

#### **Biotech Showcase 2019**

January 9, 2019

The matters discussed in this presentation include forward looking statements which are subject to various risks, uncertainties, and other factors that could cause actual results to differ materially from the results anticipated. Such risks and uncertainties include but are not limited to the success of AgeX Therapeutics and its affiliates in developing new stem cell-based products and technologies; results of clinical trials of such products; the ability of AgeX and its licensees to obtain additional FDA and foreign regulatory approval to market products; competition from products manufactured and sold or being developed by other companies; the price of and demand for such products; the ability of AgeX and its subsidiaries to maintain patent and other intellectual property rights; and the ability of AgeX to raise the capital needed to finance its current and planned operations. Any statements that are not historical fact (including, but not limited to statements that contain words such as "will," "believes," "plans," "anticipates," "expects," "estimates") should also be considered to be forward-looking statements. As actual results may differ materially from the results anticipated in these forward-looking statements they should be evaluated together with the many uncertainties that affect the business of AgeX and its other subsidiaries, particularly those mentioned in the cautionary statements found in AgeX's Securities and Exchange Commission filings. AgeX disclaims any intent or obligation to update these forward-looking statements.

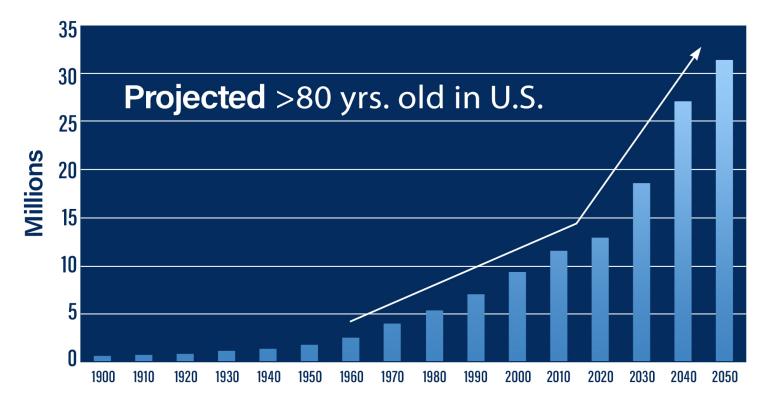


#### Mission

AgeX Therapeutics is focused on the development of young cell-based regenerative therapies for the treatment of human aging.



#### Aging and chronic degenerative disease

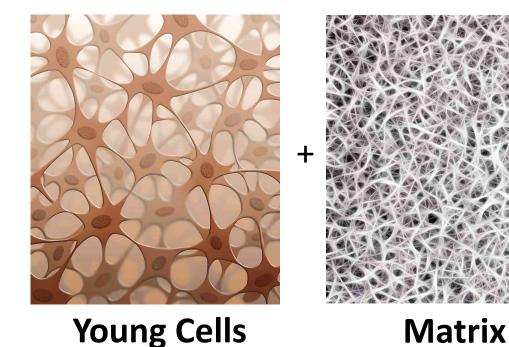


- 80% of \$2.5T health care costs associated with chronic disease.
- 80% of elderly have at least one chronic disease, 68% have two or more.



# The Ideal Technology Platform

- Young replacement cells of all kinds
- Cells capable of regeneration
- A path to an off-the-shelf product
- An injectable mix of cells/matrix to regenerate 3-D tissue



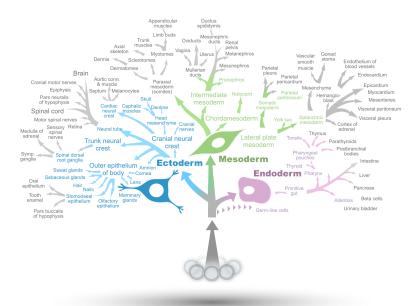




# The Ideal Technology Platform

#### Twin Technologies: Cells & Matrix

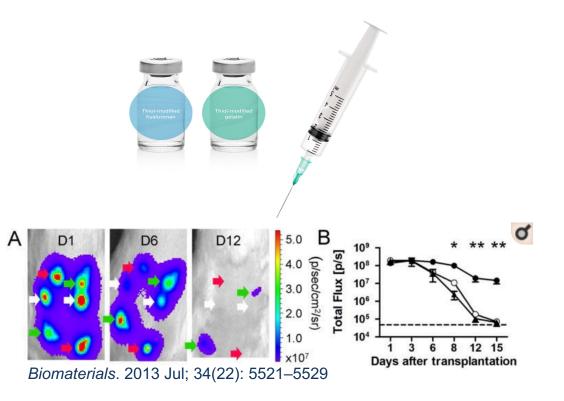
#### Pluripotent Cell-Based Therapeutics



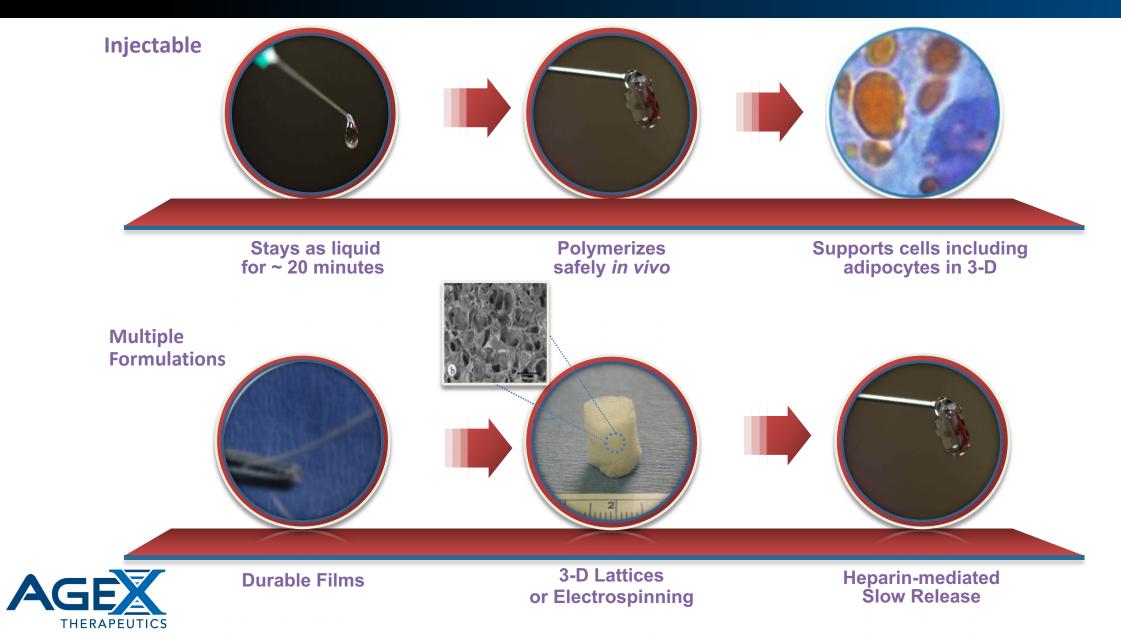
- Pluripotent Stem Cells (PSCs) allow the manufacture of all young human cell types on an industrial scale
- Engineered for allogeneic use
- Our cells are government (NIH) approved







# HyStem – Unique Properties & Applications



# History of the Biotechnology Revolutions

#### Recombinant DNA Technology



- 1974 Gene cloning technology developed
- 1976 Moratorium on rDNA research initiated led to established guidelines on rDNA research
- 1989 First \$B product EPO
- Today, products from the use of rDNA technology are ubiquitous
- >140 clinical trials
- Current Global Market \$75 B



- 1975 Hybridoma technology developed
- 1997- First \$B Product Rituximab
- Advances in Mab Engineering
- Today, eight of the 20 bestselling biotechnology drugs in therapeutic monoclonal antibodies
- > 200 clinical trials
- Current Global Market \$44 B

#### **Regenerative Medicine**



- 1998 First Pluripotent Stem Cells isolated
- 2001 U.S. Federal funding restriction (reversed in 2009)
- 2010 1<sup>st</sup> hES Clinical trial
- Future 1<sup>st</sup> \$B product



# Numerous Products Performing Well in Trials

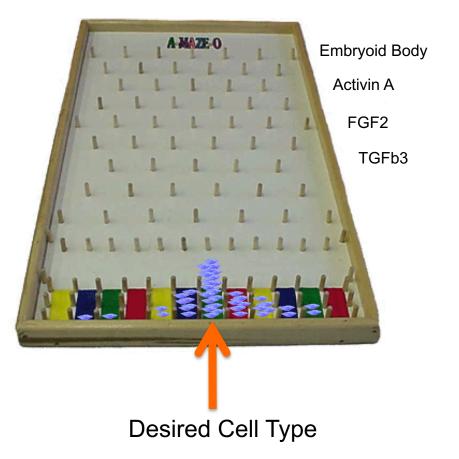
- Retinal Pigment Epithelial cells (OpRegen) Agerelated macular degeneration (BioTime Phase II)
- Oligodendrocyte Progenitor Cells (OPC1) Spinal cord injury (Asterias Phase II)
- Dendritic cells (VAC2) Cancer immunotherapy (Asterias/CRUK Phase I)



# Pluripotency – The Competitive Edge

The >1000-fold complexity of cell types derived from hPS cells leads to unique challenges:

- How manufacture with cGMP?
- How produce allogeneic product?
- Identity Lot-to-lot variability in composition
- Purity Contamination with unknown cell types





#### cGMP Manufacture



# Cell Stem Cell Correspondence

#### The Generation of Six Clinical-Grade Human Embryonic Stem Cell Lines

Jeremy Micah Crook,<sup>1,3,\*</sup> Teija Tuulikki Peura,<sup>2</sup> Lucy Kravets,<sup>1</sup> Alexis Gina Bosman,<sup>2</sup> Jeremy James Buzzard,<sup>1</sup> Rachel Horne,<sup>1</sup> Hannes Hentze,<sup>1</sup> Norris Ray Dunn,<sup>1,3</sup> Robert Zweigerdt,<sup>1,3</sup> Florence Chua,<sup>1</sup> Alan Upshall,<sup>1</sup> and Alan Colman<sup>1,3</sup> <sup>1</sup>ES Cell International Pte Ltd., Singapore 138667 <sup>2</sup>Sydney IVF, Sydney, NSW 2000, Australia <sup>3</sup>Present address: Institute of Medical Biology, Singapore Stem Cell Consortium, Singapore 138648. <sup>\*</sup>Correspondence: jeremy.crook@imb.a-star.edu.sg DOI 10.1016/j.stem.2007.10.004

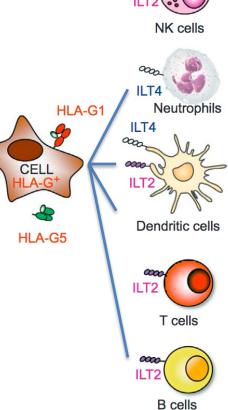
First publication describing the derivation of clinical-grade GMP hES cell lines

- Comprehensive, multiple stage donor consent
- FDA approved, GMP human fibroblast feeder cell line
- Six karyotypically normal hES cell lines successfully derived
- Screened for panel of adventitious agents
- NIH Registered



# UniverCyte<sup>™</sup>: HLA-G for Allogeneic Immunotolerance

- It appears that the primary role of HLA-G is to suppress maternal immune response to pregnancies.
- Appears to disarm multiple arms of immune system

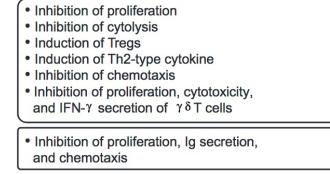


- Inhibition of cytotoxicity
  Inhibition of IFN-γ secretion
  - Inhibition of MICA/NKG2D activation
  - Inhibition of chemotaxis

• Inhibition of reactive oxygen species production and phagocytosis

Induction of tolerogenic DC

- Inhibition of maturation
  - <sup>1</sup> MHCII presentation pathway
  - $\$  Costimulatory molecules and IL12 secretion
  - Induction of anergic and suppressor T cells
  - Inhibition of NK cell activation

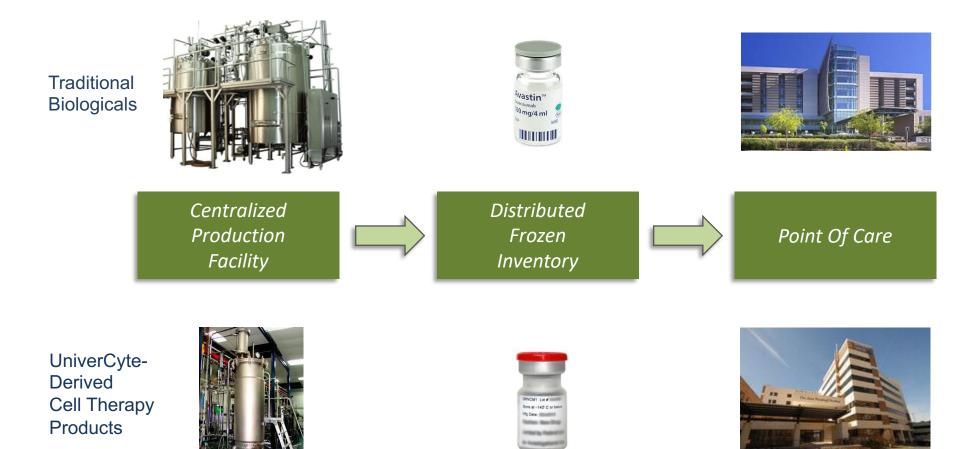


Adv. Immunol. (2015) 127:33-144



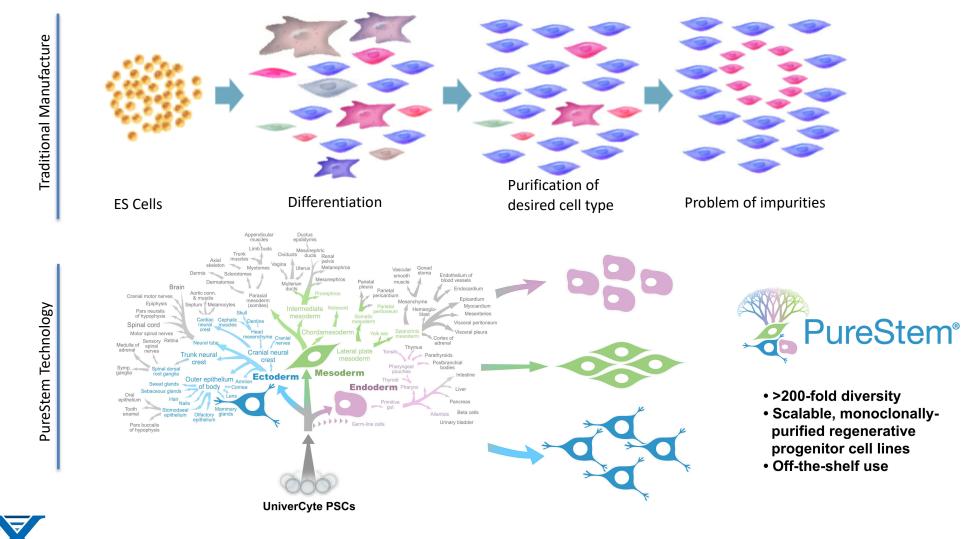
# Value of the UniverCyte Pluripotent Platform

#### Classical biologics off-the-shelf business model



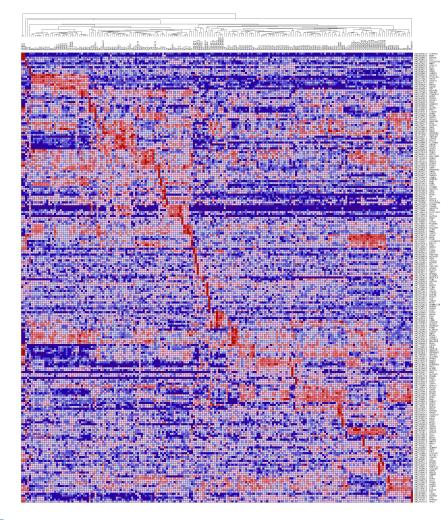


#### Universal *PureStem<sup>TM</sup>* Technology





#### PureStem-Based Manufacture





> 200 diverse human embryonic progenitor cell types isolated in a clonally pure and scalable format.



#### Example of PureStem Line Scalability

#### Estimated Cell Number If Scaled Cells Presently in Inventory to Passage 30

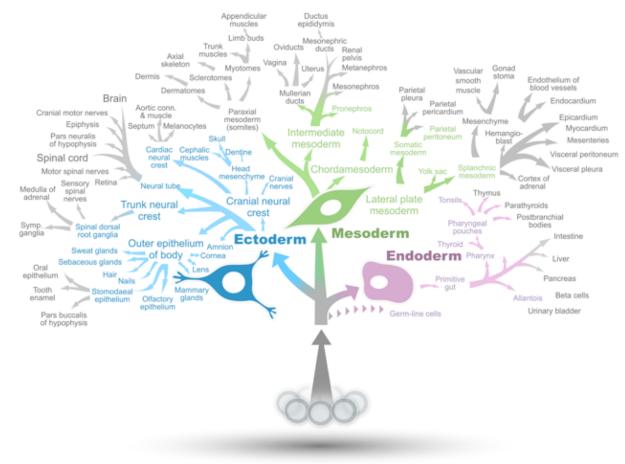
#### CELL LINE

4D20.8 Example	Cell Number in Millions	Passage Number	Approximate treatments if require 100 million cells per treatment		
	100	P9	1		
	300	P10	3		
	900	P11	9		
	2700	P12	27		
	8100	P13	81		
	24300	P14	243		
	72900	P15	729		
	218700	P16	2187		
	656100	P17	6561		
	1968300	P18	19683		
	5904900	P19	59049		
	17714700	P20	177147		
	53144100	P21	531441		
	159432300	P22	1594323		
	478296900	P23	4782969		
	1434890700	P24	14348907		
	4304672100	P25	43046721		
	12914016300	P26	129140163		
	38742048900	P27	387420489		
	1.16226E+11	P28	1162261467		
	3.48678E+11	P29	3486784401		
	1.04604E+12	P30	10460353203		



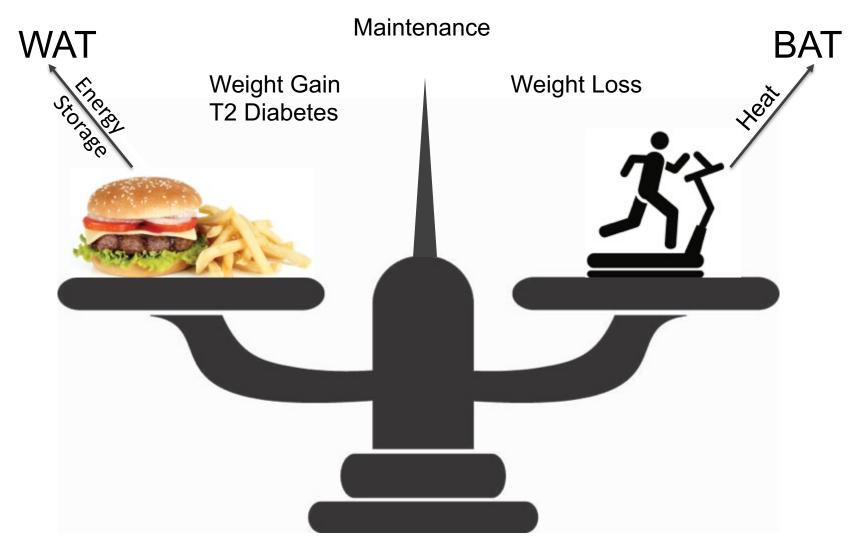
# Identification of Low-Hanging Fruit

- Key applications in age-related degenerative disease
- Disease characterized by loss of cells
- Not addressable with current modalities



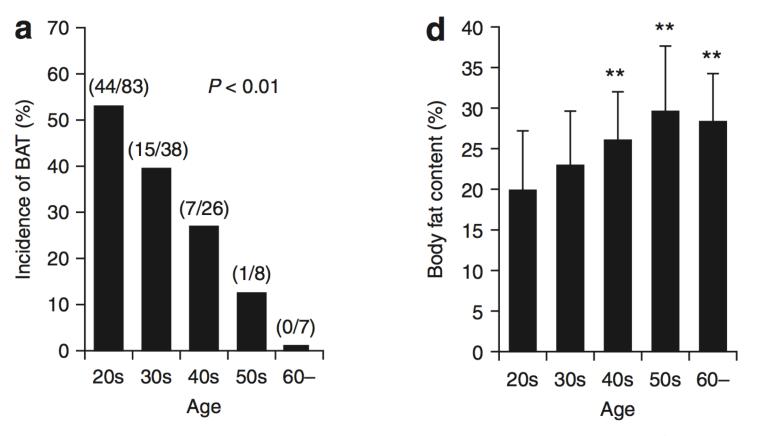


#### Brown Adipose Cells Regulate Metabolism





#### Brown Adipose Cells Regulate Metabolism

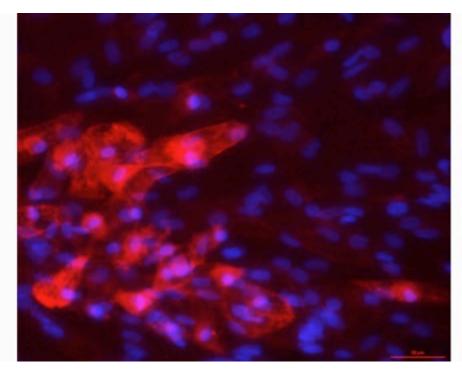


Obesity (2011) 19, 1755–1760. doi:10.1038/oby.2011.125

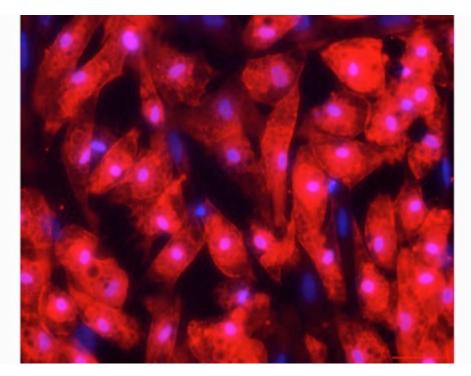


# AgeX-BAT1 Properties

#### Stained for Brown Adipocyte Marker UCP1



**Tissue-Sourced Brown Adipocytes** 

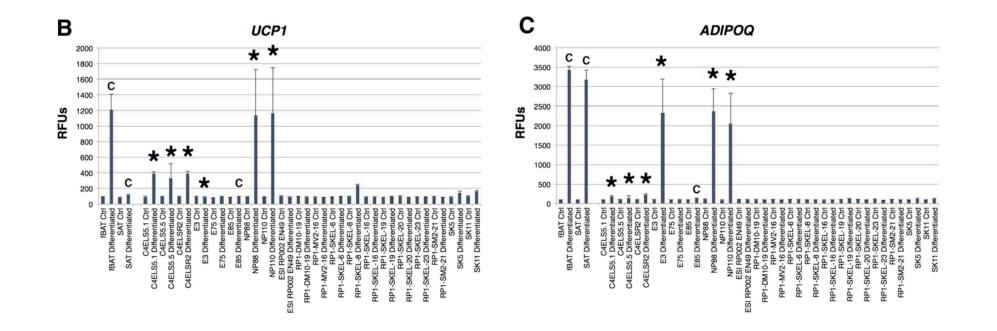


PureStem Brown Adipocytes

West et al. Stem Cell Research & Therapy (2019) 10:7



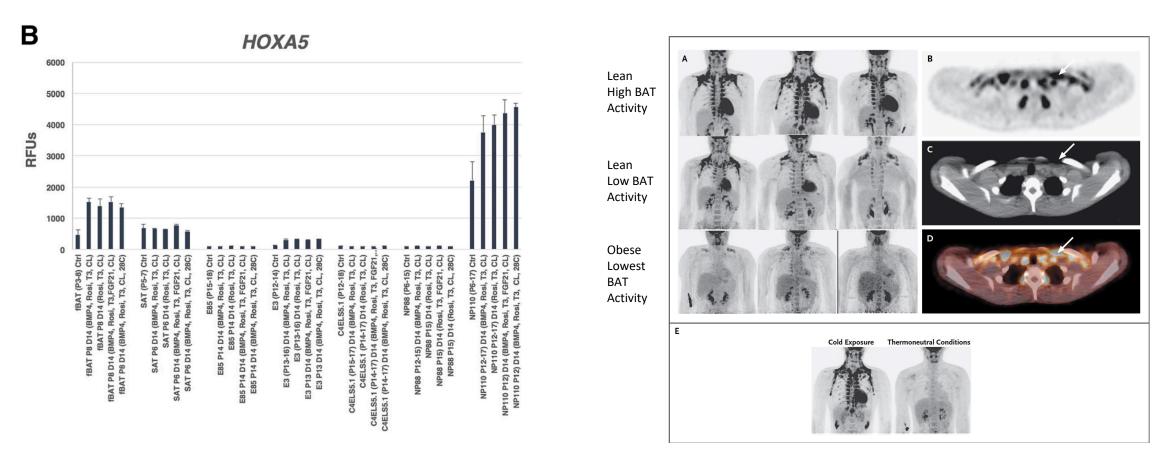
## AgeX-BAT1 Properties





West et al. Stem Cell Research & Therapy (2019) 10:7

# AgeX-BAT1 Properties



West et al. Stem Cell Research & Therapy (2019) 10:7





- 30M Americans have diabetes<sup>1</sup> 1:3 Americans will have diabetes by 2050
- The global market for diabetes mellitus and obesity is set to rise from \$70.8 billion in 2015 to <u>\$163.2 billion by 2022</u>, at a strong compound annual growth rate of 12.7%, according to business intelligence firm GBI Research.
- Competing products commonly target insulin secretion, glucose excretion, incretins such as GLP-1, or attempt to activate existing BAT or cause browning of white fat.

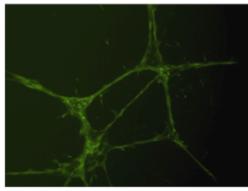
1) Centers for Disease Control and Prevention. National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States. US Department of Health and Human Services; Atlanta, GA: 2014.

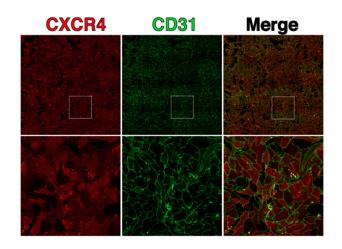


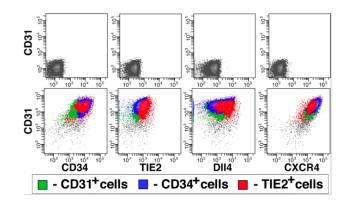
# AgeX-VASC1 Purity

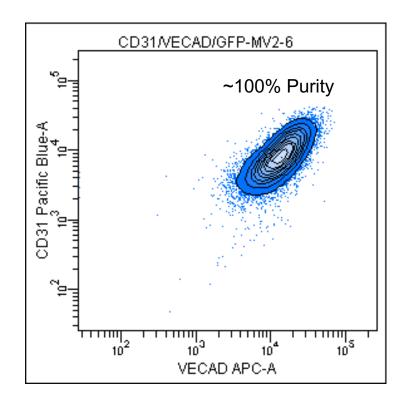
#### Monoclonal Endothelium

#### GFP Endothelium (168 hrs)





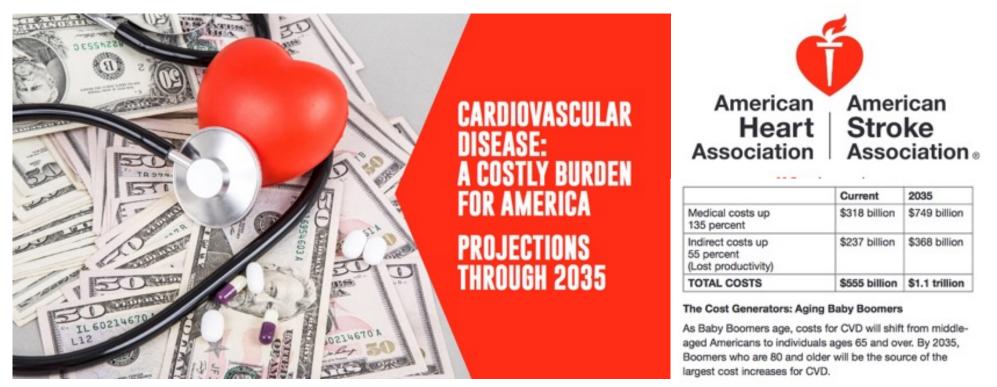






## Cardiovascular Market

#### > \$Trillion Market Worldwide

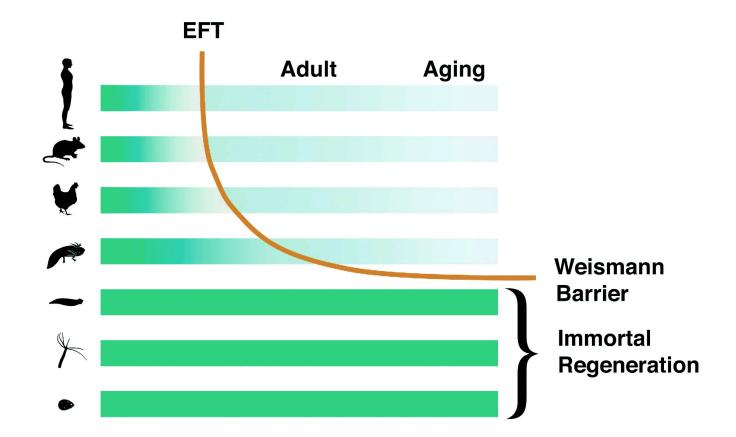


http://www.heart.org/idc/groups/heart-public/@wcm/@adv/documents/downloadable/ucm\_491543.pdf



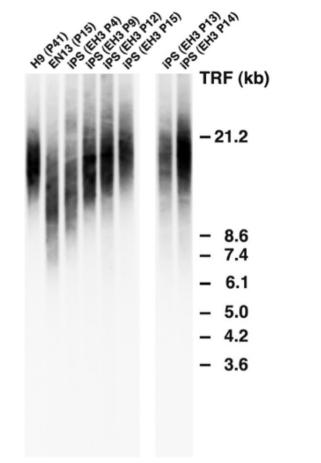
#### Induced Tissue Regeneration (iTR)

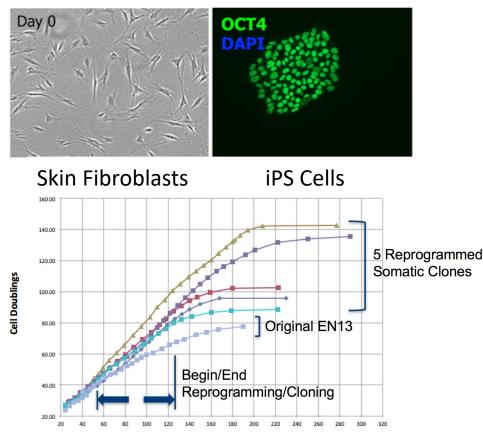
#### Innate regeneration in humans restricted to early development





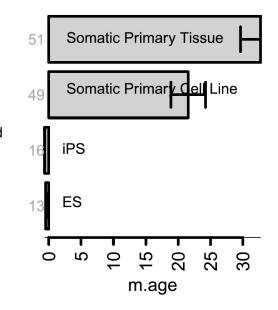
## Reversing the Aging of Human Cells Back to Pluripotency





#### Reprogramming Methylation Age

A Data 77 p = 1e−14



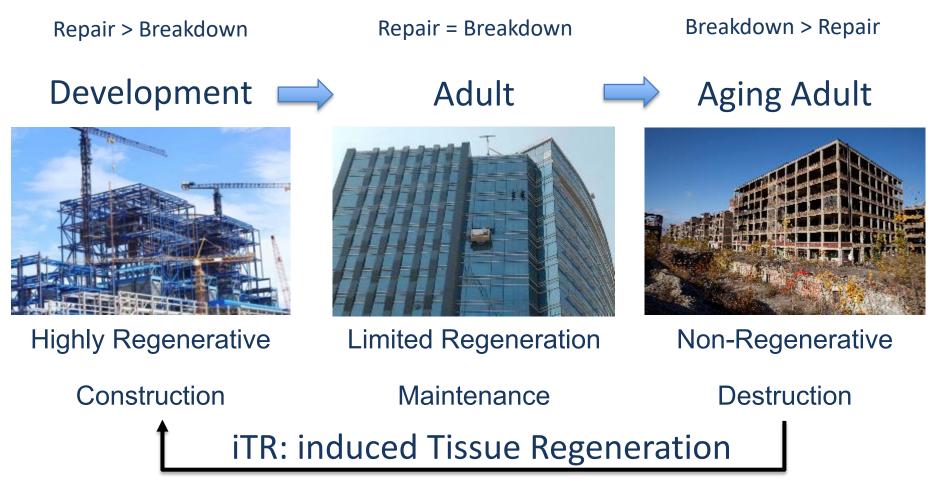
Regen Med 2010 May;5(3):345-63

Time (Days)

Genome Biol. 2013;14(10):R115

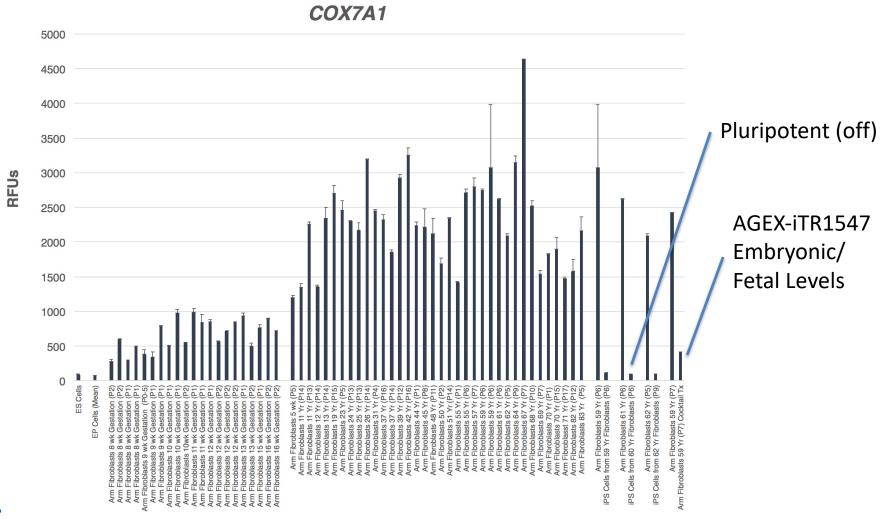


# Reversing the Aging of Human Cells Back to Regeneration



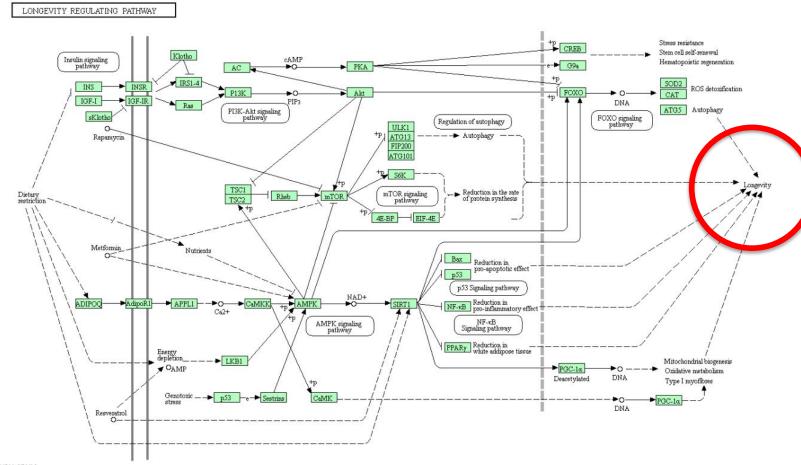


#### An Example of an iTR Gene





# Toward a Unified Theory of Aging



A growing consensus that modulating these metabolic pathways effect aging, but how?

A complex analysis by AgeX scientists suggests that insights from regenerative biology will lead to a unified theory of aging.

04211 6/21/16 (c) Kanehisa Laboratories

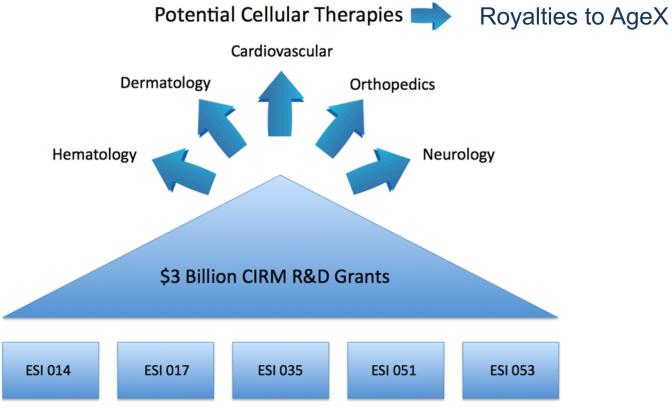


	Pre-Clinical		Phase I	Phase II	Phase III/Pivotal
THERAPEUTICS					
AGEX-BAT1 (Brown Adipocytes)	T2D				
AGEX-VASC1 (Vascular Progenitors)	MI				
AGEX-iTR1547 (NCE in HyStem)	CHF				
Renelon <sup>™</sup> (Repurposed Drug) 510(k) Scarless Healin			510(k) Clearance		
RESEARCH PRODUCTS					
Universal cGMP ES Cells, Cytiva	Marketed Research Products				
DATABASE PRODUCTS					
GeneCards/LM Discovery	Marketed NGS Interpretation				
<b>CANCER DIAGNOSTICS &amp; THERAPY</b>					
Cancer Stem Cell EFT Dx & Tx		To be Partnered for Cancer Dx			



## Licensing of GMP Stem Cell Master Cell Bank

- Ownership of bank remains with AgeX
- Narrowly-defined products owned/sold by partner
- Running royalty not limited by patent expiration





AgeX GMP UniverCyte Master Cell Banks

#### **ESI BIO Research Product Division**

- Markets cells for drug screening
- Manufacture and Marketing of Cytiva for GE Healthcare

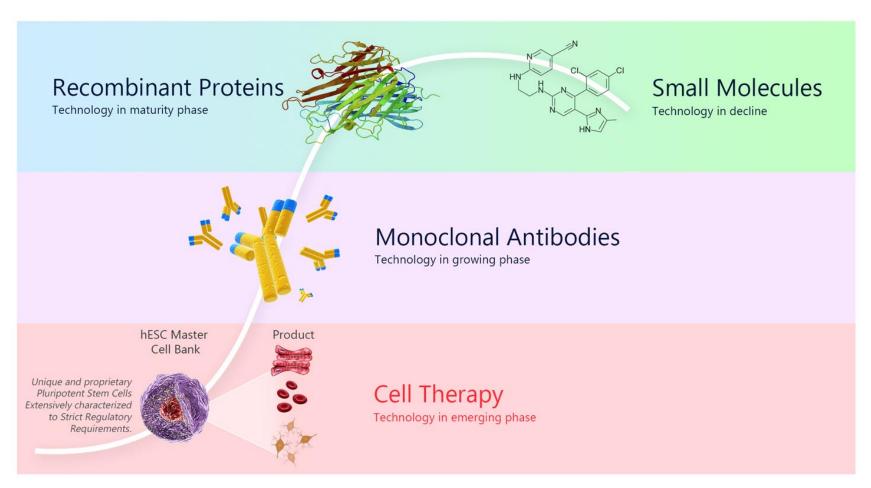






#### Asset Life of Pluripotent Platform

Potentially long lifespan due to lack of regulatory pathway for generics or biosimilars





- Aging: The demographic trend of our time
- Largest challenge is chronic degenerative diseases of aging
- Straightforward therapeutic strategy: Young cells for aged tissues
- Proprietary manufacturing technology yielding highly scalable, purified, identified, and regenerative cells for applications in age-related degenerative disease
- A proprietary path to off-the-shelf allogeneic application
- A proprietary injectable matrix

