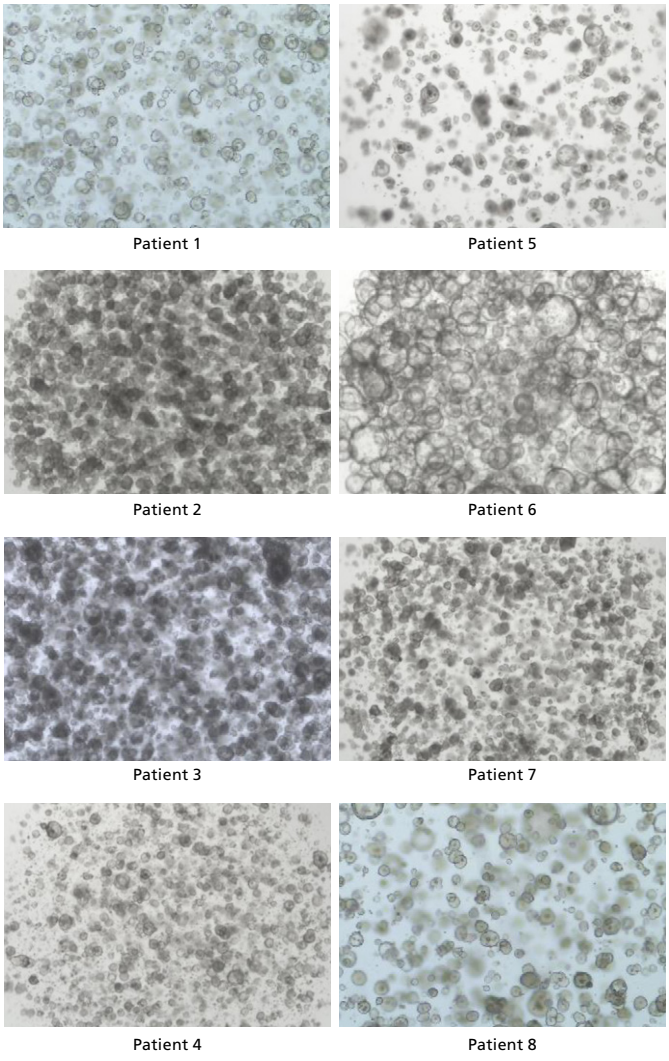


Figure 6. IntestiCult™ Organoid Growth Medium (Human) Enables Organoid Growth Across Different Patients

Organoids were established in published medium[33] from colorectal tumor biopsy samples, then switched to IntestiCult™. Organoids were passaged twice in IntestiCult™ and imaged at the end of the second passage (day 6 - 12). Data used with permission from Hubrecht Organoid Technology.

TECHNICAL BULLETIN

Read the protocol for culturing cancer-derived organoids in IntestiCult Organoid Growth Medium (Human).

www.stemcell.com/Intestinal-Cancer-Organoids

WEBINAR

From Stem Cells to Organoids: Modeling the Gastrointestinal Tract

www.stemcell.com/Huch_Webinar

TECH RESOURCE CENTER

Learn More About Organoids and Their Applications

www.stemcell.com/Organoids

Pancreatic Organoids

PancreaCult™ Organoid Growth Medium (Mouse) enables the growth of pancreatic exocrine organoids from pancreatic ducts, duct fragments, single cells, or organoid fragments.

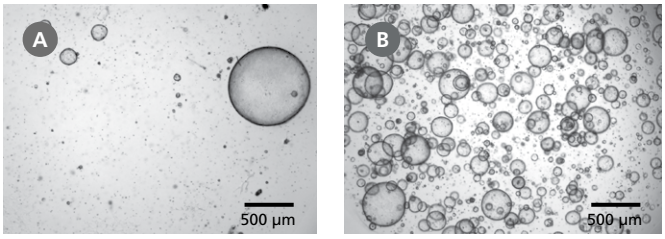


Figure 7. Pancreatic Exocrine Organoids Provide a Model for Pancreatic Carcinomas.

Pancreatic ducts were isolated from KPC mice ($Kras^{+/LSL\text{-}G12D}$; $Trp53^{+/LSL\text{-}R172H}$; Pdx1-Cre) and cultured in PancreaCult™ Organoid Growth Medium (Mouse). Organoids were imaged on day 4 of primary culture (A) and day three after the first passage (B). An activated KRAS genotype was retained in organoids during culture. Data used with permission from Dr. David Tuveson.

Prostate Organoids

ProstaCult™ Organoid Growth Medium (Mouse) is a serum-free cell culture medium for the establishment and long-term maintenance of mouse prostate organoids.

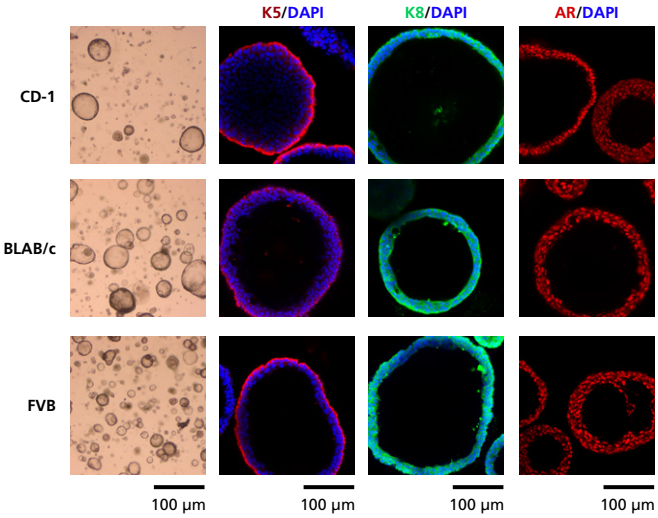


Figure 8. Prostate Organoids can be Established from Multiple Mouse Strains

Prostate organoids were derived from multiple mouse strains and cultured in ProstaCult™ Organoid Growth Medium (Mouse). The organoids exhibit a polarized, bilayered epithelium containing luminal cells that express androgen receptor (AR) and keratin 8 (K8), and basal cells that express Keratin 5 and 14 (K5, K14). Organoids can be passaged every 7 days, maintained indefinitely, and are karyotypically stable for at least 10 passages. They are also amenable to cryopreservation. Similar marker expression was observed in n=12 independent experiments.

Products for Culturing Organoids

PRODUCT	TYPE OF ORGANOID	CATALOG #
IntestiCult™ Organoid Growth Medium (Mouse)	Intestinal	06005
IntestiCult™ Organoid Growth Medium (Human)	Intestinal	06010
PancreaCult™ Organoid Growth Medium (Mouse)	Pancreatic	06040
HepatiCult™ Organoid Growth Medium (Mouse)	Hepatic	06030
ProstaCult™ Organoid Growth Medium (Mouse)	Prostate	06050
Gentle Cell Dissociation Reagent	Intestinal	07174
Anti-Adherence Rinsing Solution	All	07010
Reversible Strainers, 37µm/70µm/100µm	All	27250/27260/27270
CryoStor® CS10	All	07930

Brain Tumor Research

Multipotent neural stem-like cells, known as brain tumor stem cells (BTSCs) or cancer stem cells, have been identified and isolated from different grades (low and high) and types of brain cancers, including gliomas and medulloblastomas.[40,41] Similar to neural stem cells (NSCs), these BTSCs exhibit self-renewal, high proliferative capacity and multi-lineage differentiation potential in vitro.

BTSCs can either be cultured as free-floating aggregates (neurospheres) or as an adherent monolayer of cells. For both methods, cells are plated in a defined, serum-free medium in the presence of a mitogenic factor, such as EGF and/or bFGF. In the neurosphere system, cells are cultured in the absence of a culture substrate, which causes the cells to grow as non-adherent clusters - the neurospheres. Importantly, the neurosphere assay may be a clinically relevant functional read-out for the study of BTSCs, with recent research suggesting that renewable neurosphere formation in cultured human glioma samples may be a significant predictor of increased risk of rapid tumor progression and patient death.[42-44] Adherent monolayer culture has recently been shown to enable pure populations of glioma-derived BTSCs to be expanded in vitro.[45]

The standardized NeuroCult™ culture system provides a wide range of species-specific media and supplements, for the proliferation and differentiation of human, mouse and rat neural stem and progenitor cells from normal or tumor CNS tissue. Components for all NeuroCult™ media and supplements adhere to STEMCELL Technologies' renowned quality control standards, which include prescreening raw materials before manufacturing, and performance testing in relevant assays.

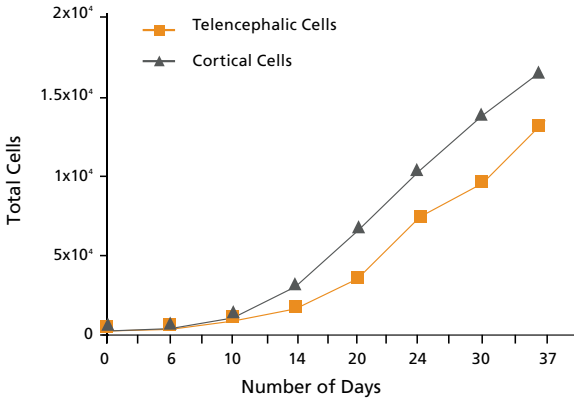


Figure 9. NeuroCult™ NS-A Proliferation Medium Supports the Growth of Neural Cells as Neurospheres

Total cell expansion for fetal human telencephalic and cortical cells cultured as neurospheres with complete NeuroCult™ NS-A Proliferation Medium containing rh EGF, rh bFGF and heparin (n = 2).

NeuroCult™ media and dissociation reagents have been used to:

- Dissociate human glioblastoma and oligodendroglioma samples[46]
- Culture human glioblastoma-derived[47-49] and oligodendroglioma-derived[50] tumorspheres
- Culture cells obtained from mouse models of medulloblastoma[51] and glioma[52] as tumorspheres
- Differentiate brain tumor stem cells into neurons, astrocytes and oligodendrocytes[51,52]
- Passage/dissociate tumorspheres[53]

Products for Brain Tumor Stem Cell Research

PRODUCT	CATALOG #
NeuroCult™ NS-A Proliferation Kit (Human)*	05751
NeuroCult™-XF Proliferation Medium*	05761
NeuroCult™ NS-A Differentiation Kit (Human)	05752
NeuroCult™ Proliferation Kit (Mouse)*	05702
NeuroCult™ Differentiation Kit (Mouse)	05704
NeuroCult™ NS-A Proliferation Kit (Rat)*	05771
NeuroCult™ NS-A Differentiation Kit (Rat)	05772

*Requires supplementation with rh EGF (Catalog #78006). When culturing cells obtained from adult mouse, rh bFGF (Catalog #78003) and Heparin (Catalog #07980) are also required.

WALLCHART
SnapShot: Glioblastoma Multiforme
www.stemcell.com/GlioblastomaWallchart

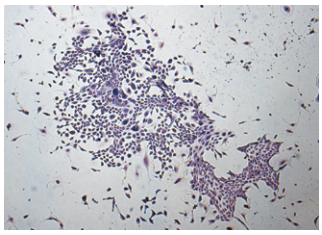
Breast Cancer Research

Understanding the organization of the mammary epithelial cell hierarchy is important for identifying the cell-of-origin for different types of human breast tumours, characterizing the cells that drive tumor growth, and understanding how different oncogenic mutations influence homeostasis within the normal mammary epithelium. Adherent and non-adherent in vitro colony-forming assays are valuable approaches for interrogating the functional heterogeneity present within normal human and mouse mammary tissue, within mammary tissue of genetically modified mice, and human breast tumor samples.

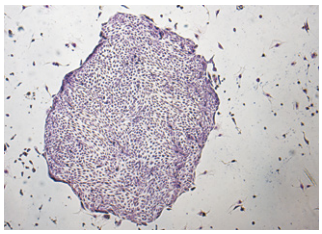
Culture and assay normal and malignant mammary cells using the defined MammoCult™ and EpiCult™ cell culture media. EpiCult™ media support the growth of human- and mouse-derived mammary epithelial cells in adherent culture. MammoCult™ is the most-published commercially-available medium for culture of human mammospheres derived from normal human mammary tissue and tumorsphere formation from multiple breast cancer cell lines.

Mammary Epithelial Colony and Sphere Images

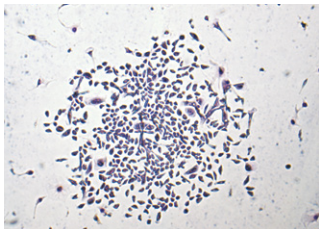
Examples of Colonies Derived From Human and Mouse Mammary Epithelial Progenitors



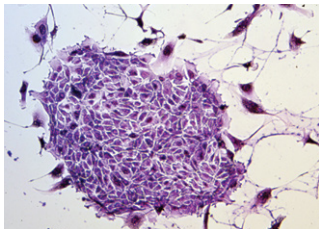
Normal Human Mixed-Lineage Colony



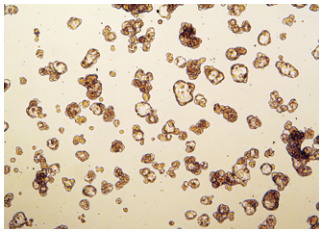
Normal Human Pure Luminal Cell Colony



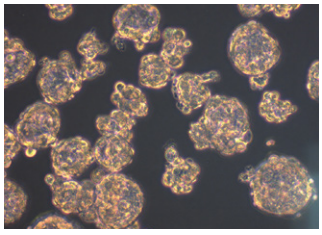
Normal Human Pure Myoepithelial Cell Colony



Normal Mouse Mammary Epithelial Colony



Mammospheres from Primary Normal Human Mammary Epithelial Cells



Tumorspheres from MCF7 Human Breast Cancer Cell Line

Products for the Assay and Culture of Primary Mammary Progenitor Cells

PRODUCT	APPLICATION	CATALOG #
EpiCult™-B (Human)	Colony-forming cell assay for differential assessment of progenitor content	05601
EpiCult™-B (Mouse)	Colony-forming cell assay for assessment of progenitor content	05610
EpiCult™-C (Human)	Short-term culture of primary human mammary epithelial cells	05630
MammoCult™	Generation of robust human mammospheres and tumorspheres in optimized and defined culture conditions	05620
ALDEFLUOR™	Identification, enumeration and isolation of viable normal and cancer cells on the basis of their ALDH activity	01700

MammoCult™ can be used to culture tumorspheres from primary breast cancer tissue and a variety of breast cancer cell lines including MCF7, MCF10A, SKBR3, MDA-MB-231, AU565, SUM149 and BT474.

Learn more at **www.stemcell.com/MammoCult**.

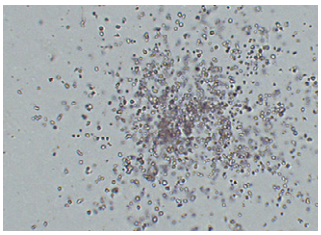
WALLCHART
SnapShot: Breast Cancer
www.stemcell.com/BreastCancerWallchart

Leukemia Research

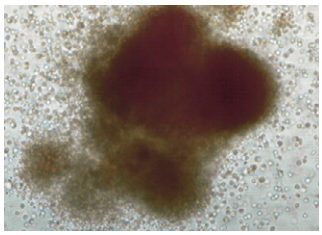
Leukemic cells have the capacity for clonogenic growth in vitro.[54] Often, culture methods and media used for the study of normal hematopoiesis are also useful for functional studies of leukemic cells. Leukemic cells can be cultured in colony-forming unit (CFU) assays in MethoCult™ medium, long-term culture-initiating cell (LTC-IC) assays in MyeloCult™ medium or in serum-free conditions with StemSpan™ serum-free expansion medium. Applications include research into the mechanisms underlying malignant transformation and cancer progression, or evaluating the responsiveness of patient cells to chemotherapeutic agents, such as specific inhibitors of the BCR-ABL tyrosine kinase in Chronic Myeloid Leukemia (CML).[55]

Hematopoietic Colony Images

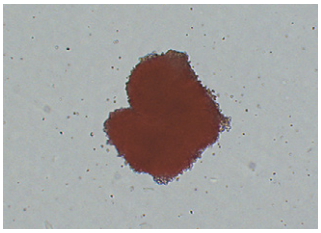
Examples of Colonies Derived From Human Hematopoietic Progenitor Cells



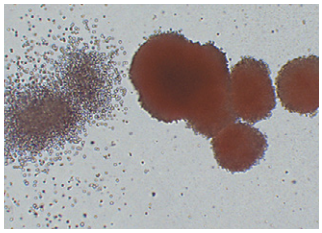
Human CFU-GM



Human CFU-GEMM

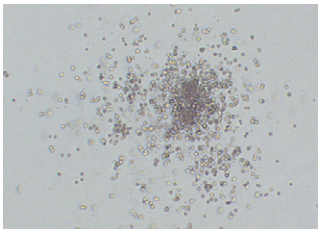


Human BFU-E

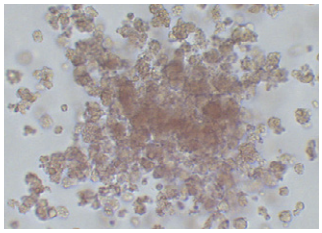


Human CFU-GM & BFU-E

Examples of Colonies Derived From Mouse Hematopoietic Progenitor Cells



Mouse CFU-M



Mouse BFU-E

Learn more at **www.stemcell.com/StemSpan**.

Products for the Assay and Culture of Hematopoietic Stem and Progenitor Cells

PRODUCT	CATALOG #	APPLICATION
StemSpan™ Leukemic Cell Culture Kit	09720	Serum-free medium and supplements for the culture, expansion, and drug screening of hematopoietic cells **www.stemcell.com/StemSpan**
StemSpan™ Serum-Free Expansion Medium	09600 09605 09850 09855	
StemSpan™ CD34⁺ Expansion Supplement	02691	
MethoCult™ for Human Cells	04100 04230 04236 04330	Methylcellulose-based media, available in a wide range of formulations for the detection of CFU-E, BFU-E, CFU-GM (including CFU-G and CFU-M), and CFU-GEMM in bone marrow and blood **www.stemcell.com/MethoCult**
	04034 04434 04435 04436	
	04035 04534 04535 04536	
MethoCult™ for Mouse Cells	03434	Methylcellulose-based media, available in a wide range of formulations for the detection of BFU-E, CFU-GM and CFU-GEMM in bone marrow, spleen, peripheral blood and fetal liver **www.stemcell.com/MethoCult**
	03534	
	03334 03234 03231	
MyeloCult™	05100 05300	Myeloid long-term culture medium for primitive hematopoietic cells **www.stemcell.com/MyeloCult**
UM729	72332	Small molecules that enhances the self-renewal of human hematopoietic stem cells in vitro

WALLCHART
Human Hematopoietic Progenitors
www.stemcell.com/HumanHemaWallchart

T Cell Therapy Research

Your breakthrough today can become the therapy of tomorrow. That's why we develop reagents and protocols to enable T cell therapy research and manufacturing. Because production of human T cells for cell therapy is a complex, multi-step process, there are many opportunities for optimization to obtain maximum yield while retaining desired end phenotype and function.

Explore optimized protocols and reagents for human T cell research:

Products for T Cell Therapy Research

PRODUCT	CATALOG #	APPLICATION
EasySep™ Human T Cell Isolation Kit	17951	Isolate highly purified human T cells in as little as 8 minutes using EasySep™ immunomagnetic cell separation technology. **www.EasySep.com**
EasySep™ Human CD4+ T Cell Isolation Kit	17952	
EasySep™ Human CD8+ T Cell Isolation Kit	17953	
EasySep™ Release Human CD3 Positive Selection Kit	17751	Isolate highly purified human T cells free of magnetic particles using EasySep™ Release positive selection technology. **www.EasySepRelease.com**
EasySep™ Release Human CD4 Positive Selection Kit	17752	
ImmunoCult™ Human CD3/ CD28 T Cell Activator	10971	Activate human T cells without the use of beads, feeder cells, or plate-bound antibodies. This technology is not exclusively licensed for the manufacturing of genetically modified T cells. **www.ImmunoCult.com**
ImmunoCult™ Human CD3/ CD28/CD2 T Cell Activator	10970	
ArciTect™ Cas9 Nuclease	76002	Perform high-efficiency genome editing of human primary T cells. **For more information, see pages 6-7.** **www.stemcell.com/Arcitect**
ArciTect™ crRNA	76010 / 76011 / 76012	
ArciTect™ tracrRNA kit	76016 / 76017 / 76018	
ArciTect™ Human HPRT Positive Control Kit	76013	
ImmunoCult™-XF T Cell Expansion Medium	10981	Expand functional human T cells in serum- and xeno-free culture medium optimized for rapid T cell expansion. **www.ImmunoCult.com**
StemSpan™ T Cell Generation Kit	09940	Generate $CD4^+CD8^+$ double-positive T cells—without the use of serum or stromal cells—from $CD34^+$ cord blood cells. **www.stemcell.com/StemSpan**
CryoStor® CS10, CS5 and CS2	07930 / 07933 / 07932	Cryopreserve T cells with animal component-free, cGMP-manufactured CryoStor® media. **www.stemcell.com/Cryostor**
Hypothermosol® FRS	07935	Protect cells, tissues and organs with animal component-free, cGMP-manufactured, hypothermic (2 - 8°C) preservation medium. **www.stemcell.com/HypoThermosol**

Learn more at **www.stemcell.com/T-Cell-Therapy**.

Cell Isolation for Cancer Research

Enrich cancer cells with our innovative cell separation platforms, RosetteSep™ and EasySep™, which provide an easy, fast and effective method for isolating rare cells with high purity and recovery.[56-58] With RosetteSep™, cells are isolated directly from human whole blood during density gradient centrifugation, reducing your cell isolation workflow to a single step. With EasySep™, human cells are isolated immunomagnetically by either positive or negative selection from many types of samples without the use of columns. EasySep™ can be fully automated using RoboSep™.

Circulating Tumor Cells

Enrich circulating tumor cells (CTCs) from whole blood, bone marrow and fresh or previously frozen human mononuclear cells with our optimized cell isolation products. Isolated cells are untouched and immediately ready for cell culture, DNA/RNA isolation for genetic analyses, further purification using microfluidics and other downstream assays.

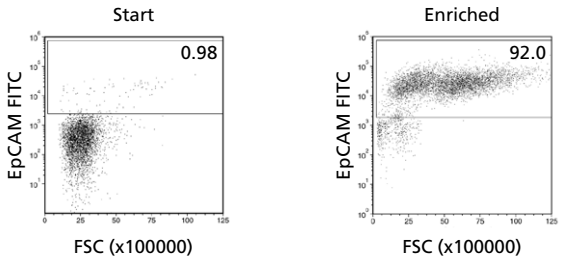


Figure 10. Typical EasySep™ Direct Human CTC Enrichment Kit Profile (Catalog #19657)

Starting with human whole blood from healthy donors, spiked with approximately 1% of CAMA cells (epithelial tumor cell line), the CTC (EpCAM+) content of non-lysed final enriched fraction is 79 ± 16 % (gated on DRAQ5+). Typically the log depletion of targeted CD45⁺ cells ranges from 2.8 to 3.2.

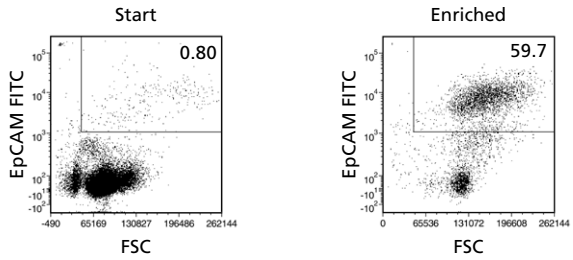


Figure 11. Typical RosetteSep™ CTC Enrichment Profile (Catalog #15177)

Starting with human whole blood from healthy donors, spiked with approximately 0.8% of CAMA cells (epithelial tumor cell line), the CTC (EpCAM⁺) content of non-lysed final enriched fraction, in the example above, is 59.7%.(gated on DRAQ5⁺). Typically the log depletion of targeted CD45⁺ cells ranges from 3.2 to 4.2.

PRODUCT	CATALOG #	RECOMMENDED FOR:
RosetteSep™ CTC Enrichment Cocktail Containing Anti-CD36	15127	Enrichment of CTCs directly by depleting hematopoietic cells from whole blood. CD36 has been shown to be expressed on a small subset of breast cancer samples.[59,60] For enrichment of CTCs from breast cancer samples we recommend using #15122 or #15137.
	15167 (5 x 15127)	
RosetteSep™ CTC Enrichment Cocktail Containing Anti-CD56	15137	Enrichment of CTCs by depleting hematopoietic cells from whole blood. CD56 has been shown to be expressed on small cell lung cancer (SCLC) and pancreatic carcinoma samples.[61-63] For enrichment of CTCs from SCLC and pancreatic carcinoma samples we recommend using #15122 or #15127.
	15177 (5 x 15137)	
EasySep™ Direct Human CTC Enrichment Kit	19657	Enrichment of CTCs directly from WB without the need for pre-processing steps such as density gradient centrifugation, sedimentation or lysis.
RosetteSep™ Human CD45 Depletion Kit	15122	Enrichment of CTCs by depleting CD45⁺ cells from whole blood.
	15162 (5 x 15122)	
EasySep™ Human CD45 Depletion Kit II*	17898	The enrichment of CTCs by depleting CD45⁺ cells from fresh or previously frozen peripheral blood human mononuclear cells (PBMCs).

*Automate EasySep™ cell isolations with RoboSep™ instruments (**www.RoboSep.com**).

Hematological Malignancies

For hematological malignancies such as Multiple Myeloma (MM) and B-Cell Chronic Lymphocytic Leukemia (B-CLL), it is important to identify underlying mutations with the highest-possible sensitivity and accuracy. Techniques to profile genetic abnormalities include fluorescence in situ hybridization (FISH), array-based comparative genomic hybridization (array-CGH) and array-based single-nucleotide polymorphism analysis (array-SNP), to name some examples. Enriching blood samples for the malignant cells prior to cytogenetic analysis has been shown to improve and enhance the sensitivity of FISH and array-based assays.[64,65]

Improve the sensitivity of your assays by enriching cells with our products optimized for MM and B-CLL:

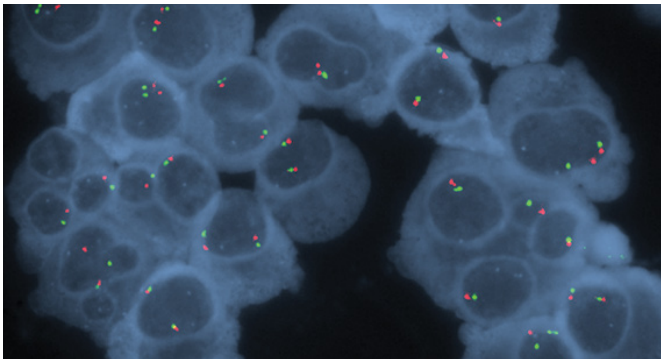


Figure 12. Enrichment of plasma cells by CD138 positive selection can enhance the sensitivity of downstream FISH analysis.

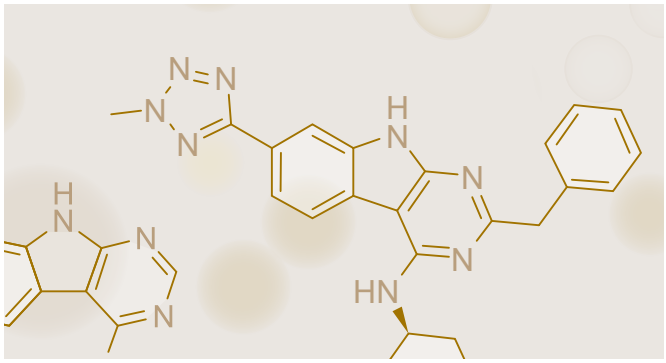
APPLICATION	PRODUCT	CATALOG #	RECOMMENDED FOR:
Multiple Myeloma (CD138) Cells	RosetteSep™ Multiple Myeloma Cell Enrichment Cocktail	15129	Enrichment of untouched multiple myeloma cells (B cells and plasma cells) from bone marrow aspirates.
		15169 (5 x 15129)	
	EasySep™ Human CD138 Positive Selection Kit II*	17877 (MNC)	Selection of highly purified CD138$^+$ cells from MNCs, bone marrow (BM) or whole blood (WB).
		17887 (BM and WB)	
B Cells From Chronic Lymphocytic Leukemia (CLL) Samples	EasySep™ Human B Cell Enrichment Kit II Without CD43 Depletion*	17963	Enrichment of untouched B cells from PBMCs of leukemia or lymphoma samples, in which B cells may express CD43.
	EasySep™ Direct Human B-CLL Cell Isolation Kit	19664	Enrichment of untouched B cells from whole blood of CLL samples, in which B cells may express CD43. Cells are enriched without the need for density gradient centrifugation, sedimentation or lysis.

*Automate EasySep™ cell isolations with RoboSep™ instruments (**www.RoboSep.com**).

Accessory Products

Small Molecules

Small molecules can be used in cancer research to understand mechanisms of cancer, identify signaling pathways, assess the effect of inhibiting certain signals, and can also be tested in vitro as potential therapeutics. For a complete listing of the small molecules available from STEMCELL Technologies, which are used in high impact cancer research, please visit **www.stemcell.com/SmallMolecules**.

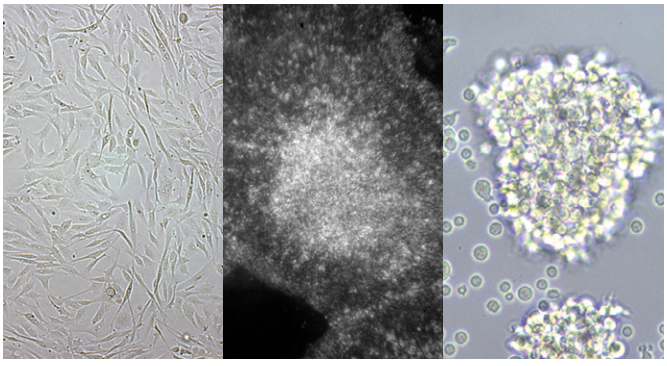


GloCell™ Fixable Viability Dyes

Easily assess cell viability with GloCell™ Fixable Viability Dyes. GloCell™ dyes irreversibly bind intracellular and cell surface amine groups, are resistant to washing and fixation, and are compatible with flow cytometry and intracellular staining protocols. Stained cells can also be cryopreserved without loss of fluorescence intensity. Learn more at **www.stemcell.com/GloCell**.

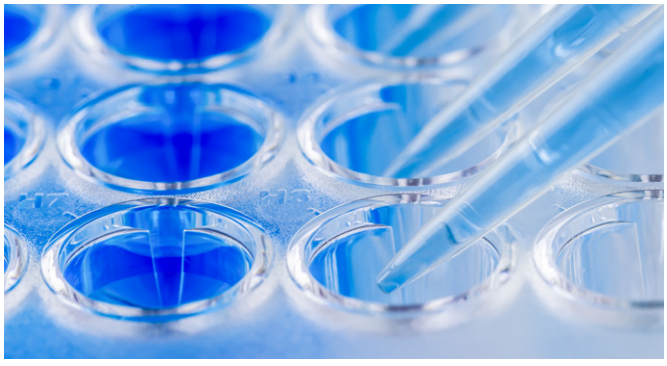
Cryopreservation and Storage Media

Preserve your cell and tissue samples with STEMCELL's suite of cGMP-manufactured, protein-free and serum-free cryopreservation and storage media products that are designed to maintain high cell viability and maximize cell recovery. CryoStor® and HypoThermosol® FRS are compatible with a range of cell types and have a US FDA Drug Master File. Learn more at **www.stemcell.com/Cryopreservation**.



ELISAs

The enzyme-linked immunosorbent assay (ELISA) is a highly sensitive assay to detect and quantify cytokines, hematological factors, hormones, peptides, and immunoglobulins produced by cells. Take the guesswork out of cell analysis by using ELISA kits that are compatible with your workflow and feature low intra- and inter-assay variability for accurate, precise, and consistent analyte quantification. Learn more at **www.stemcell.com/Elisa**.



Contract Assay Services

Contract Assay Services (CAS) is a CRO within STEMCELL Technologies. We leverage the power of specialized STEMCELL Technologies reagents within our technical expertise to provide standardized and customized cell-based assay services for pharma and biotech clients.

We work with our clients to design and execute cell-based assays to meet your needs. Our primary cell-based assays can provide clinically relevant results of the effects of small molecule compounds, including chemotherapeutic agents or biologics. We offer standardized and customized primary cell-based assays for hematopoietic, immune and mesenchymal cells.

Why Choose CAS?

QUALITY. We use the highest standards for methods, materials and processes.

COMMUNICATION. Clear, frequent communication with clients throughout the study process.

COMPLIANCE. STEMCELL Technologies is a world leader in the development of industry-standard products for stem, progenitor and other primary cells.

EXPERTISE. In-house experts are available for many cell types, media and assays.

Predicting Hematoxicity

Assays for predicting hematoxicity are critical during the development of oncology drugs. We offer gold standard colony-forming unit (CFU) assays and the new, higher throughput HemaTox™ assays. Both assays measure the effects of drugs on the growth and lineage-specific differentiation of hematopoietic stem and progenitor cells (HSPCs) into various lineages (erythroid, myeloid, or megakaryocyte (dependent upon species)). These assays can be used in toxicity testing to predict myelosuppression, anemia and thrombocytopenia, or to assess effects of potential therapeutics on cell fate or differentiation.

- CFU assays, which use a semi-solid medium, assess proliferation and differentiation potential through colony formation, which requires expertise in colony identification. CFU assays for some hematopoietic progenitor cell lineages have been validated for their ability to predict in vivo parameters, such as maximum tolerated dose[66] and C_{max}[67].
- HemaTox™ is a liquid-based assay performed in a 96-well plate, which enables higher throughput studies. HemaTox™ assays show similar drug toxicity trends as those identified in CFU assays, and allow for flexible treatment regimens and improved ability to evaluate the effects of anti-proliferative drugs in vitro.

Immune Toolkit for Immuno-oncology

We also offer support for customized immuno-oncology studies, including design and optimization of assays to evaluate the immunomodulatory effects of potential therapeutics. Types of assays and custom services include:

- Flow cytometric marker analysis
- Proliferation and viability assessments
- Quantitation of secreted proteins (e.g. ELISA and MesoScale)
- T cell assays, including activation and suppression
- Immune cell differentiation (e.g. macrophage, dendritic cells)
- Custom cell isolation and culture

Good Data Doesn't Just Happen. Let us help.
Learn more at **www.ContractAssay.com**.

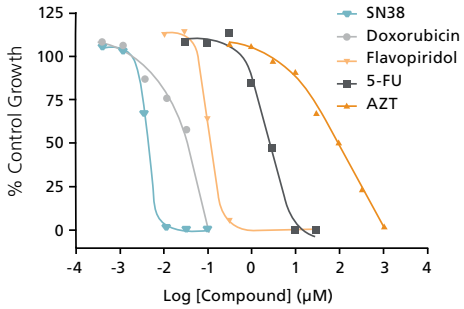


Figure 13. Dose-response curves of the effect of various cytotoxic compounds on human bone marrow-derived myeloid progenitor proliferation in the CFU assay.

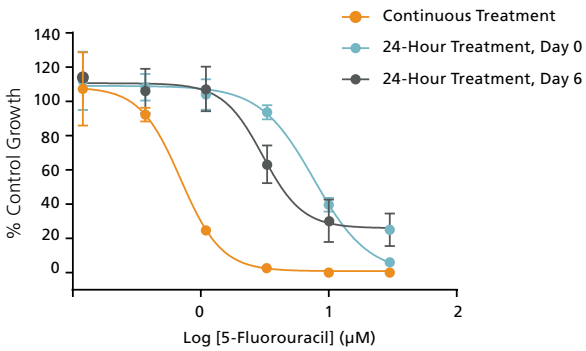


Figure 14. Dose-response curves of the effect of 5-Fluorouracil on myeloid cells in different treatment regimens, measured using the HemaTox™ assay.

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TOLL FREE PHONE 1 800 667 0322
PHONE +1 604 877 0713
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