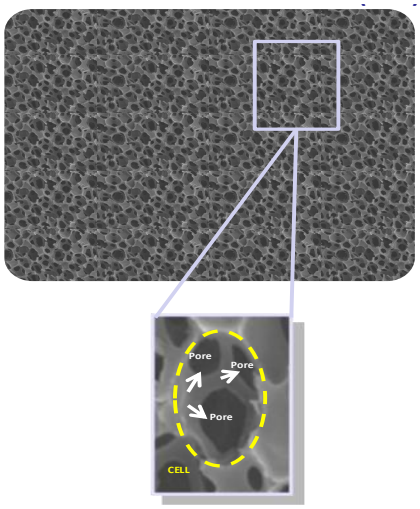
Biomerix 3D Scaffold™

The **Biomerix 3D Scaffold™** is designed to mimic the nature and function of the extracellular matrix (ECM) for stem cell research and therapeutic applications in regenerative medicine

Biomerix 3D Scaffold™
(SEM 23X)



- **Chemical Formulation**
  - Polycarbonate polyurethane-urea thermoset chemistry
- **Fully Reticulated 3D Morphology**
  - Interconnected 3D network of cells and pores
  - Open-cell, porous structure with void content of >90%
- **Demonstrated Biocompatibility with Multiple FDA Clearances**
  - Full panel of ISO 10993 biocompatibility testing completed
  - Ten regulatory clearances in the US, EU, and Canada for soft tissue repair, orthopedic, and vascular applications
- **Ideal Platform for Stem Cell Therapy & Regenerative Medicine**
  - Applications in drug discovery, tissue engineering, & cell banking
- **Available Form Factors & Pricing**
  - 25 cylindrical discs, 5 mm diameter x 2 mm thickness
  - Other custom form factors available upon request

Biomerix 3D Scaffold™ Features & Benefits

Features	Mimic *In-Vivo* Conditions	Enhance Cell Viability	Promote ECM Synthesis	Optimize 3D Cell-ECM Interactions	Provide Stable Environment	Support Cell Differentiation	Maximize Throughput
Biostable Polyurethane Chemistry					✓		✓
Interconnected 3D Network of Cells & Pores	✓	✓	✓	✓		✓	✓
High (>90%) Porosity	✓	✓	✓	✓		✓	✓
High Surface Area to Volume Ratio	✓	✓	✓	✓		✓	✓
High Affinity for Proteins & Peptides	✓	✓		✓		✓	✓
Reproducible-High Volume Manufacturing Process		✓		✓	✓	✓	✓
Biocompatible	✓	✓	✓	✓	✓	✓	✓

BIOMERIX™
Structured for Life.

Studies Evaluating Biomerix 3D Scaffold™ in Regenerative Medicine

Ex-Vivo Hematopoietic Stem Cell Niche in the Rotary Cell Culture System™

Collaboration with Dr. Stephen Navran, Synthecon Inc., TX

Objective:

- **Create a bioartificial hematopoietic stem cell niche to expand umbilical cord blood stem cells**

Methods:

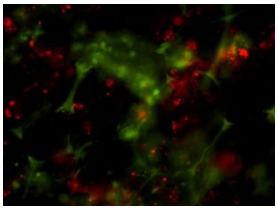
- **Bone marrow stromal cells (MSC) expressing GFP cultured on *Biomerix 3D Scaffold* in Rotary Cell Culture System**
- **Umbilical Cord Blood (UCB) cells labeled with $DiIC_{18}$-DS introduced into the bioreactor in suspension**

Results:

- **UCB cells homed to the stroma/scaffold bioartificial niche**
- **The niche construct was maintained for at least 2 weeks**

Conclusions:

- **The combination of *Biomerix 3D Scaffold* and a dynamic rotary cell culture bioreactor can create a bioartificial niche for the expansion of rare UCB stem cells**



Bone Marrow MSC and Umbilical Cord Blood Cells

Bone Marrow Hematopoetic Niche Formation in an *In Vivo* Transgenic Mouse Model

Collaboration with Dr. Daniel Kraft, Stanford University School of Medicine, CA

Objective:

- **Investigate bone marrow hematopoetic niche formation in the *Biomerix 3D Scaffold***

Methods:

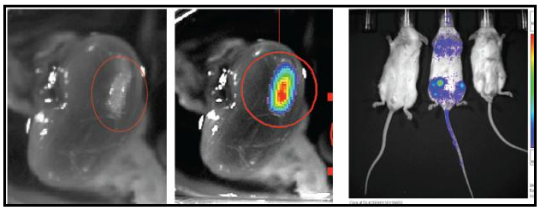
- **Marrow cells isolated from adult and fetal mice (Luciferase transgenic)**
- **Artificial marrow created in the *Biomerix 3D Scaffold***
- **Controls fabricated using intact whole bone marrow and Matrigel**
- **Constructs implanted into the renal capsule of GFP+ transgenic mice**
- **Donor cells tracked *in vivo* for up to eight months; homing of host cells to the niche tracked using GFP+**

Results:

- **Excellent results in terms of *in-vivo* viability of HSCs in the *Biomerix Scaffold,* with kidney capsule Biomerix grafts maintained *in-vivo* for up to eight months**
- ***Biomerix 3D Scaffold* allows transplanted HSCs to establish and expand**
- ***Biomerix 3D Scaffold* also formed osteogenic niche from the fetal cells**

Conclusions:

- ***Biomerix 3D Scaffold* is an excellent platform for bone marrow niche formation and expansion of hematopoetic stem cells**



Kidney with Biomerix 3D Scaffold two weeks after implantation. Note strong bioluminescent signal from donor derived marrow cells. Biomerix 3D Scaffold appeared to be somewhat hard, consistent with early bone formation (osteogenesis). Cells from the scaffold were transplanted to secondary recipient after sublethal irradiation (400Gy). Engraftment is evident (middle mouse), from Biomerix 3D Scaffold derived transplanted cells.

Ectopic Human Mesenchymal Stem Cell-Coated Scaffolds in NOD/SCID Mice: An *In-Vivo* Model of the Leukemia Niche

Collaboration with Dr. Sarah R. Vaiselbuh, Feinstein Institute for Medical Research, NY

Objective:

- **Evaluate potential of *Biomerix 3D Scaffold* to support malignant hematopoiesis within the human stromal microenvironment**

Methods:

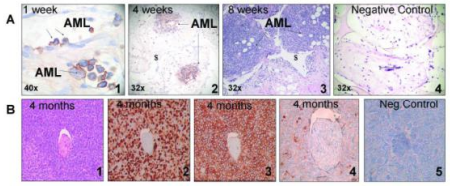
- **MSCs isolated from human bone marrow obtained electively after orthopedic surgery**
- **MSC-coated *Biomerix 3D Scaffolds* prepared *in-vitro* for 24-48 hours**
- **Ectopic MSC-coated scaffolds implanted in NOD/SCID mice and injected with primary AML cells**
- **Known leukemia CXCR4 antagonist used to treat AML niche *in-vivo***
- **Scaffolds harvested at 1, 4, 8, and 16 weeks and analyzed histologically**

Results:

- **Leukemia niche successfully maintained for 4 months in murine model, supporting a human bone marrow stromal network of human AML cells**
- **CXCR4 leukemia antagonist shown to disrupt MSC stromal formation**

Conclusions:

- ***Biomerix 3D Scaffold* provides excellent platform to create *in-vivo* disease models that can be used for targeted drug discovery**



Novel Flow-Perfusion Bioreactor with Biomerix 3D Scaffold™

Collaboration with Dr. Stephen W. Warren, New York University Medical Center, NY

Objective:

- **Demonstrate that large 3D constructs of the *Biomerix 3D Scaffold* support viable cellular distribution, density, and metabolic activity using murine preosteoblasts in a novel flow-perfusion bioreactor**

Methods:

- **Murine preosteoblastic cells seeded onto large *Biomerix 3D Scaffold* discs (24 x 6 mm)**
- **Static culture scaffolds maintained in culture plates**
- **Dynamic culture scaffolds loaded into custom flow-perfusion bioreactor designed to optimize chemotransportation**
- **Scaffolds harvested at 0, 2, 4, 6, and 8 days and analyzed histologically**

Results:

- **Flow-perfusion culture promotes cellular viability in the *Biomerix 3D Scaffold* with significantly higher cellular density and metabolic activity compared to static culture**

Conclusions:

- **Large constructs of the *Biomerix 3D Scaffold* support chemotransportation & viable cellular activity in a flow-perfusion bioreactor, and may enable prefabrication of biological constructs large enough to solve clinical problems**