

## World Stem Cell Summit 2018

January 25, 2018

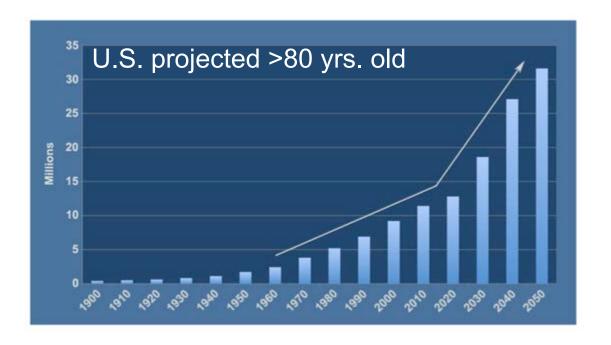
#### Safe Harbor Statement

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 products and technologies; results of clinical trials of such products; the ability of Agex and BioTime 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; 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. Forward-looking statements involve risks and uncertainties, including, without limitation, risks inherent in the development and/or commercialization of potential products, uncertainty in the results of clinical trials or regulatory approvals, need and ability to obtain future capital, and maintenance of intellectual property rights. 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 BioTime and its other subsidiaries, particularly those mentioned in the cautionary statements found in BioTime's Securities and Exchange Commission filings. BioTime and AgeX disclaim any intent or obligation to update these forward-looking statements.



#### The Market

#### Aging: The demographic trend of our time



- 80% of \$2.5T health care costs associated with chronic disease.
- Age-related chronic degenerative diseases typically have few effective drug targets.



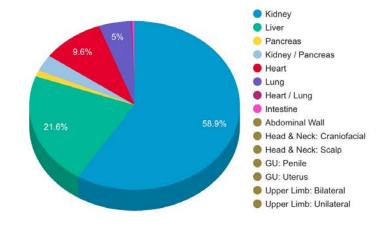
#### Tissue Transplantation Risk Profile

#### National data

#### Transplants By Organ Type January 1, 1988 - November 30, 2017 Based on OPTN data as of January 4, 2018

- 1yr Survival
- Kidney >95%
- Liver >90%
- Pancreas >95%.
- Kidney/Pancreas >95%
- Heart >85%

Organ	Transplants
Kidney	423,480
Liver	155,252
Pancreas	8,544
Kidney / Pancreas	22,852
Heart	68,677
Lung	35,606
Heart / Lung	1,227
Intestine	2,906
Abdominal Wall	1
Head & Neck: Craniofacial	5
Head & Neck: Scalp	1
GU: Penile	1
GU: Uterus	10
Upper Limb: Bilateral	6
Upper Limb: Unilateral	4
Total	718,572

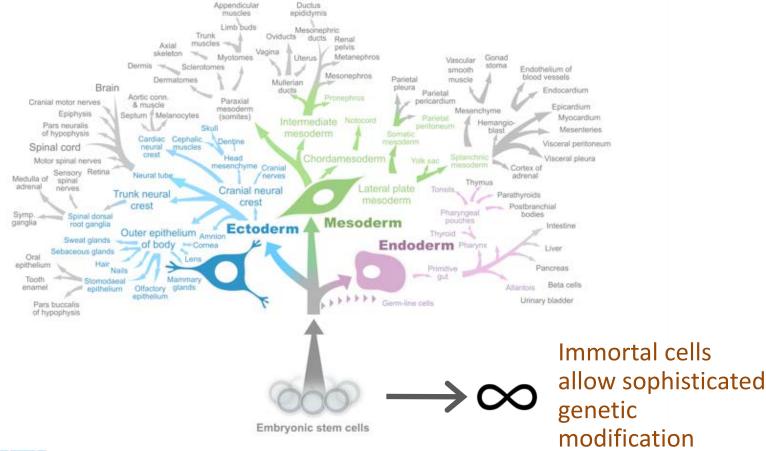


United Network for Organ Sharing



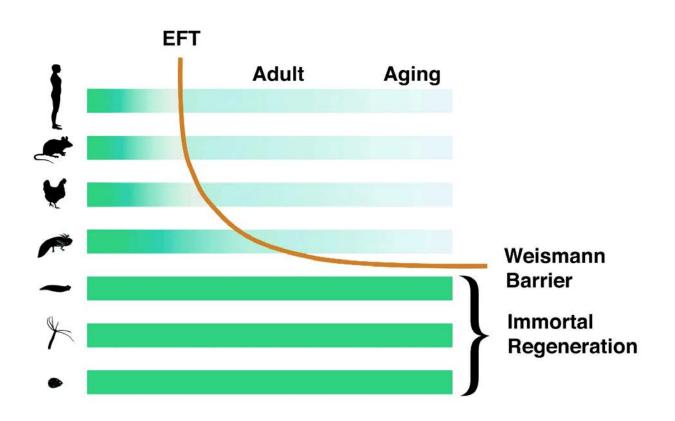
#### Pluripotency

- Scalable source of all human cell types
- Regen phenotype



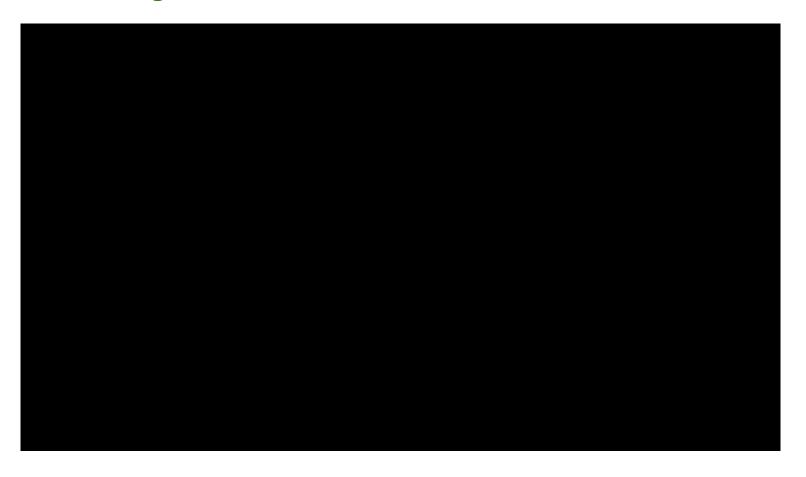


#### Innate Regeneration in Humans Restricted to Embryonic Development



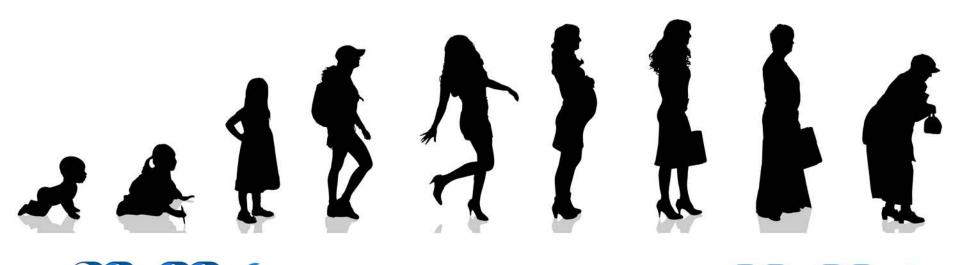


#### Planaria regeneration





#### The Nature of the Antagonistic Pleiotropy



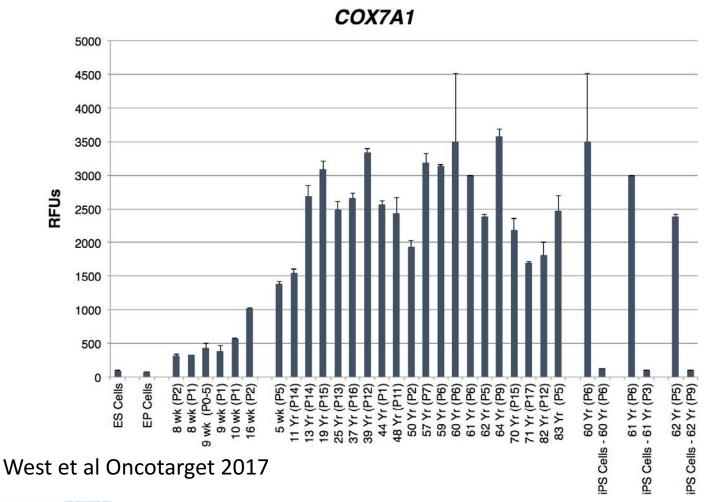
Regeneration OFF in somatic cells after EFT reduces cancer in young



Leads to disrepair/fibrosis relative lack of apoptosis in senescent cells/lipofuscin



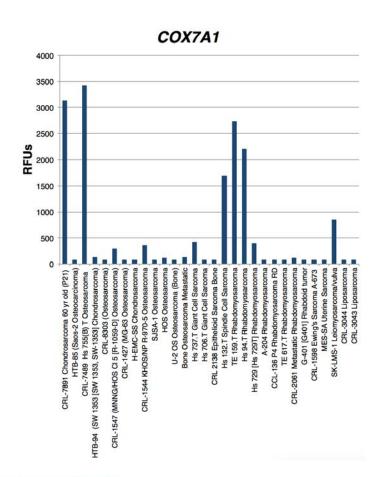
#### A Marker of EFT

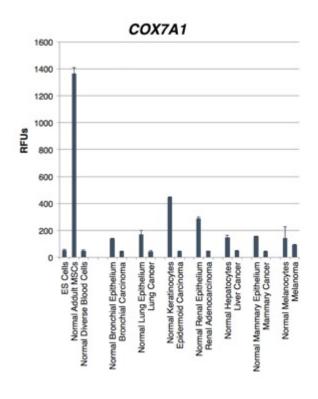




#### A Marker of EFT

#### Reversed in the Majority of Cancers

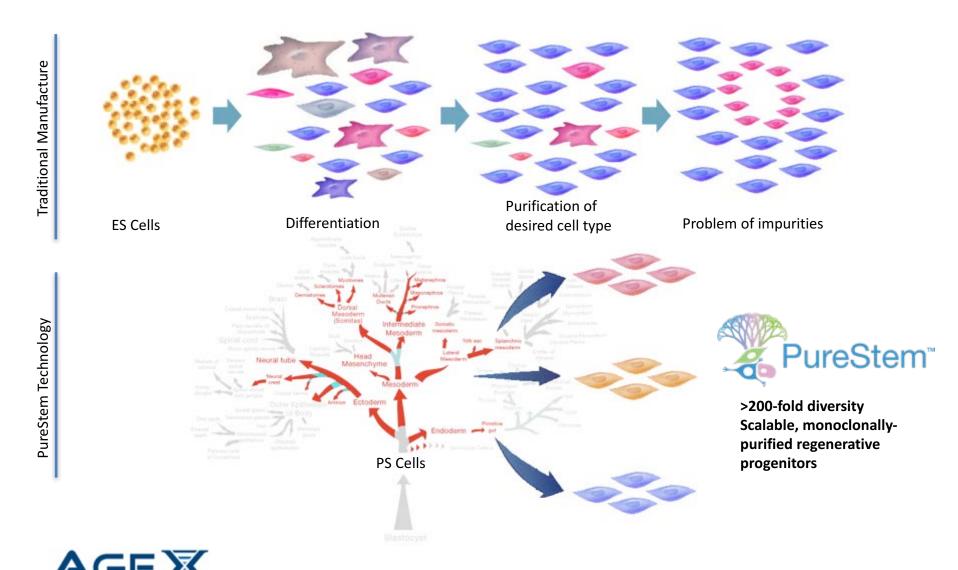




West et al Oncotarget 2017

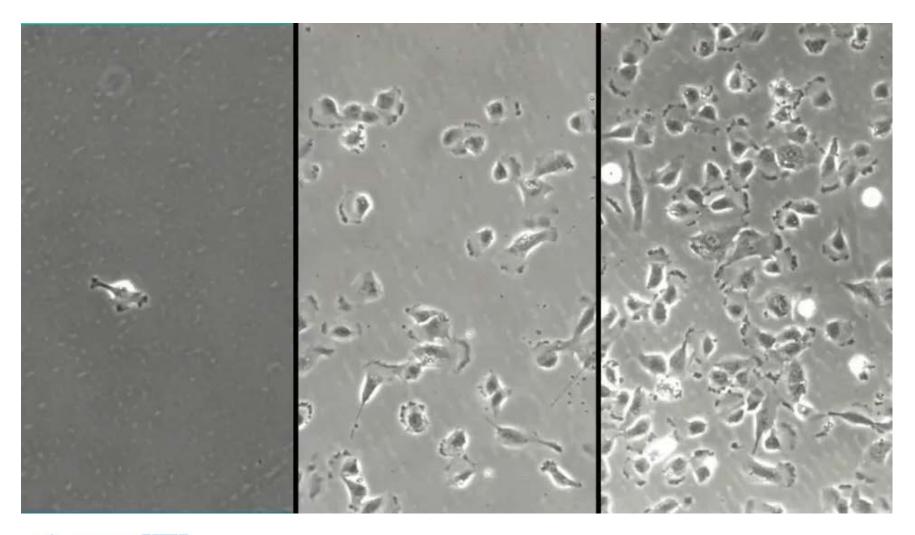


#### 2<sup>nd</sup> Generation - Universal *PureStem<sup>TM</sup>* Technology



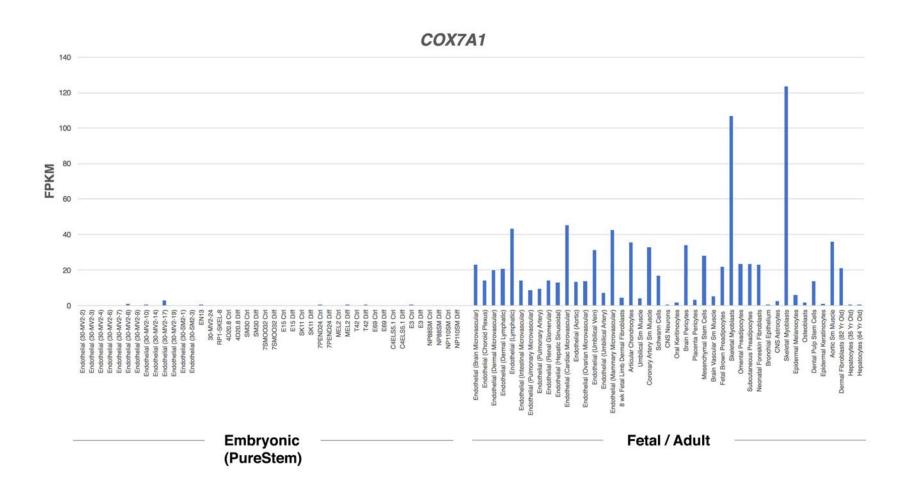


#### 2<sup>nd</sup> Generation - Universal *PureStem<sup>TM</sup>* Technology





#### Regenerative Phenotype of hESC-Derivatives





#### COX7A1 Data in GEO

#### Example of Heart Regeneration:

- Some amphibians regenerate heart throughout life
- Embryonic mammalian heart can regenerate but that capacity is lost shortly after birth



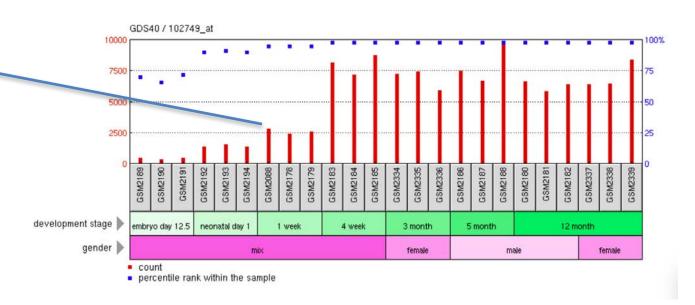
#### COX7A1 Data in GEO



Title Cardiac development, maturation and aging

Organism Mus musculus

Note low levels even postnatal





#### The Heart Model:



#### OPEN

# Epigenomic Reprogramming of Adult Cardiomyocyte-Derived Cardiac Progenitor Cells

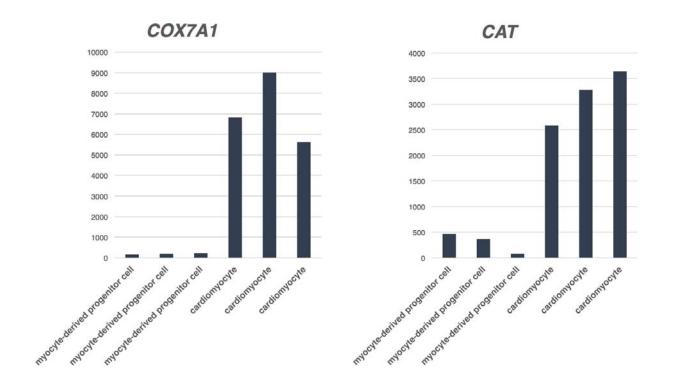
Received: 13 March 2015 Accepted: 14 October 2015 Published: 14 December 2015

Yiqiang Zhang<sup>1,2</sup>, Jiang F. Zhong<sup>3</sup>, Hongyu Qiu<sup>4</sup>, W. Robb MacLellan<sup>1</sup>, Eduardo Marbán<sup>2</sup> & Charles Wang<sup>5</sup>

Zhang Y et al Sci Rep 2015 Dec 14;5:17686



#### The Heart Model:



Zhang Y et al Sci Rep 2015 Dec 14;5:17686

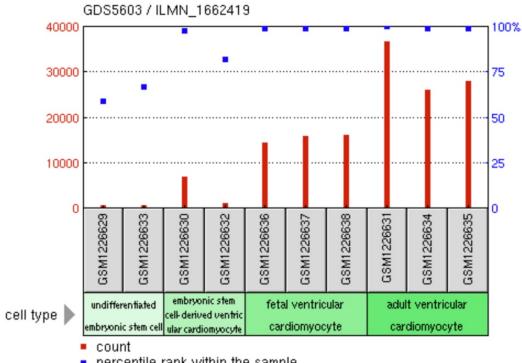


#### COX7A1 Data in GEO

**Profile** GDS5603 / ILMN\_1662419

Title Ventricular cardiomyocytes generated in vitro from embryonic stem cells

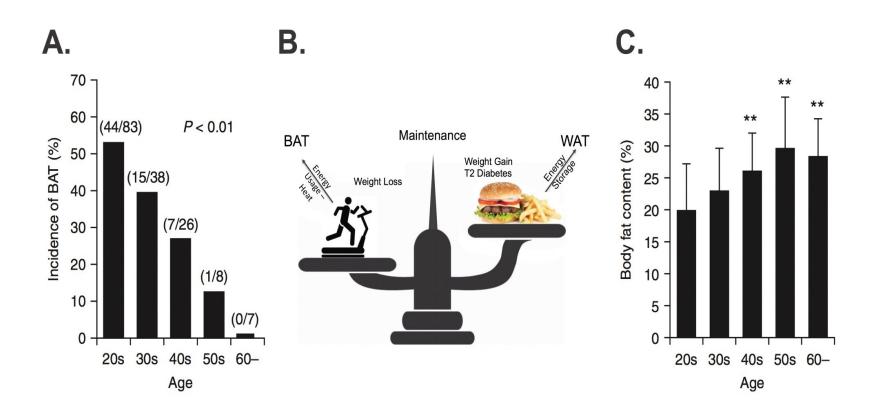
Organism Homo sapiens



percentile rank within the sample



#### Brown Adipose Cells Regulate Metabolism



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



#### Brown Adipose Cells Regulate Metabolism

# New Powers of Brown Fat: Fighting the Metabolic Syndrome

Jan Nedergaard,<sup>1,\*</sup> Tore Bengtsson,<sup>1</sup> and Barbara Cannon<sup>1</sup>
<sup>1</sup>The Wenner-Gren Institute, Stockholm University, Stockholm 106 91, Sweden
\*Correspondence: jan@metabol.su.se
DOI 10.1016/j.cmet.2011.02.009

#### **ORIGINAL ARTICLE**

#### Reversal of Type 1 Diabetes in Mice by Brown Adipose Tissue Transplant

Subhadra C. Gunawardana and David W. Piston

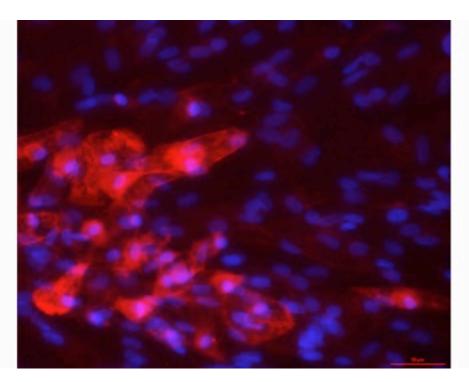
# Brown adipose tissue regulates glucose homeostasis and insulin sensitivity

Kristin I. Stanford, Roeland J.W. Middelbeek, Kristy L. Townsend, Ding An, Eva B. Nygaard, Kristen M. Hitchcox, Kathleen R. Markan, Kazuhiro Nakano, Michael F. Hirshman, Yu-Hua Tseng, and Laurie J. Goodyear

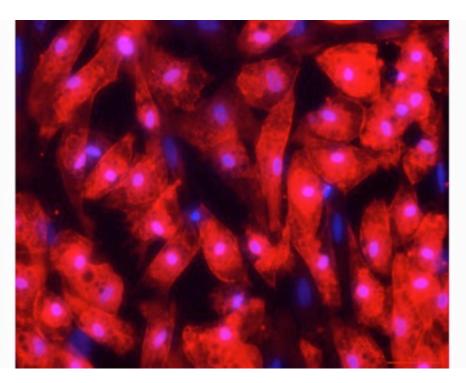
Section on Integrative Physiology and Metabolism, Joslin Diabetes Center, Harvard Medical School, Boston, Massachusetts, USA.



#### Stained for Brown Adipocyte Marker UCP1

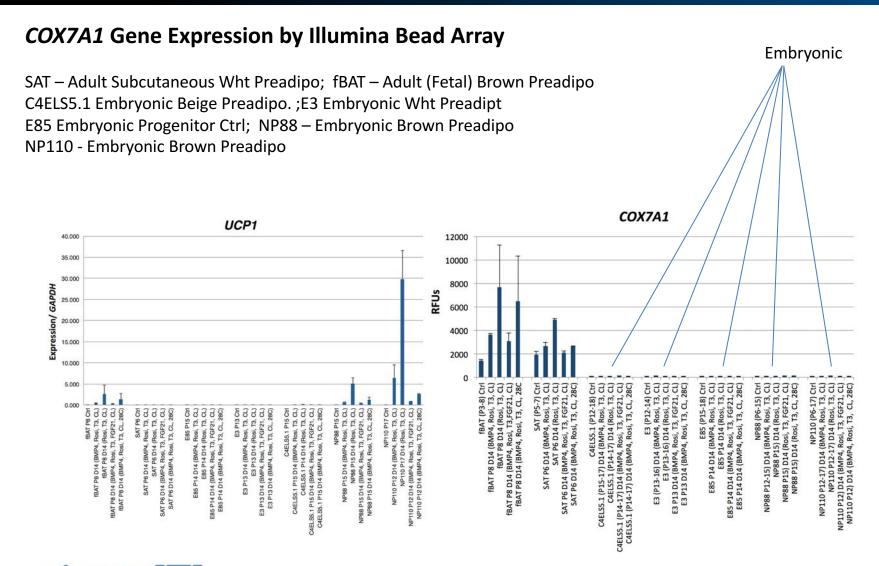


Tissue-Sourced Brown Adipocytes

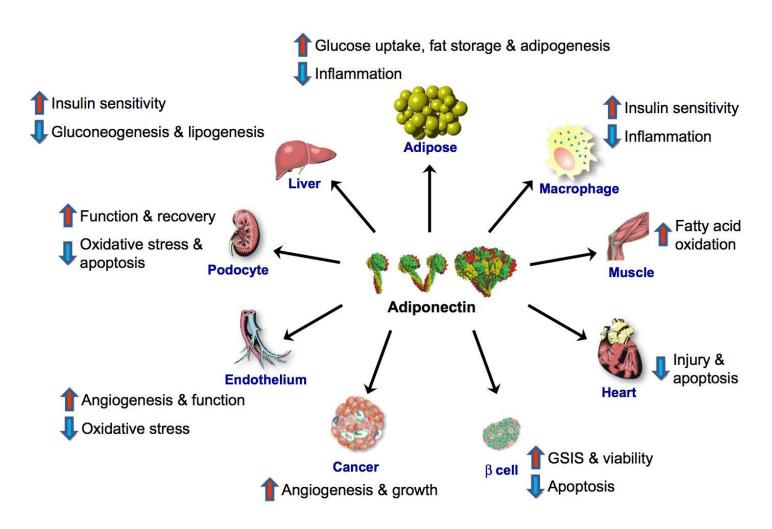


PureStem Brown Adipocytes



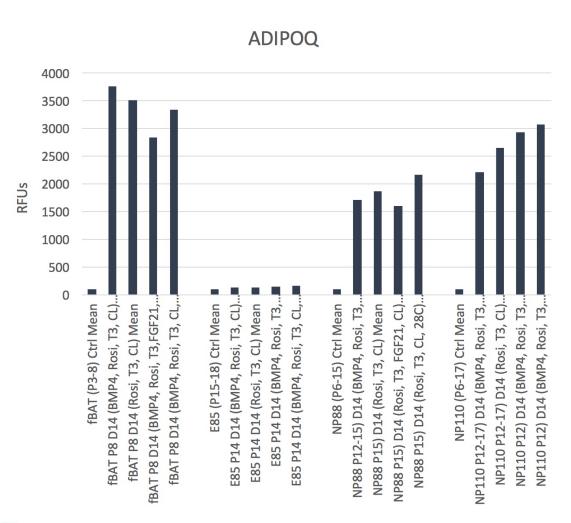








MOLECULAR METABOLISM 2 (2013) 133-141





#### Obesity/T2D Market

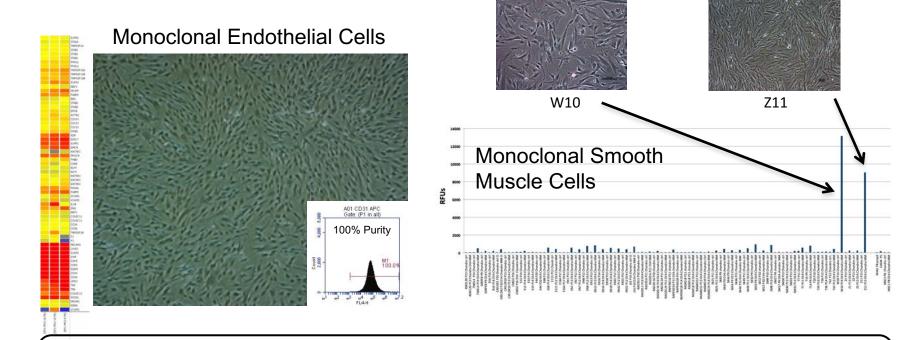
- 30M Americans have diabetes<sup>1</sup> 1:3 Americans will have diabetes by 2050
- The global market for diabetes mellitus and obesity is set to rise from \$70.8 billion in 2015 to \$163.2 billion by 2022, at a strong compound annual growth rate of 12.7%, according to business intelligence firm GBI Research.

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

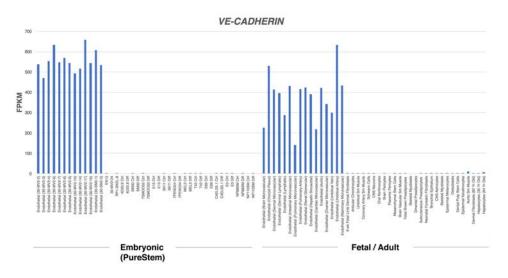
#### Regenerative Vascular Progenitors

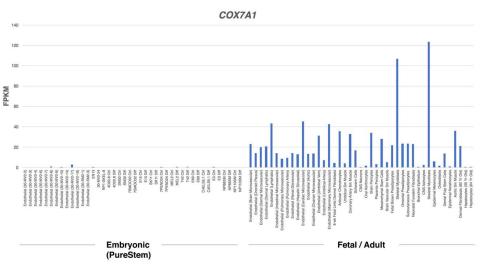


- Highly scalable with high purity & potency
- Extensive IP estate
- Formulated in HyStem



#### AGEX-VASC1







#### Cardiovascular Market

#### > \$Trillion Market Worldwide





life is why\*

	Current	2035
Medical costs up 135 percent	\$318 billion	\$749 billion
Indirect costs up 55 percent (Lost productivity)	\$237 billion	\$368 billion
TOTAL COSTS	\$555 billion	\$1.1 trillion

#### The Cost Generators: Aging Baby Boomers

As Baby Boomers age, costs for CVD will shift from middleaged Americans to individuals ages 65 and over. By 2035, Boomers who are 80 and older will be the source of the largest cost increases for CVD.

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



### Induced Tissue Regeneration- iTR

# Renelon<sup>TM</sup>: Repurposed Drug Formulated in HyStem for Local Delivery

**Embryonic** 



Fetal - Adult



**Aging Adult** 



Highly Regenerative



Limited Regeneration



Non-Regenerative

Construction

Maintenance

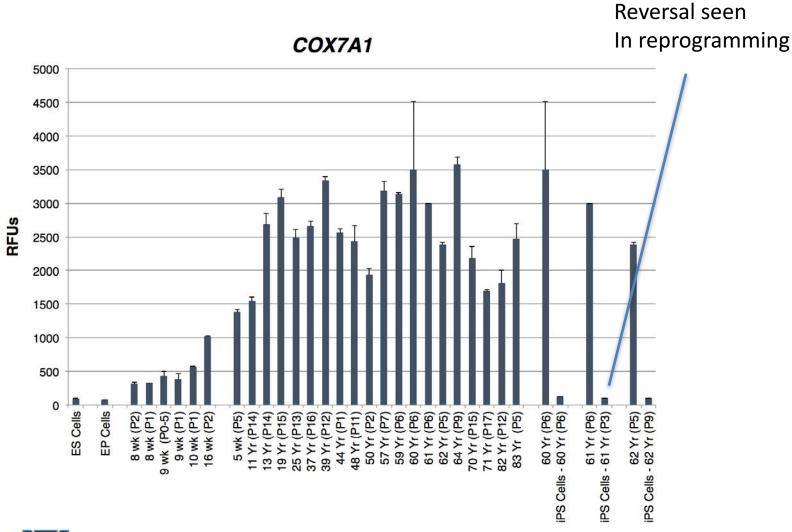
Destruction

iTR: induced Tissue Regeneration

Renelon™



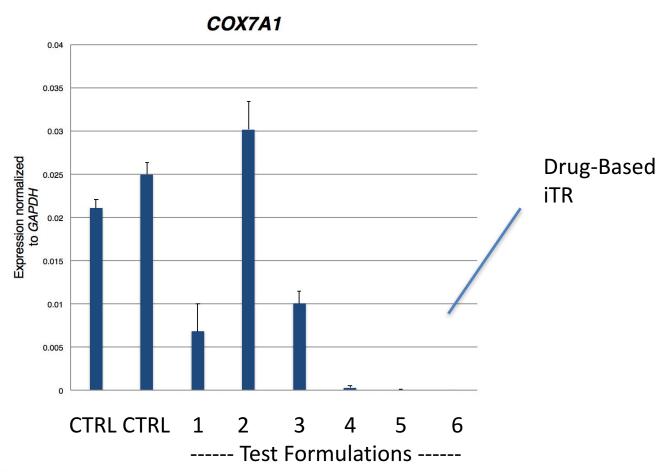
#### A Marker of EFT





#### Induced Tissue Regeneration- iTR

#### Small Molecule-Based iTR





#### Summary

- Pluripotency offers a means of manufacturing diverse regenerative progenitors to address degenerative diseases of aging: The demographic trend of our time
- AgeX focused on three therapeutic programs with potential to address large causes of mortality in U.S.
  - T2D/Obesity
  - Ischemic Disease: The leading causes of mortality & disability in an aging population
  - iTR1: Repurposed drug targeting the scarless tissue regeneration

