

The AlphaSTEM Test™ Service

*A New Technology from Asymmetrex for
Evaluating the Effects of Drug Candidates on
Natural Adult Tissue Stem Cells
Including Efficacy and Safety*

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First, a few tissue stem cell concepts:

Importance for health, disease, drug effects

- Rare cells in the tissues of children and adults that are essential for tissue cell renewal and repair.
- Positive-acting drugs could increase healing.
- Negative-acting drugs could cause intolerable chronic organ failure.

A Stem Cell Drug Evaluation Need

Convenient and routine identification and evaluation of tissue stem cell-active drugs is a long-standing unmet need in the pharmaceutical industry.

Why?

No practical means to *specifically* quantify adult tissue stem cells for drug evaluation assays.

Previously Available Technologies

Preclinical assays

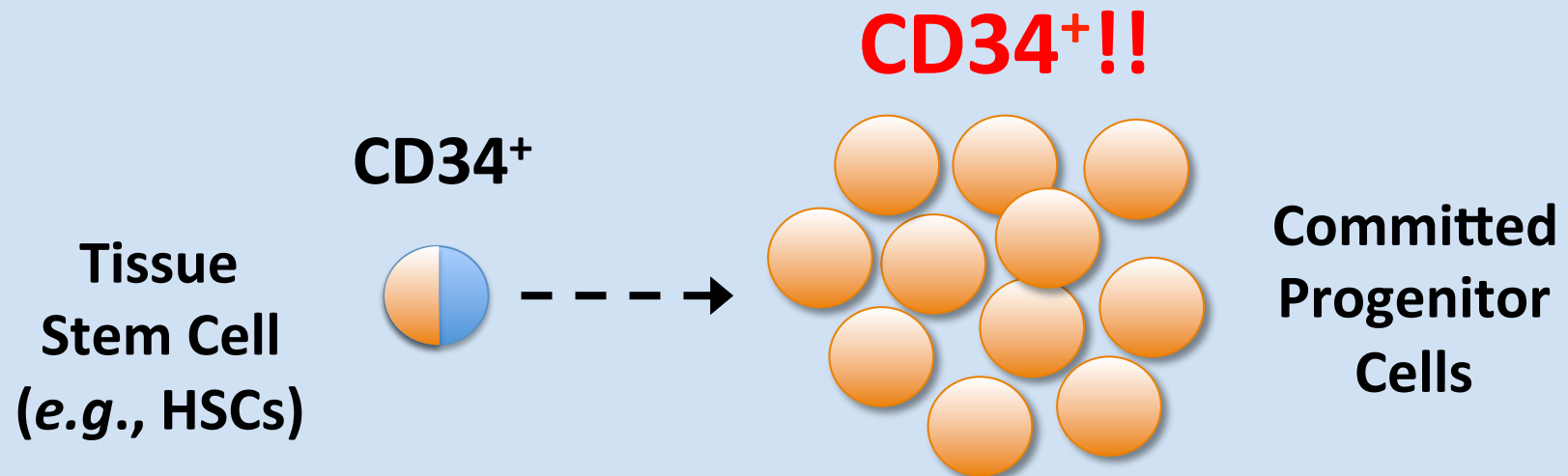
- Colony forming assays are unreliable and not specific
- SCID mouse assays are long, costly, non-quantitative
- Animal dosing is long, costly, and sometimes insensitive for chronic organ failure caused by stem cell toxicity

Clinical trials

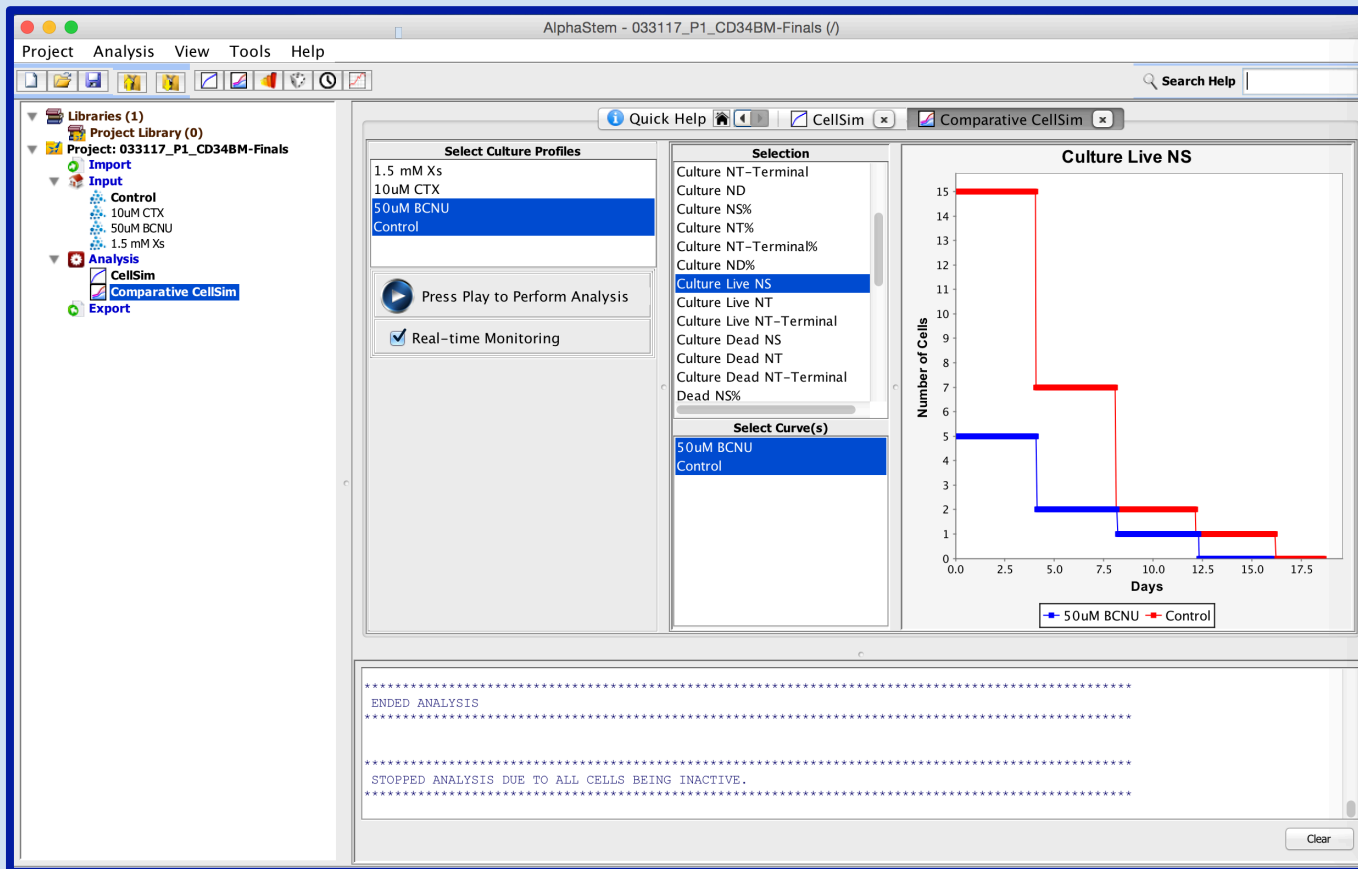
- Toxicity often not noted until in phase II, III, or later
- Very expensive
- Patients at risk for injury by unknown stem cell-toxic candidates

Why hasn't it been possible to specifically count adult tissue stem cells for drug discovery?

Poor Specificity Biomarkers
Also expressed on progenitor cells.



Using Computational Simulation The AlphaSTEM Test™ Software Can Count Tissue Stem Cells Specifically



The AlphaSTEM Test™

- **Validated for 4 Human Tissue Stem Cell Types (Hematopoietic, Liver, Lung, Mesenchymal)**
- **Validated for detecting SC-activating agents**
- **Validated for detecting SC-toxic agents**

The AlphaSTEM Test™ Service

Cell Count Data
From Control vs.
Test Articles

AlphaSTEM Test™
Computational
Simulation

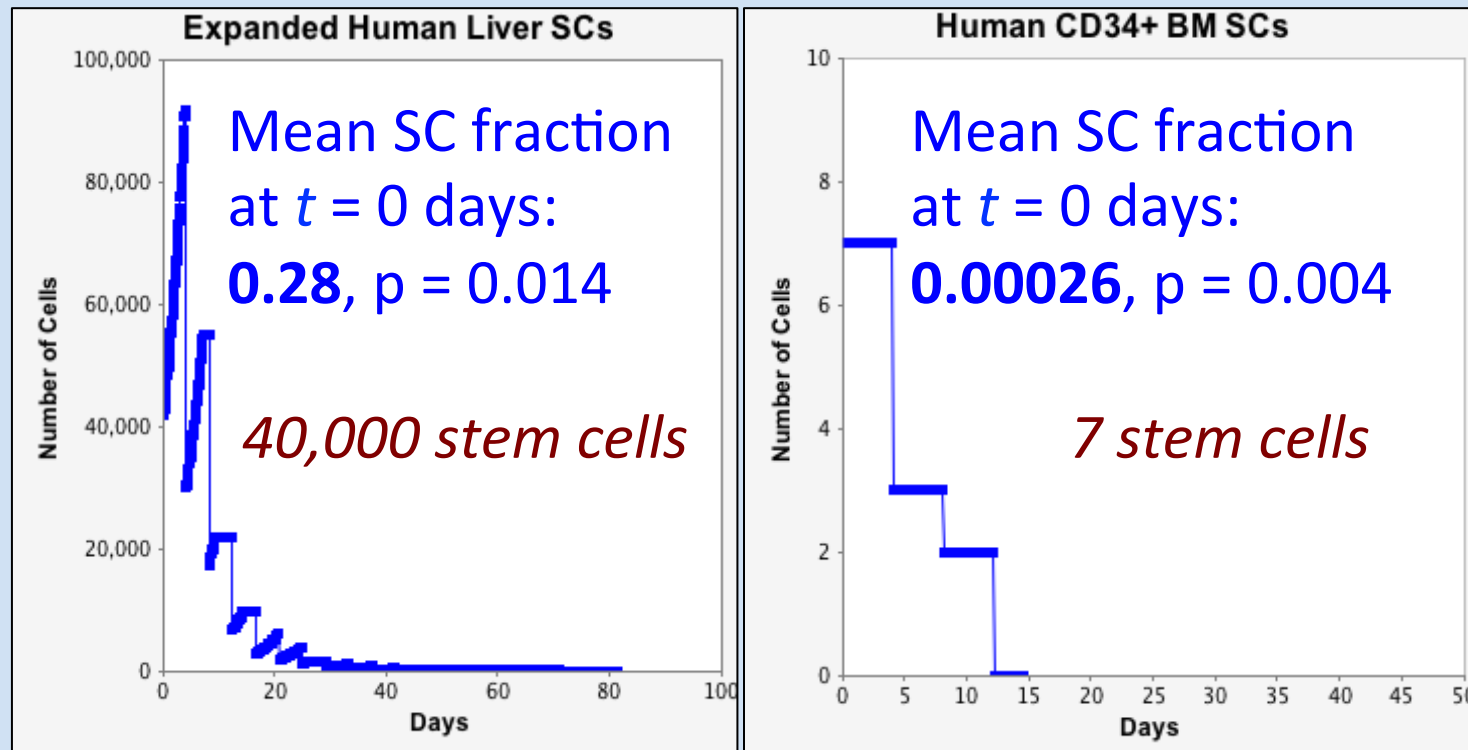
- Neutral Results
- Activating Results
- Toxic Results

For more information visit:

<http://asymmetrex.com/our-services/alphastem-test/>

Detecting Differences in the Cell Kinetics of Different Types of Adult Tissue Stem Cells

(AlphaSTEM Test™ Outputs)



Quantifying Tissue Stem Cell-Active Drugs

Xanthosine, activating (+); BCNU, toxic (-)

Parameter	Liver	CD34+	CD34+	
			Xs (+)	BCNU (-)
<u>Stem Cells</u>				
Initial Fraction	0.28 (0.014)	2.6e-4 (0.004)	3.5e-3 (0.001)	1.3e-4 (0.001)
Symmetric Rate	0.24 (0.048)	1.3e-3 (NS)	3.2e-3 (0.037)	0.0 (NS)
Sym CC Time	30h (2e-4)	7.8h (<1e-4)	9.4h (NS)	8.2h (NS)
Asym CC Time	16h (1e-4)	7.0h (2e-4)	6.6h (NS)	7.6h (NS)
<u>Non-stem cycling cells</u>				
CC Time	18h (3e-4)	6.8h (<1e-4)	8.2h (NS)	6.4h (NS)

Detecting Tissue Stem Cell Toxicity

<u>Drug</u>	<u>Liver Stem Cells</u>	<u>Bone Marrow Stem Cells</u>
<i>Cytoxan</i>	(indeterminate) ¹	Toxic
<i>BCNU</i>	Toxic	Toxic
<u><i>Idarubicin</i></u>	Toxic	Toxic

¹may require evaluation at a higher concentration

Tissue stem cell-toxic drug candidates cause chronic organ failure.

In the U.S., an estimated \$4-5 billion is loss yearly due to failure of such drugs in animal studies and phase II and III clinical trials.

The AlphaSTEM Test™ could save the Pharma industry billions each year by detecting these problem candidates early and at much less cost.

For a Brief Video Presentation Of the AlphaSTEM Test™

Visit:

<https://www.dropbox.com/s/yry16pwul8t6rzv/Asymmetrex.mp4?dl=0>