AGEX THERAPEUTICS

The Reversal of the Aging of Human Cells: Strategies for Clinical Implementation

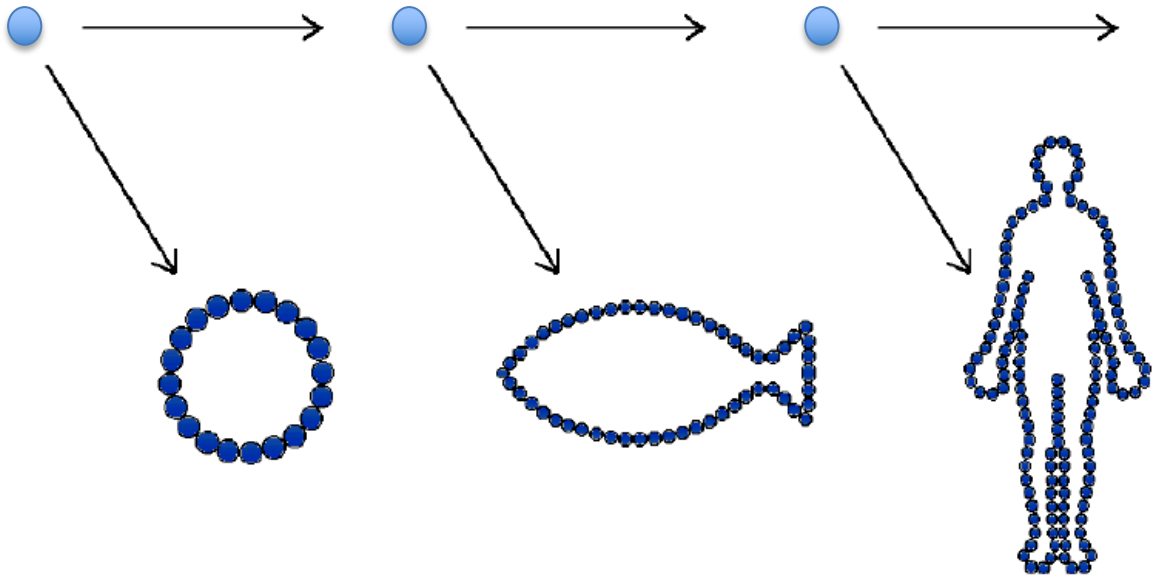
July 11, 2019

Forward Looking Statements

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.

AGEX THERAPEUTICS

Some Initial Observations

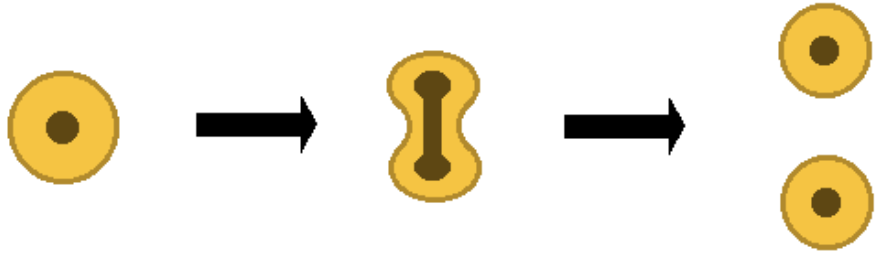


- The “germ-line” is a lineage of cells that continually creates new young people. The cells that formed us have not aged for billions of years (otherwise we would not be here).
- Aging is a phenomenon unique to the soma (all of the cells in the body other than germ-line cells). Aging is activated during cell differentiation. It is also completely reversible by, say, cloning, otherwise cloned animals would be born old.

AGEX THERAPEUTICS

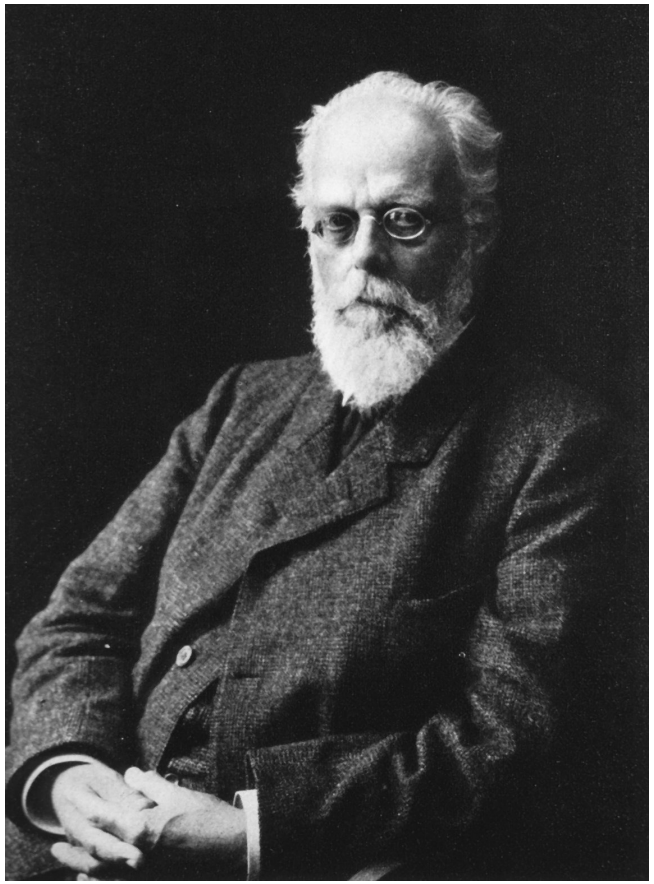
Some Initial Observations

August Weismann's prediction: Developmental loss of somatic immortality & regeneration



"Death takes place because a worn-out tissue cannot for ever renew itself, and because a capacity for increase by means of cell-division is not everlasting, but finite."

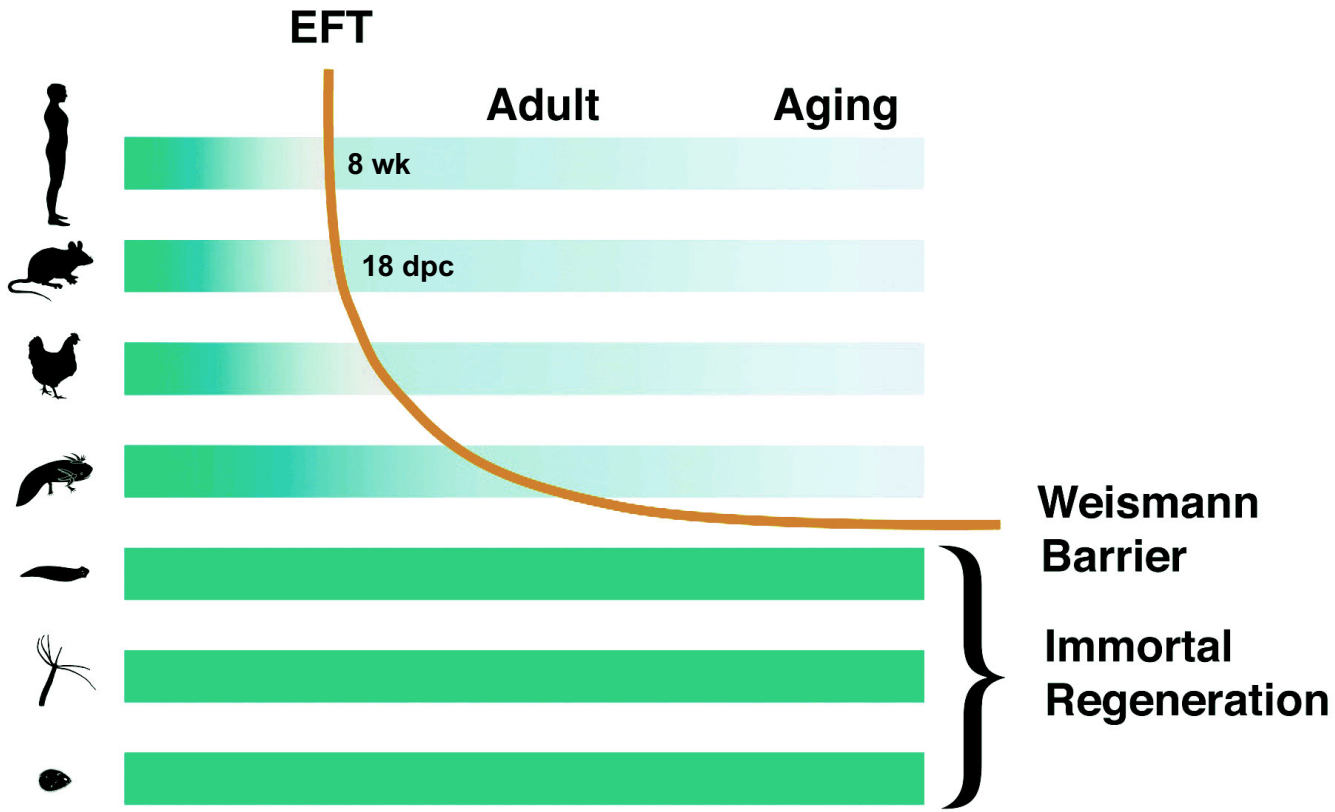
- A. Weismann, 1891



AGEX THERAPEUTICS

Some Initial Observations

Profound regeneration in humans is restricted to early embryonic development



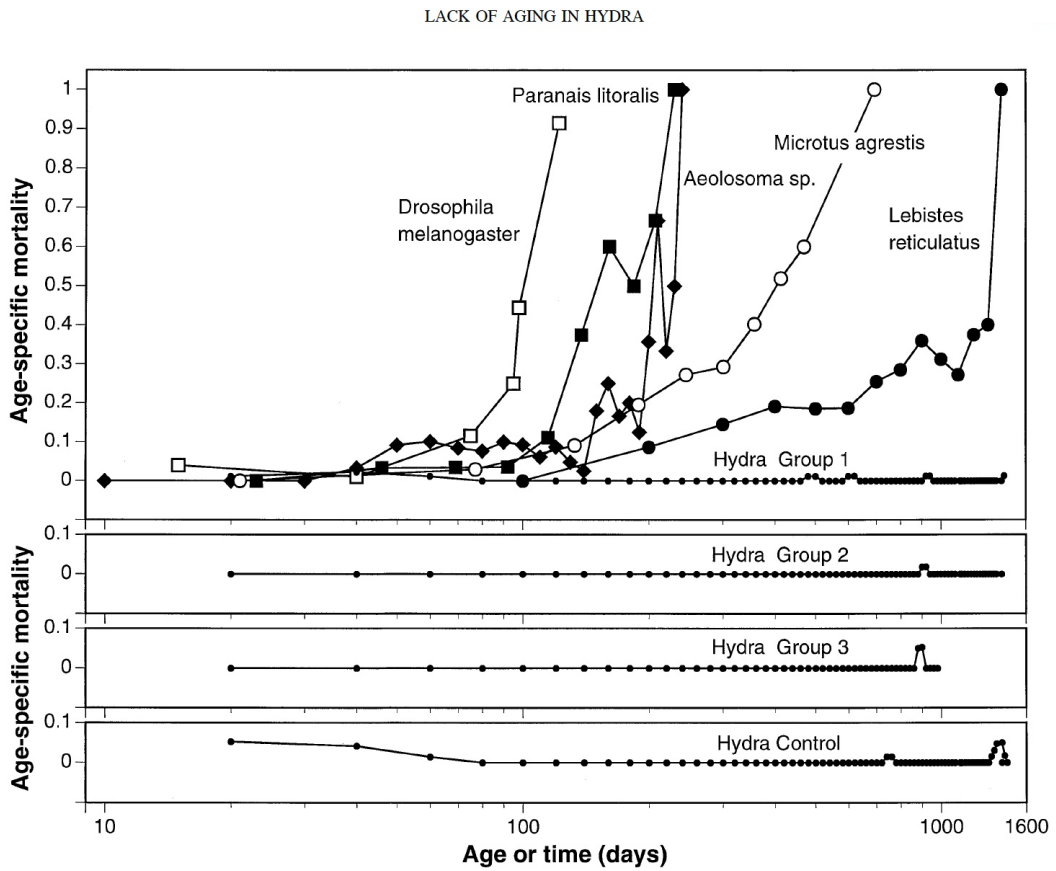
AGEX THERAPEUTICS

Some Initial Observations

Animals with somatic cells that have both replicative immortality and profound regenerative potential (immortal tissue regeneration or “iTR”) often do not age.

Some examples are:

- Hydra (data right)
  (*Exp Geront* 1998 33 (3) 217–225)
- Planaria
  (*Ageing Res Rev* 201416:66-82)
- Lobsters
  (*FEBS Lett* 1998 13;439(1-2):143-6)



Experimental Gerontology, Vol. 33, No. 3, pp. 217–225, 1998

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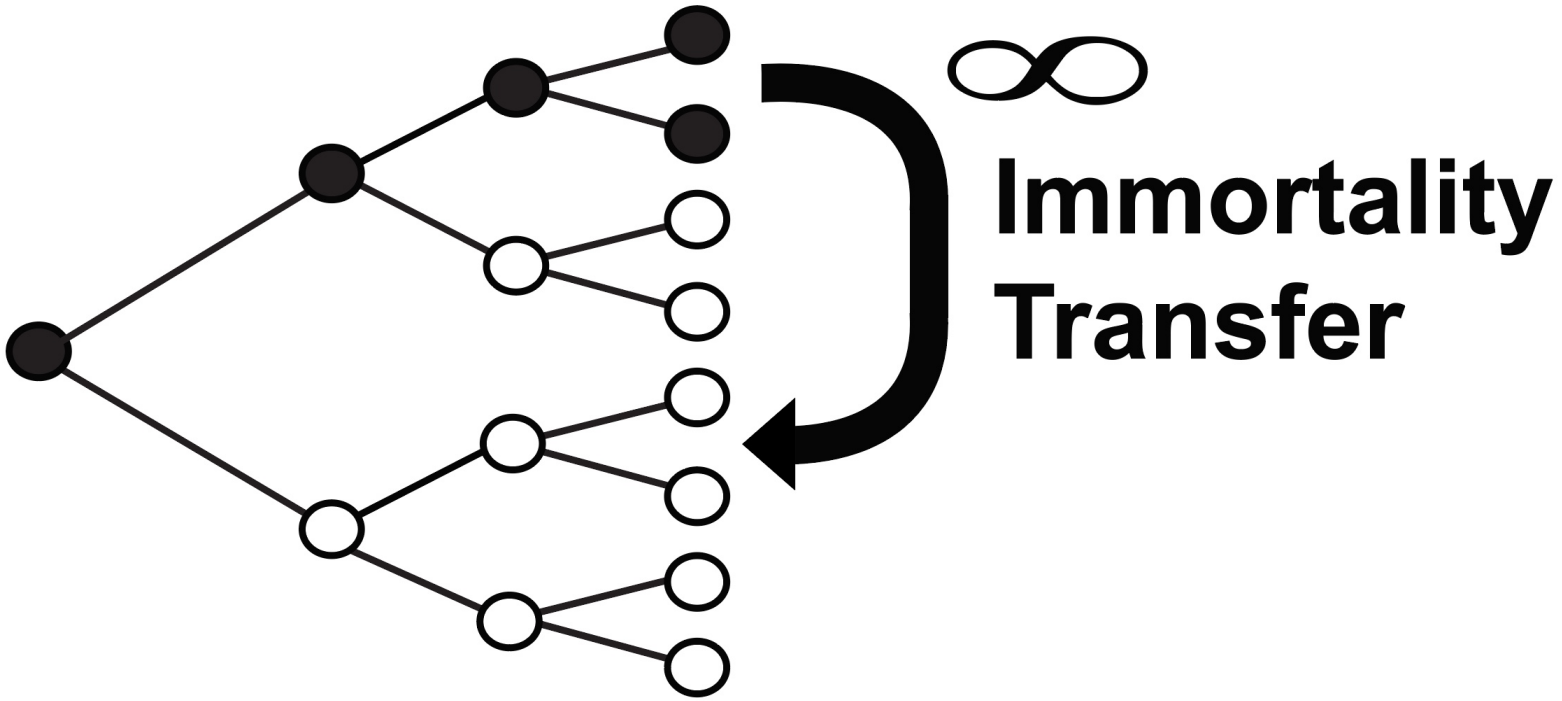
Translatable Technologies for Immortality Transfer



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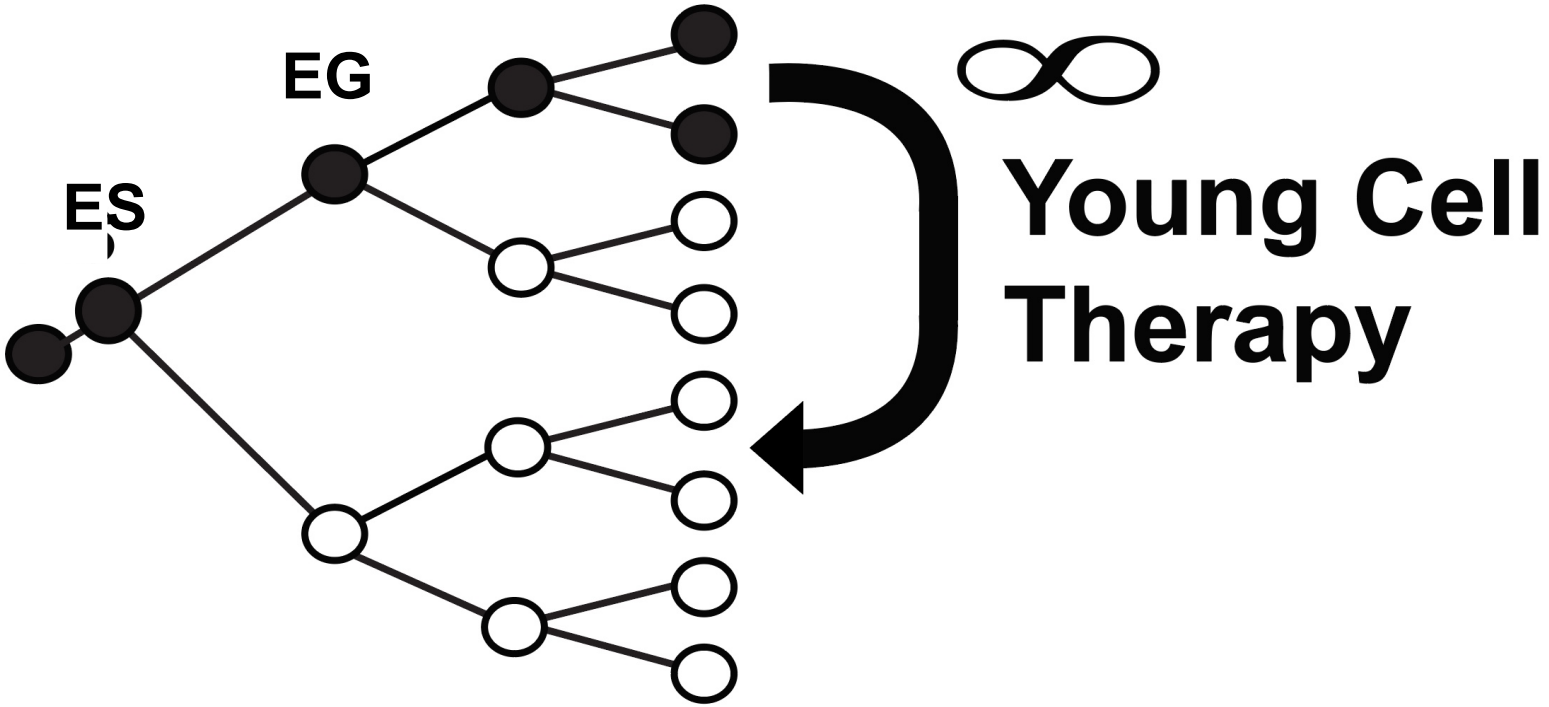
Pluripotency & Regenerative Medicine



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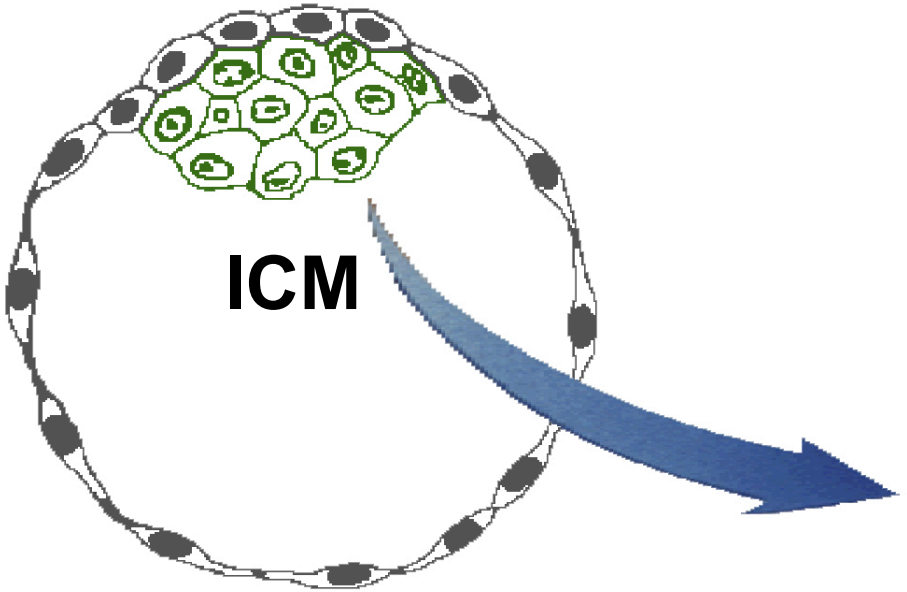
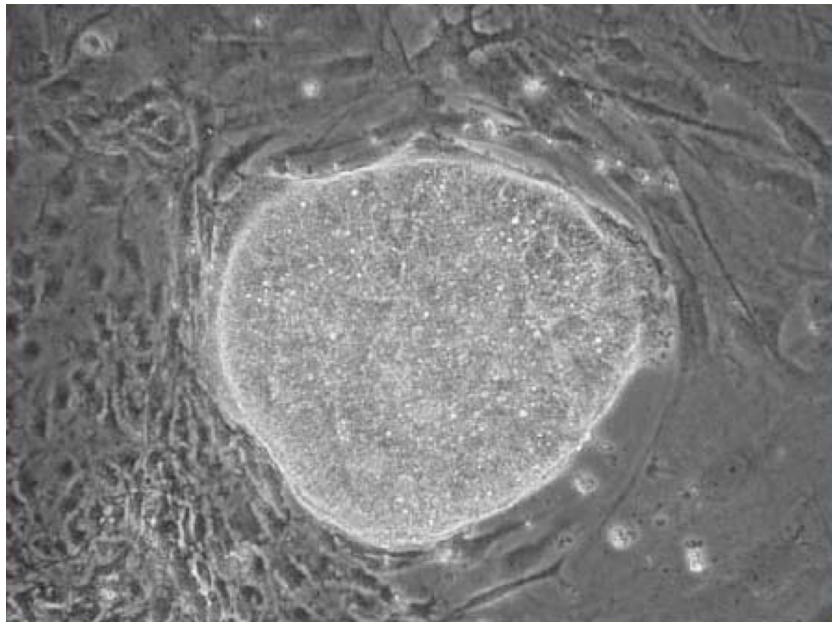
Pluripotency & Regenerative Medicine





Human ES Cells

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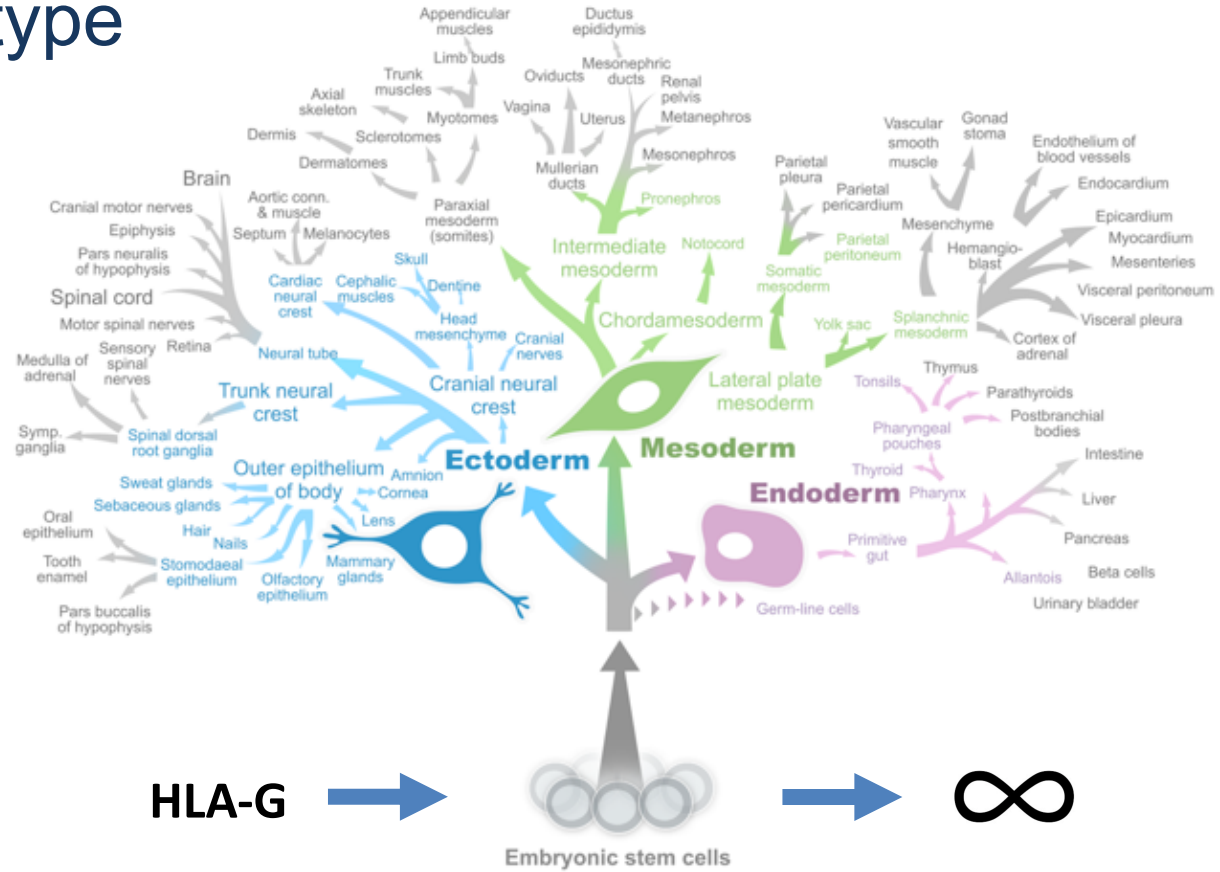
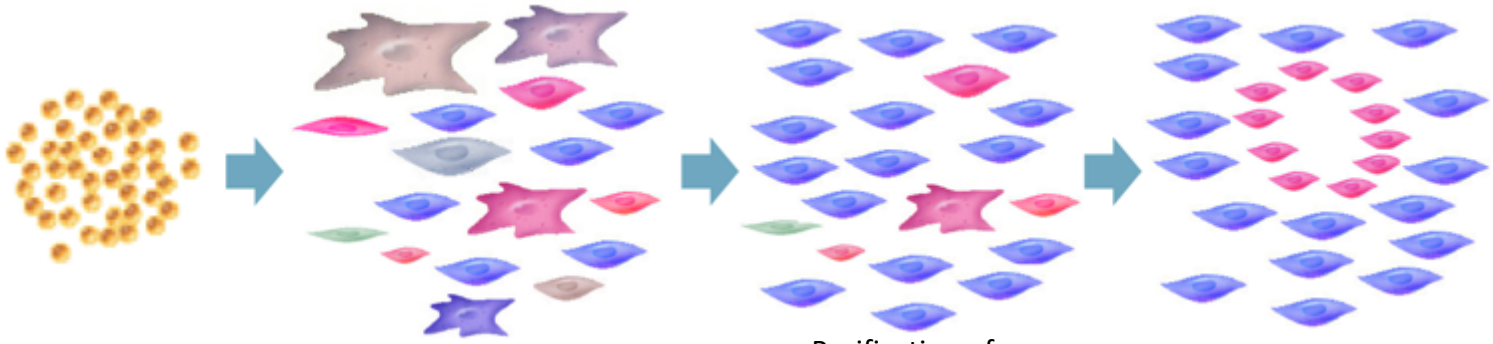
Pluripotency Combined with UniverCyte™ Technology

- Scalable source of all young human cell types
- Reduced Immunogenicity
- Regen phenotype



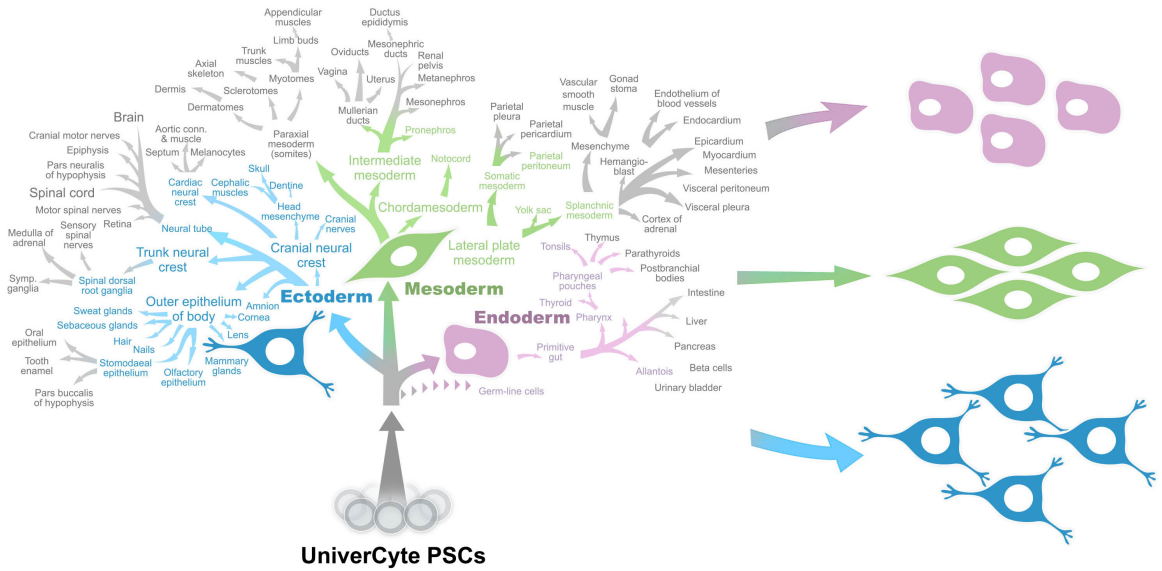
Universal *PureStem*™ Technology

Traditional Manufacture



ES Cells | Differentiation | Purification of desired cell type | Problem of impurities

PureStem Technology



UniverCyte PSCs

PureStem®

- **>200-fold diversity**
- **Scalable, monoclonally-purified regenerative progenitor cell lines**
- **Off-the-shelf use**

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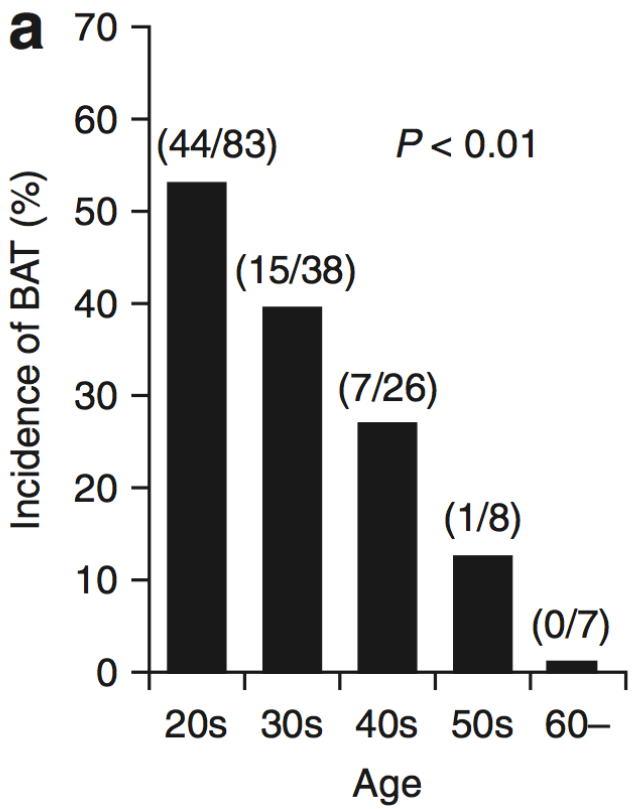
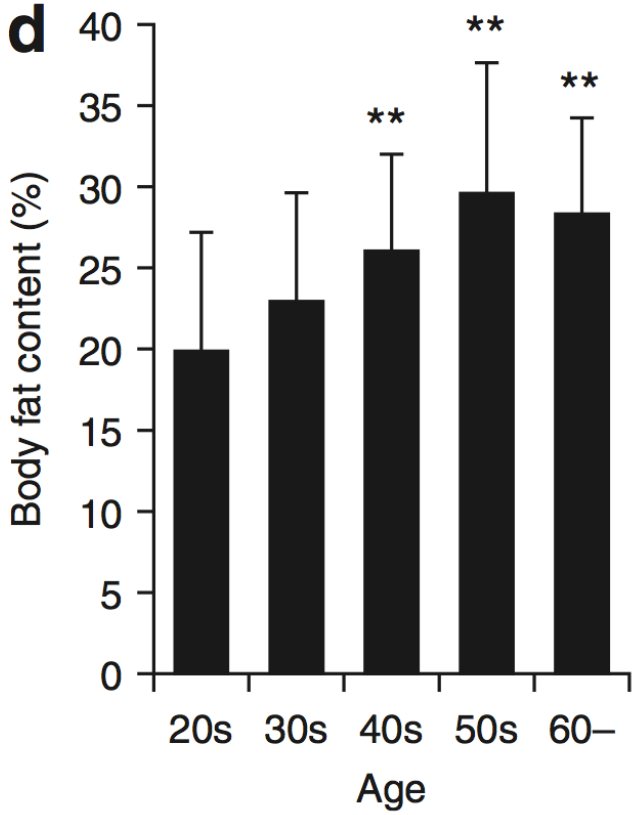
Age-Related BAT Loss





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

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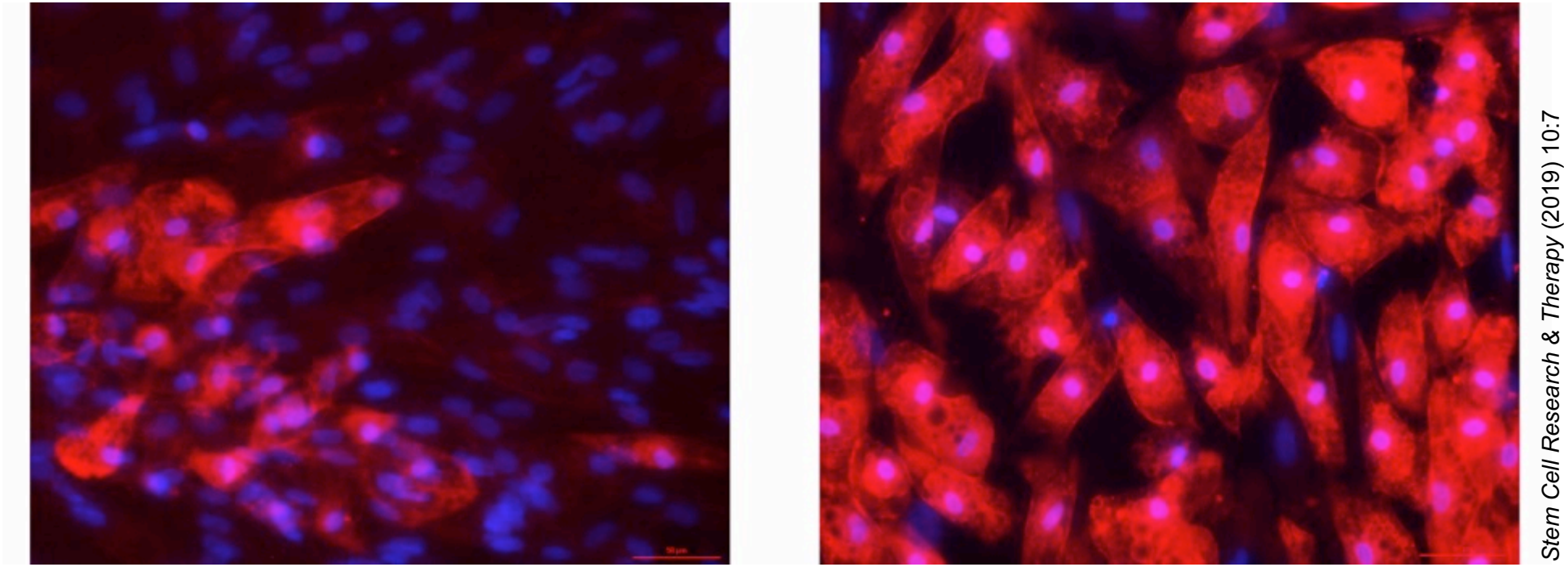
AgeX-BAT1 Properties

Stained for Brown Adipocyte Marker UCP1



Stem Cell Research & Therapy (2019) 10:7

Tissue-Sourced Brown Adipocytes

PureStem Brown Adipocytes

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Obesity/T2D Market/Competition

- 30M Americans have diabetes[1] 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.
- 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.

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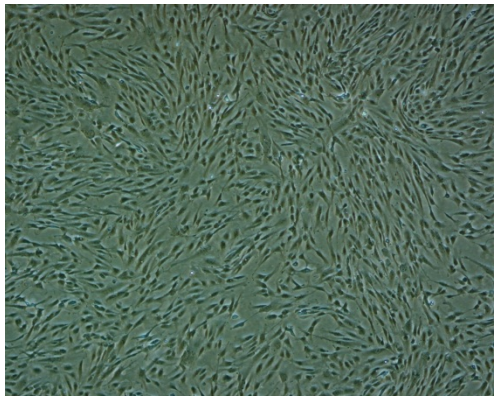
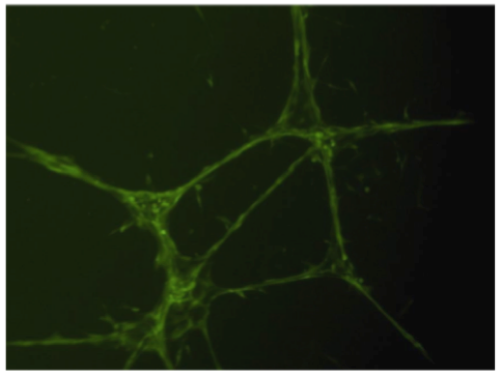
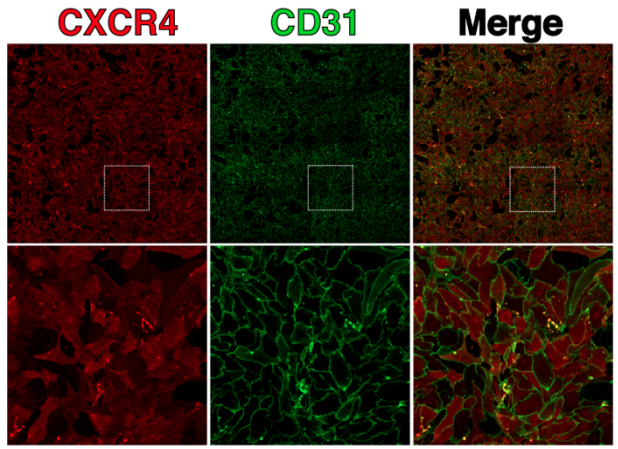
AgeX-VASC1 Purity

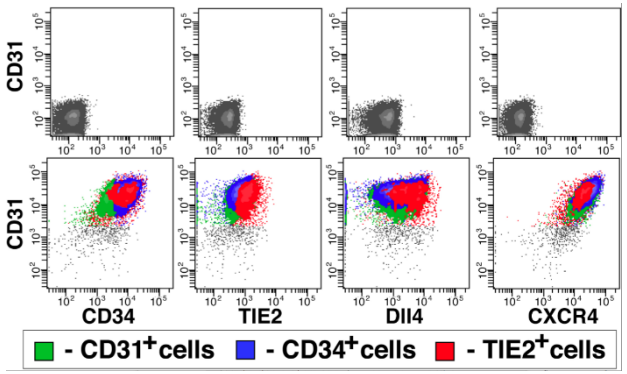
Monoclonal Endothelium

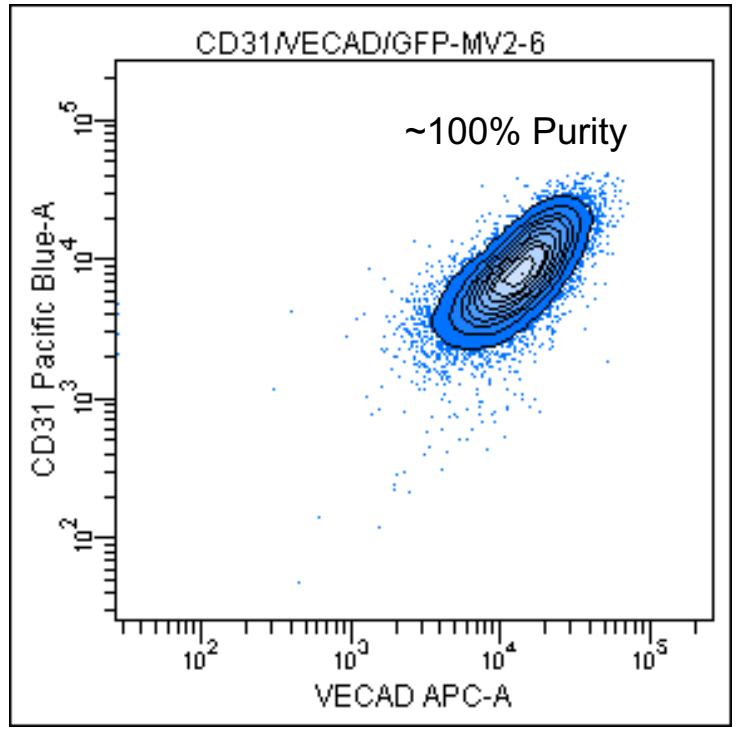


GFP Endothelium (168 hrs)









Cardiovascular Market

> $Trillion Market Worldwide

American Heart Association | American Stroke Association

	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 middle-aged 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

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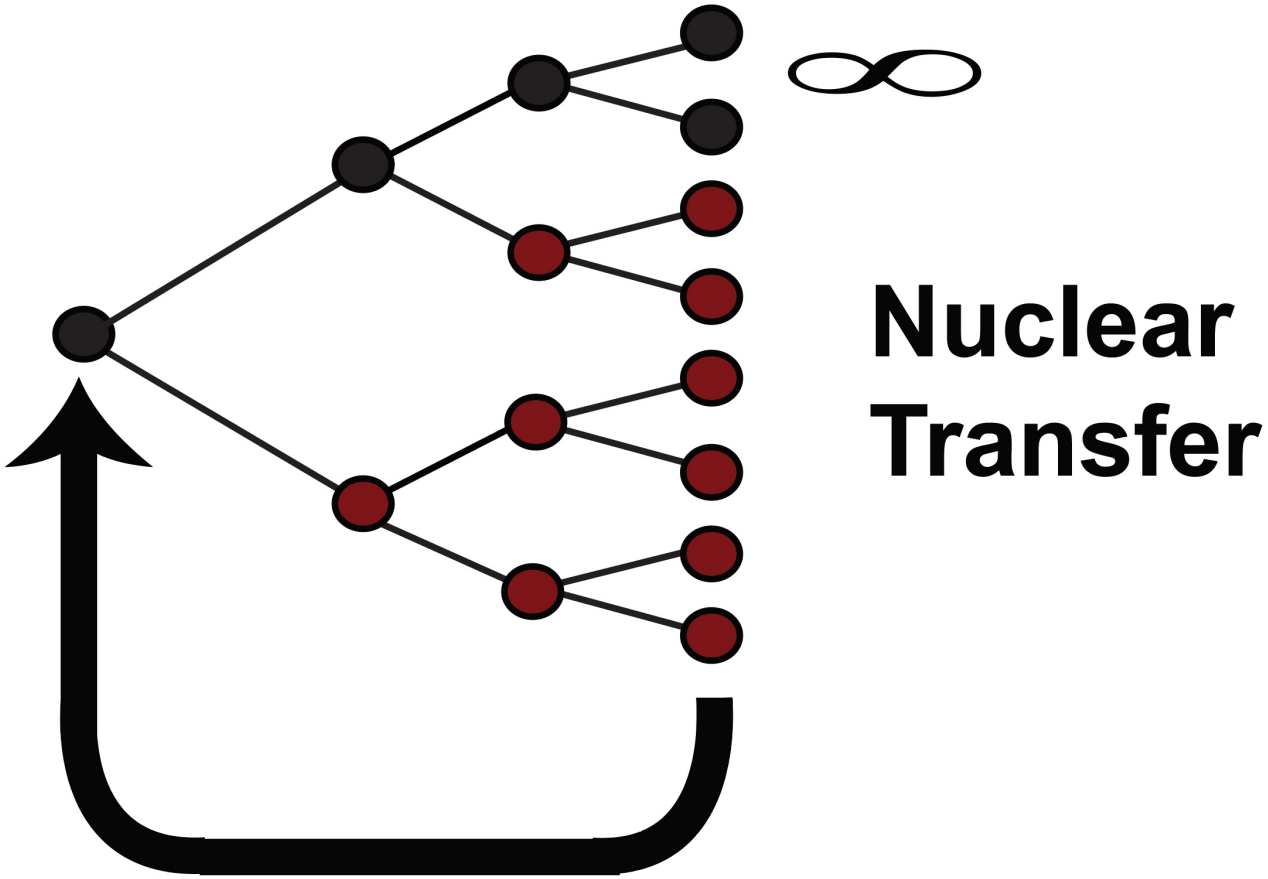
The Reversal of Aging

Cloning (SCNT) reverses the aging of somatic cells: What are the active molecules in the egg cell that accomplish age-reversal?



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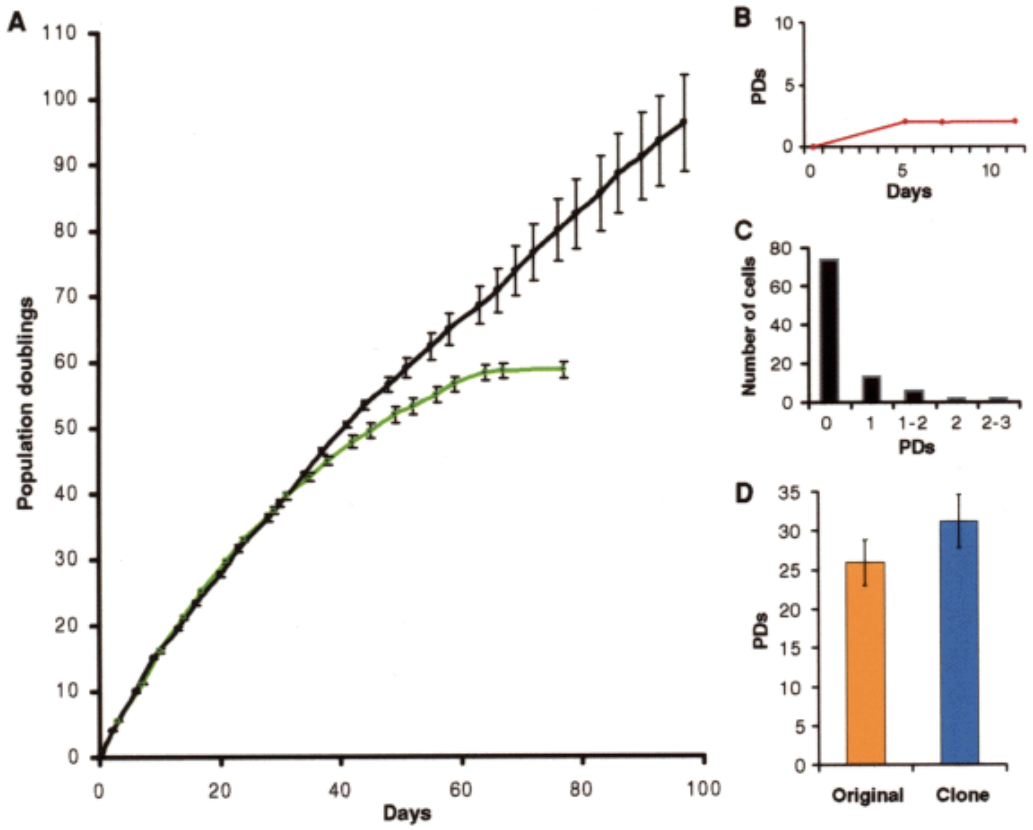
The Reversal of Aging



Science 288: 665 (2000)

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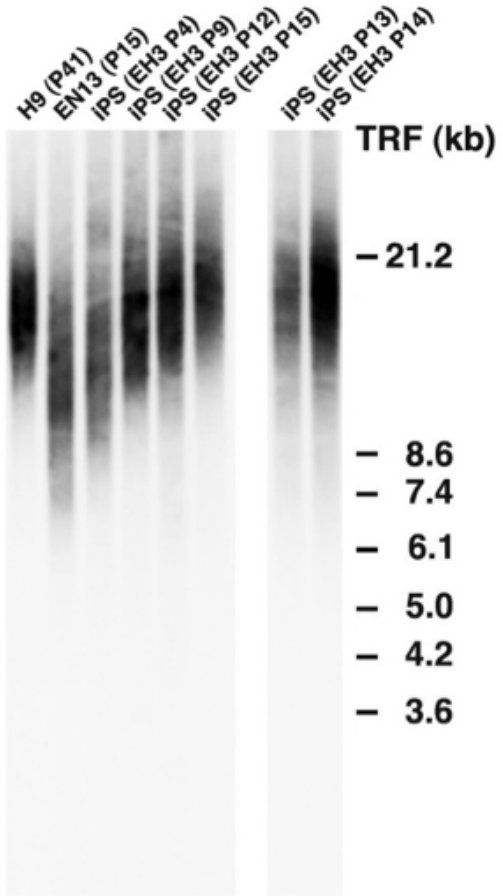
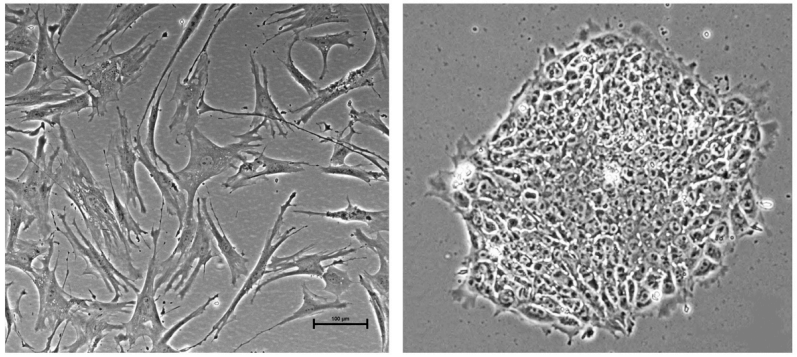
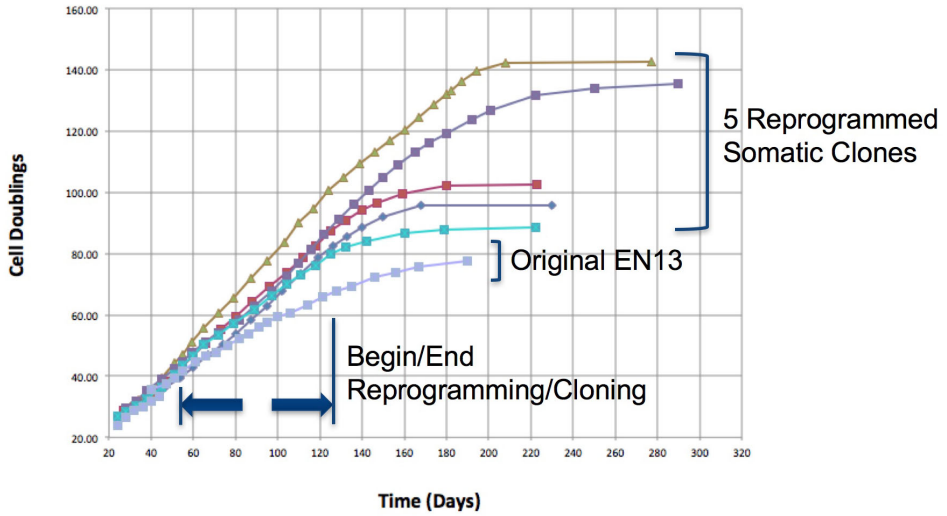
The Reversal of Aging by Transcriptional Reprogramming



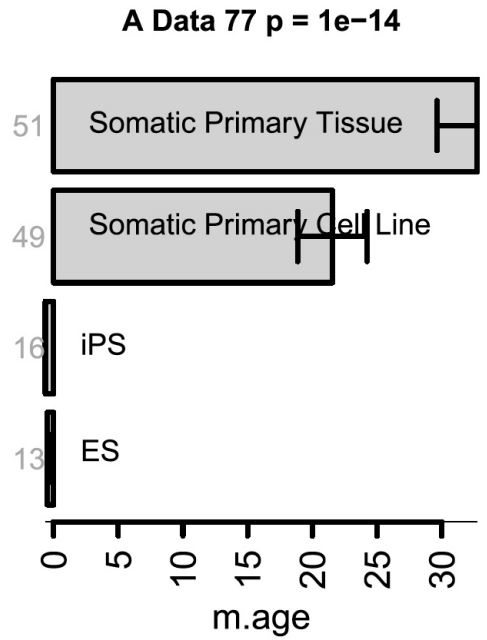
Regen Med 2010 May;5(3):345-63



Skin Fibroblasts iPS Cells



Reprogramming Methylation Age



Horvath
Genome Biol. 2013;14(10):R115

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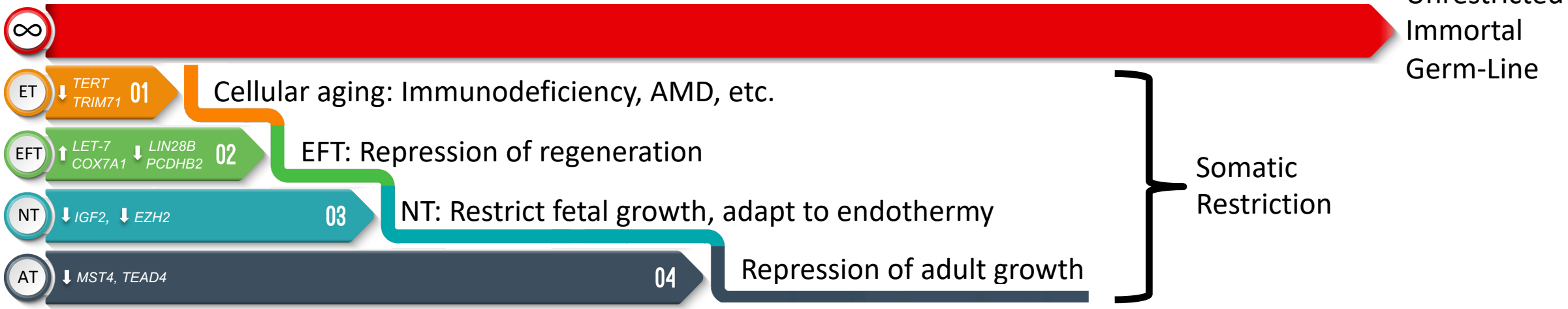
Is Age-Reversal *In Vivo* Clinically Achievable?

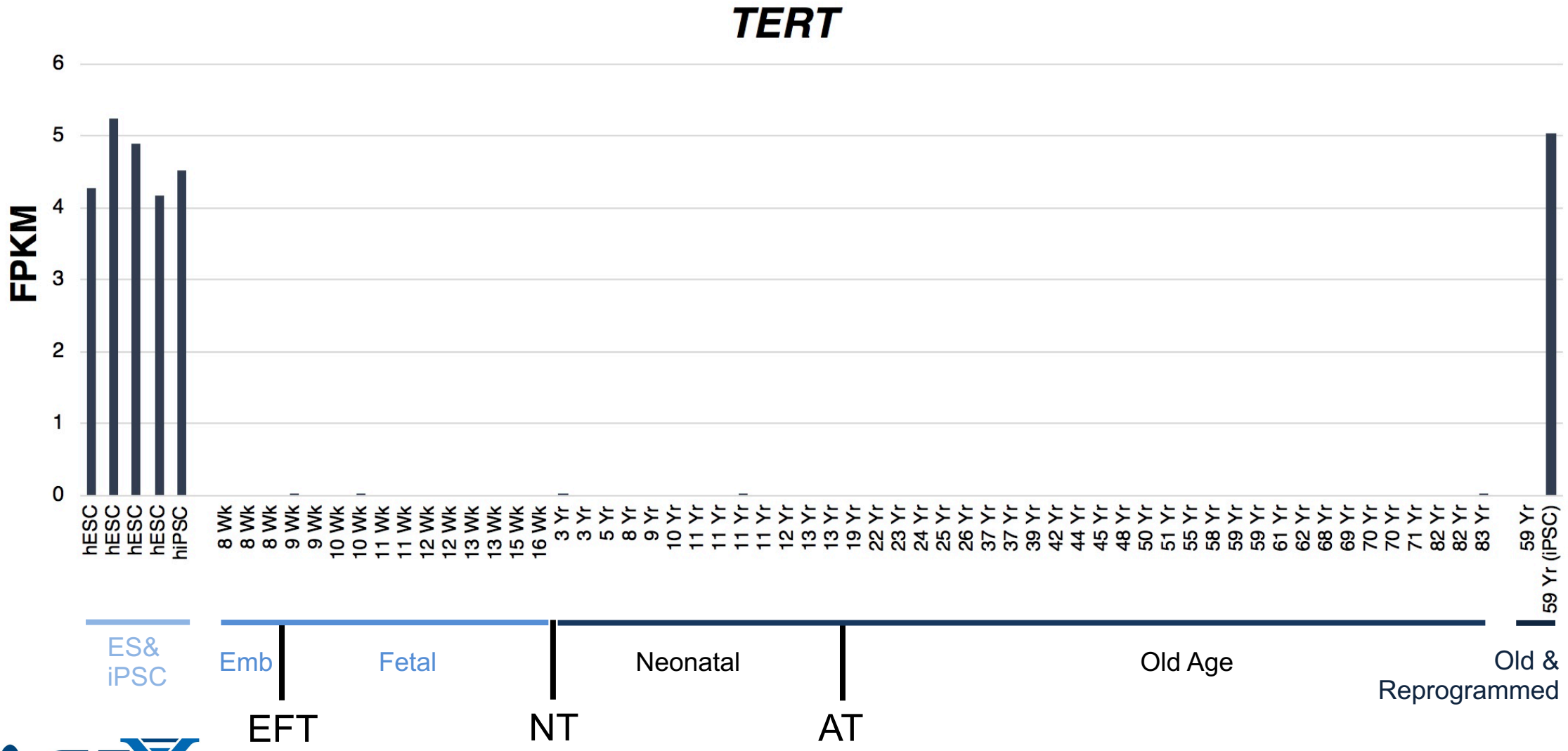
AGEX THERAPEUTICS

The Problem: Immortality Repressed Early



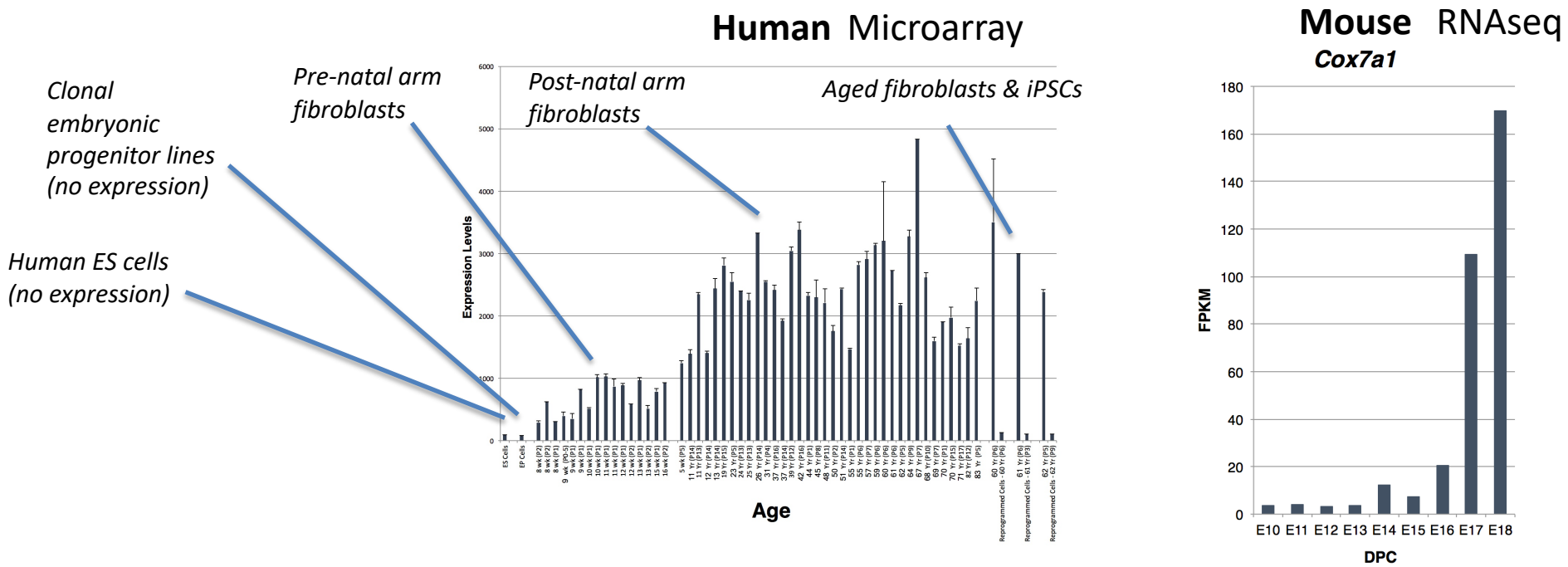
AGEX THERAPEUTICS

Telomerase *(TERT)* Expression During Development

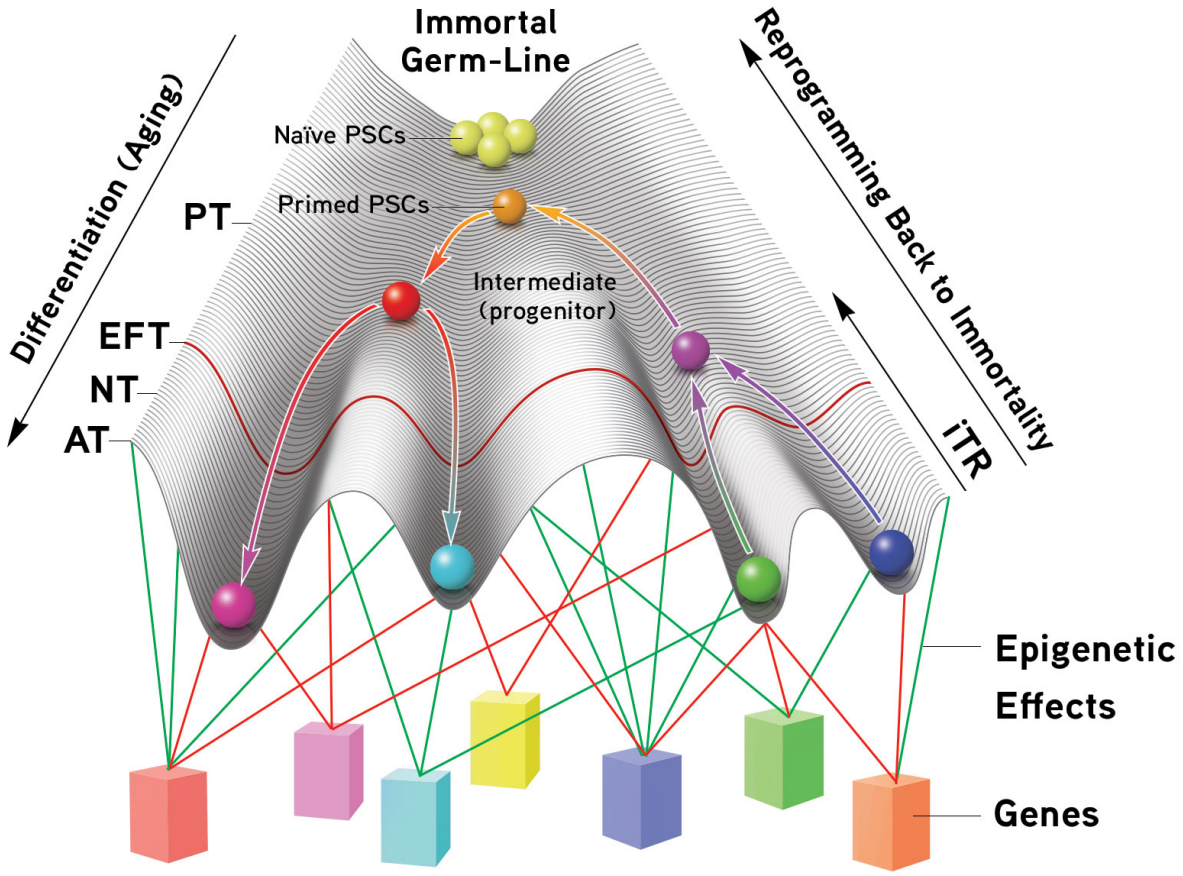


COX7A1 as an EFT Marker

Repression of regeneration coincides with switch to OXPHOS at the Embryonic-Fetal Transition (EFT).



Goal of Immortal Tissue Regeneration



- The goal is **not** to reprogram cells to pluripotency *in vivo*.
- Instead, the goal is to reprogram only before the Weismann Barrier to unlock regeneration.
- Need to separately activate telomerase for iTR.

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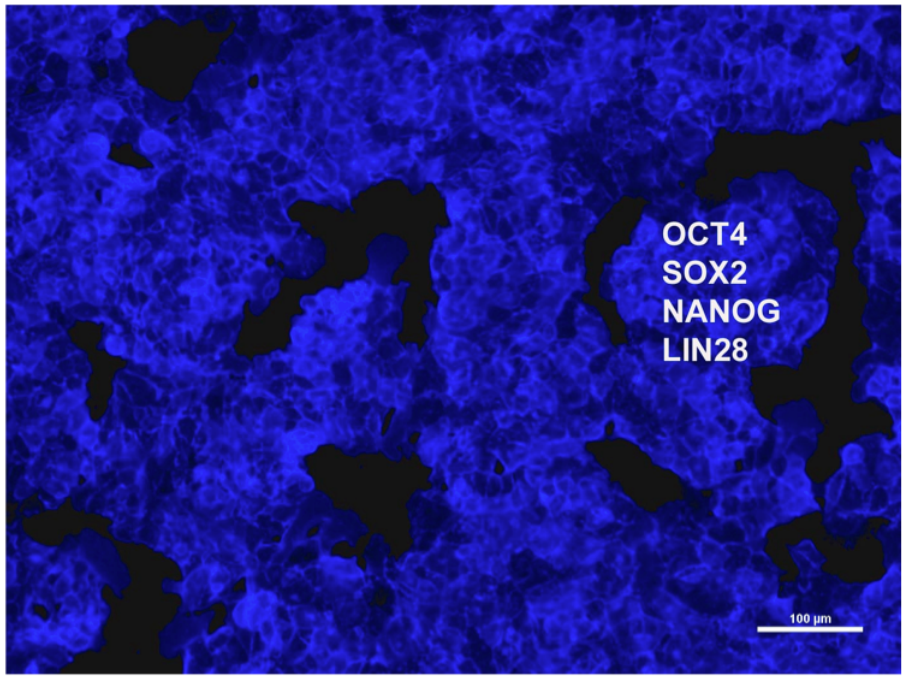
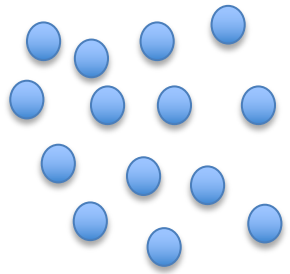
iTR (Immortal Tissue Regeneration) Strategy

Twin Strategies in Development



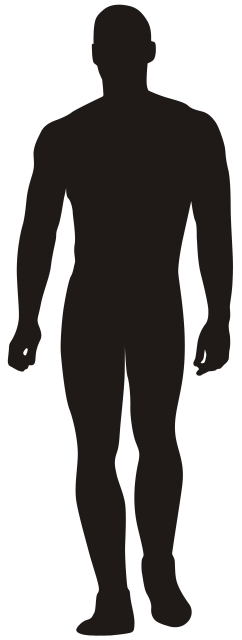
ReCyte1 EC Cell Line

Load with
Telomerase mRNA



Exosomes

Small Molecule
Cocktail (iTR 1547)

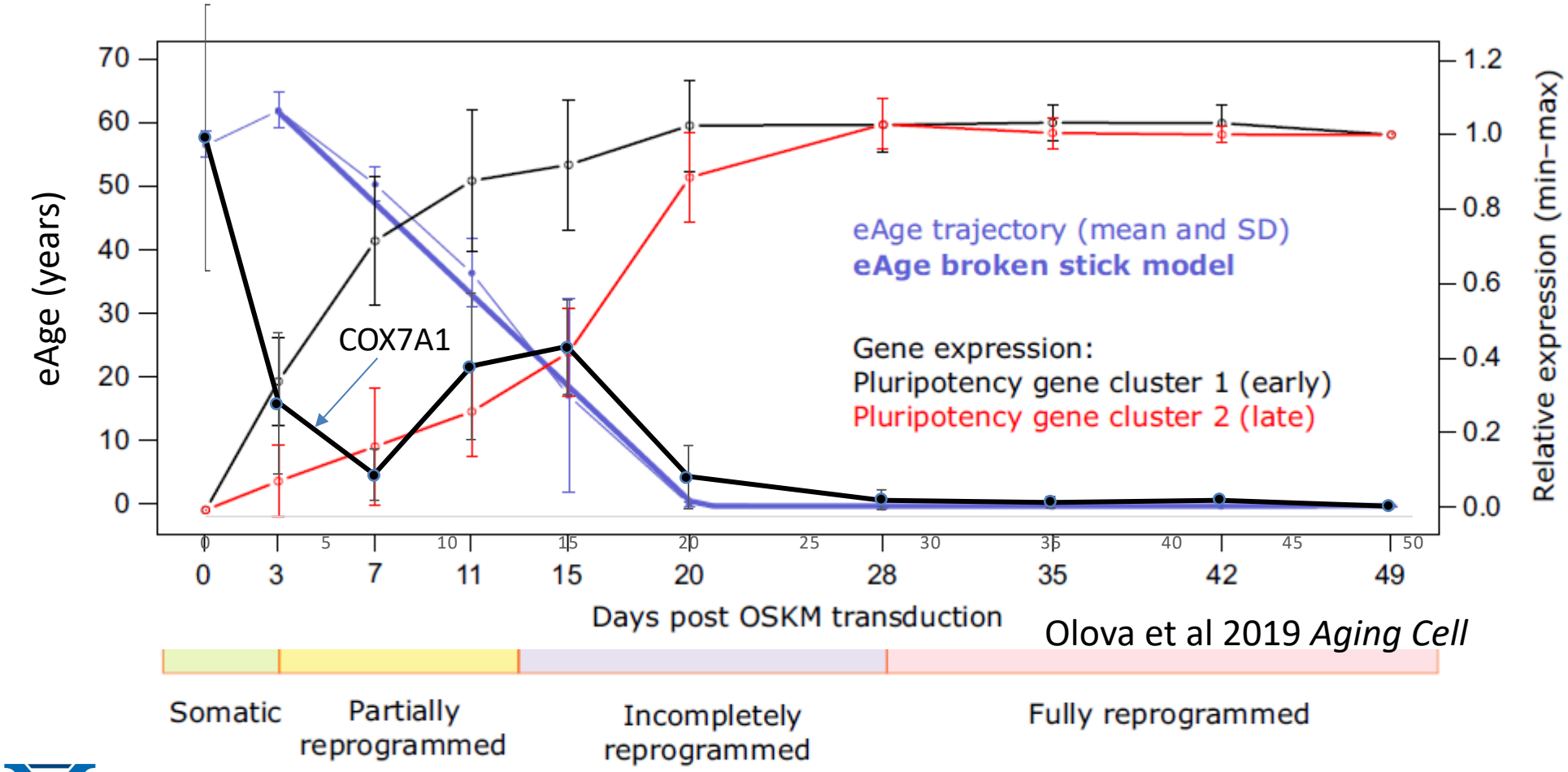


***In Vivo* Applications**

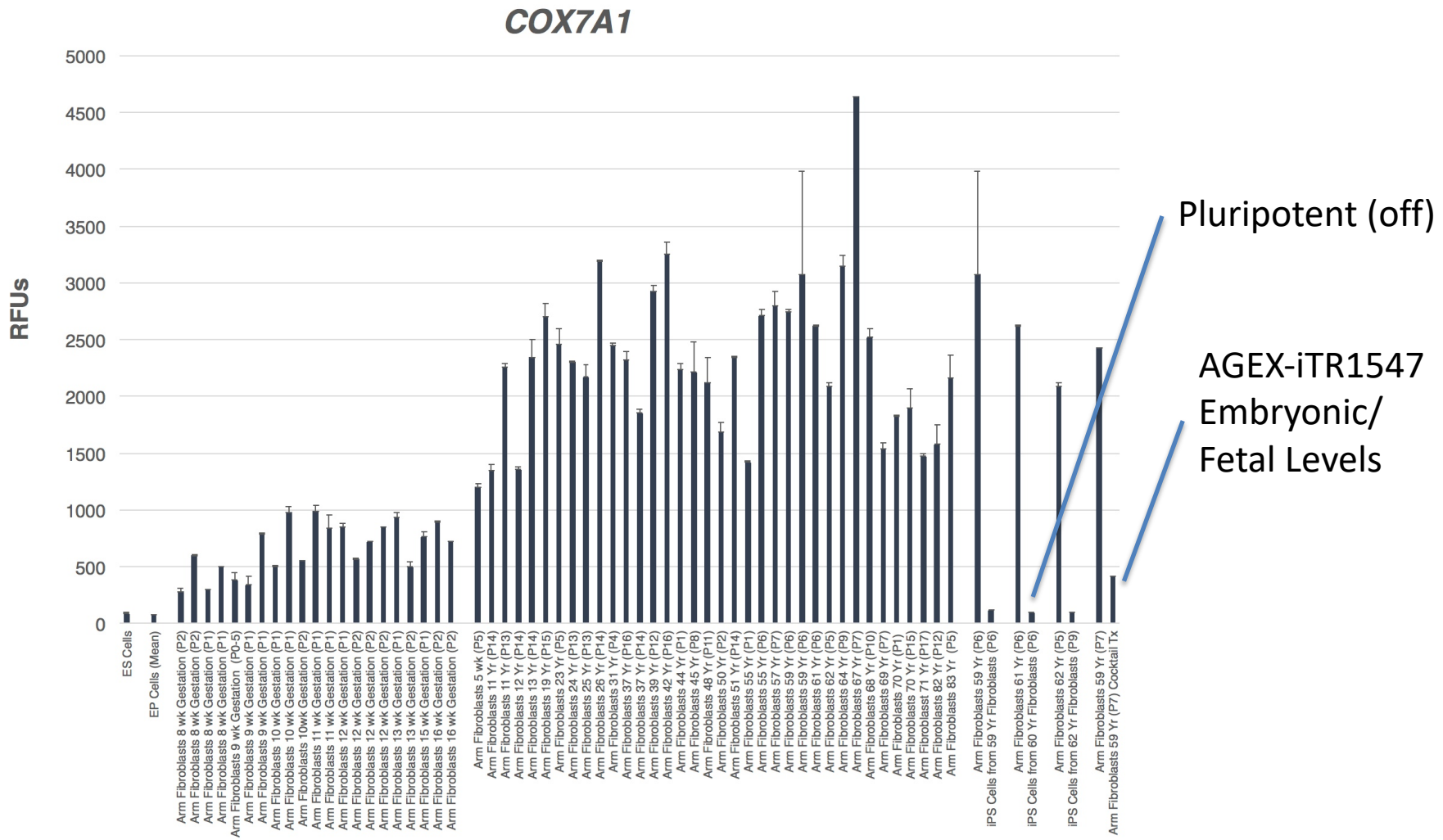
AGEX THERAPEUTICS

iTR Therapeutic Temporal Window

Timeline of epigenetic age, *COX7A1* and pluripotent gene expression during reprogramming



iTR1547 – Small Molecule-Based Reprogramming



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Summary

- Upstream triggers that lead to aging and senescence may begin as early as embryonic phases of development.
- The UniverCyte™ Pluripotency platform allows the industrial-scale manufacture of hundreds of young cell types for use in regenerative therapy.
- The transient expression of telomerase and regeneration (iTR) has the potential to reverse the aging of cells *in vivo* for diverse applications in age-related degenerative disease.

AGEX THERAPEUTICS

"If there were no regeneration there would be no life.
If everything regenerated there would be no death."

Richard J. Goss
- Principles of Regeneration (1969)

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