AGEX THERAPEUTICS

A Leader in Precision Gerontology

Precision Reprogramming Of Human Aging

NYSE American: AGE

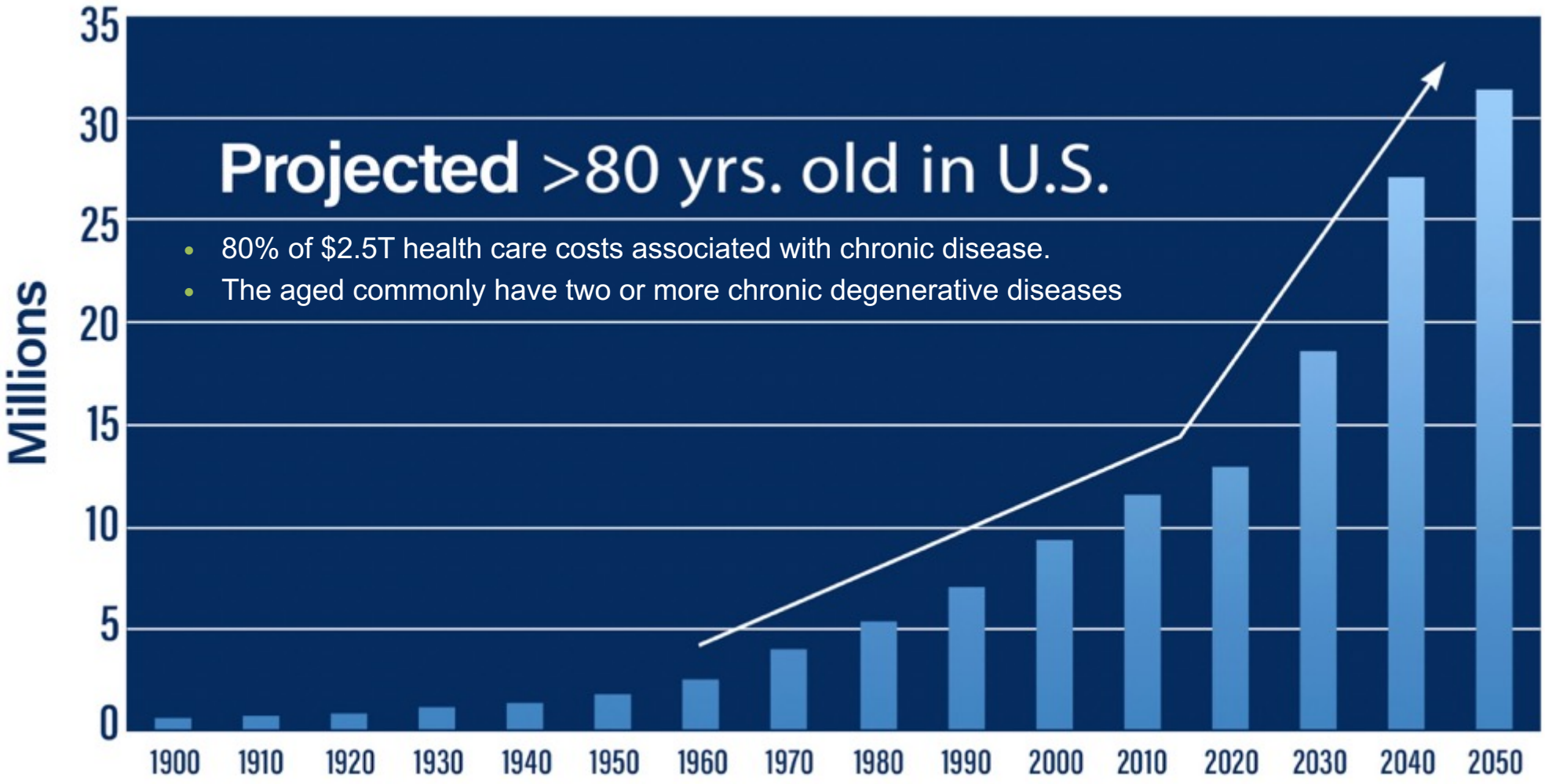
September 20, 2022

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

The Opportunity in Age-Related Degenerative Disease

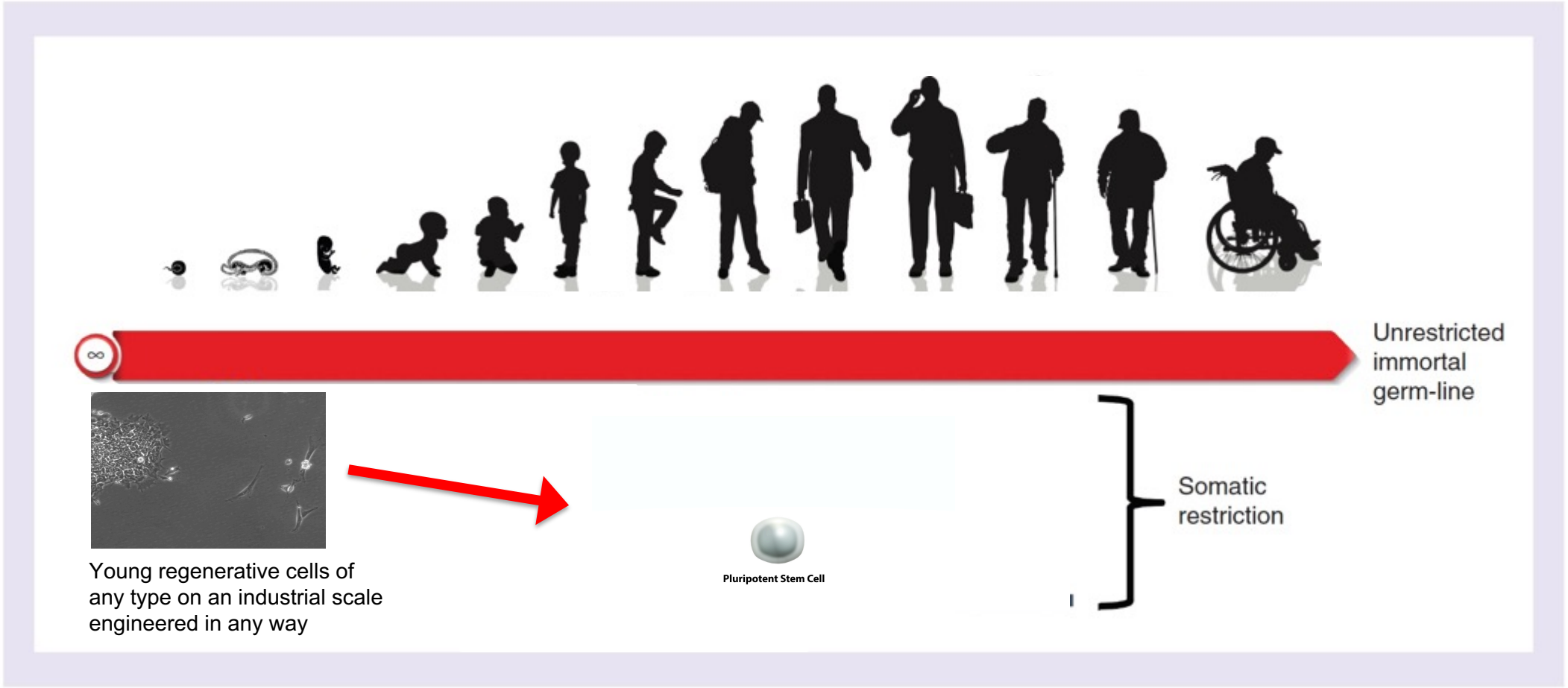


U.S. Census Bureau

AGEX THERAPEUTICS

How it Works: Somatic Cell Aging

Human ES cells are Pluripotent & Immortal



Regen Med. 2019 Sep;14(9):867-886.

AGEX THERAPEUTICS

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AGEX THERAPEUTICS

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- 2019 – Bayer acquires BlueRock
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- 2021 – SANA IPO $6B M. Cap.
  2022 – LCTX $670M Roche
- Future – 1st $B product

AGEX THERAPEUTICS

Value of the *UniverCyte* Allogeneic Cellular Therapeuticss

Classical biologics off-the-shelf business model

Traditional Biologicals

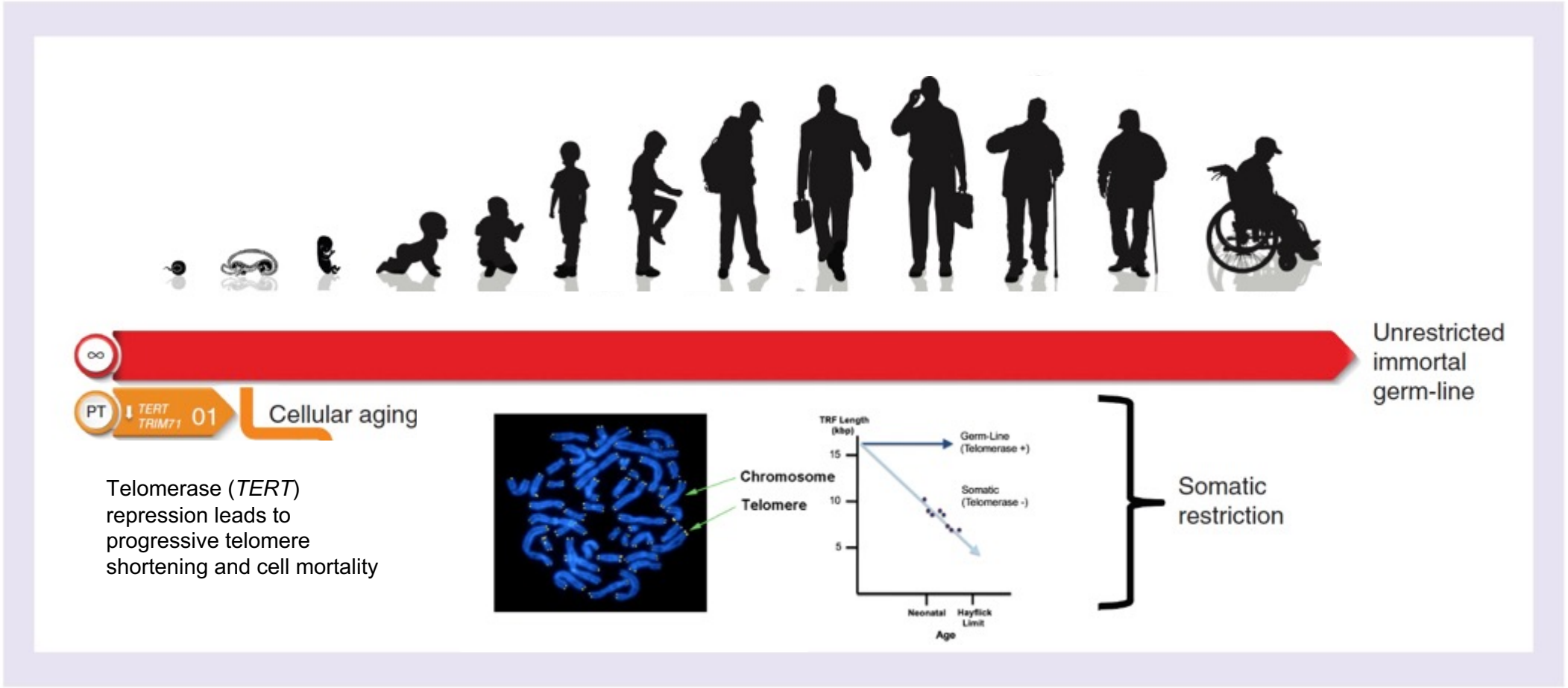
Centralized Production Facility → *Distributed Frozen Inventory* → *Point Of Care*

UniverCyte-Derived Cell Therapy Products

AGEX THERAPEUTICS

How it Works: Somatic Cell Aging

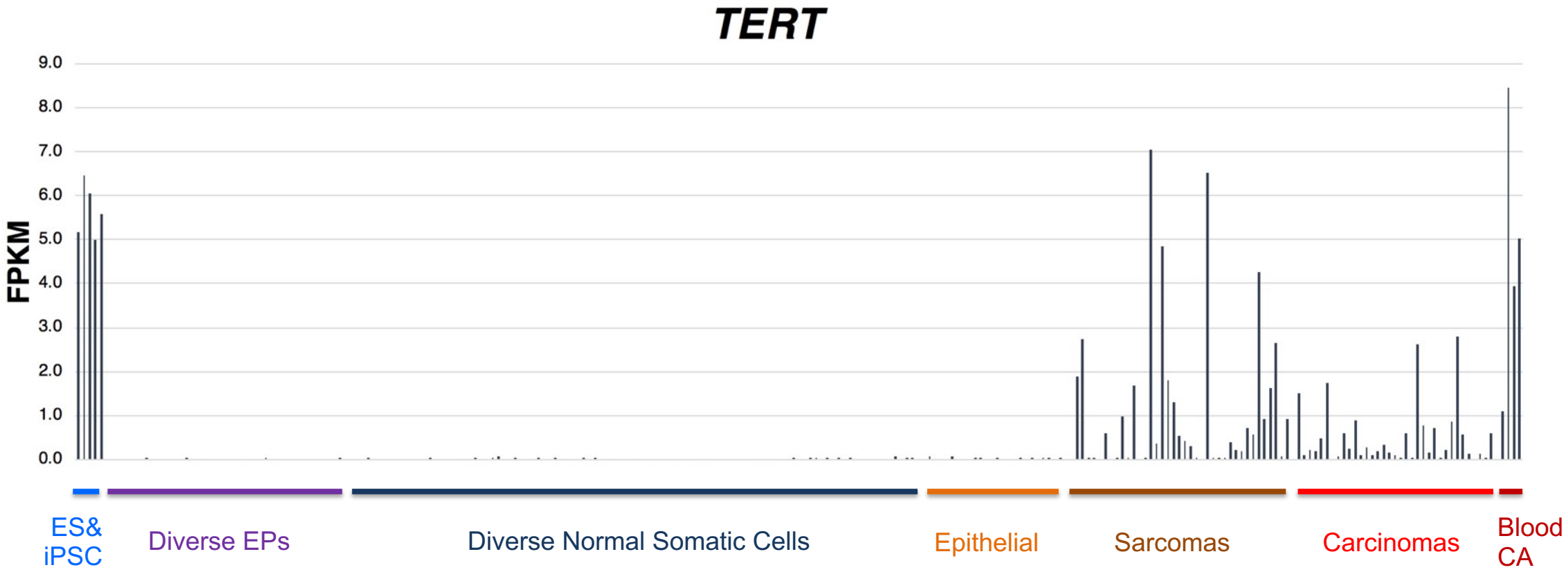
Somatic cells turn off telomerase and therefore age



Regen Med. 2019 Sep;14(9):867-886.

AGEX THERAPEUTICS

Antagonistic Pleiotropy



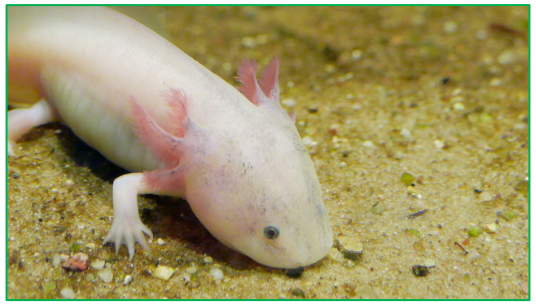
AGEX THERAPEUTICS

How it Works: Regeneration

If repression of regeneration at EFT doesn't occur, animals regenerate

Unrestricted immortal germ-line

Example of regeneration remaining on in somatic cells



Somatic restriction

Regen Med. 2019 Sep;14(9):867-886.

AGEX THERAPEUTICS

Timing of Mouse Emb-> Fetal Transition

Experimental

Confocal Microscopic Analysis of Scarless Repair in the Fetal Rat: Defining the Transition

Steven R. Beanes, M.D., Fei-Ya Hu, D.D.S., Chia Soo, M.D., Catherine M. H. Dang, M.D., Mark Urata, D.D.S., M.D., Kang Ting, D.M.D., D.M.Sc., James B. Atkinson, M.D., Prosper Benhaim, M.D., Marc H. Hedrick, M.D., and H. Peter Lorenz, M.D.

Los Angeles, Calif.

Plast. Reconstr. Surg. 2002 Jan;109(1):160-70.

wound harvest was used for controls. The wounds were fixed and stained with hematoxylin and eosin, antibody to type I collagen, and Sirius red for confocal microscopic evaluation. No E14 rat fetuses survived to wound harvest. Wounds created on E16 fetal rats healed completely and without scarring. E16 fetal rat hair follicle formation and collagen architecture was similar to that of normal, non-wounded skin. Wounds created on E18 fetal rats demonstrated slower healing; only 50 percent were completely healed at 72 hours compared with 100 percent of the E16 fetal rat wounds at 72 hours. Furthermore, the E18 wounds healed with collagen scar formation and without hair follicle formation. Confocal microscopy demon-

AGEX THERAPEUTICS

Timing of Mouse Emb-> Fetal Transition

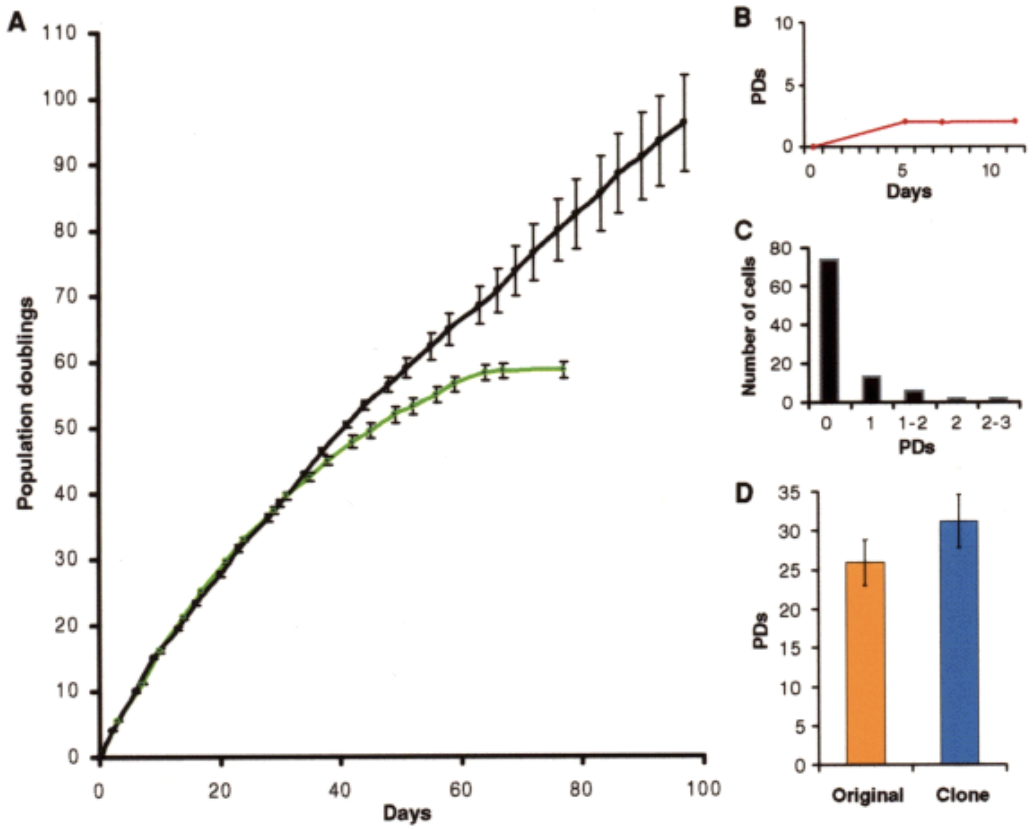
Data For Carnegie Stages Comparison Graph (Species/Days)

Species	Stage	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23
Human[2]	Days	20	22	24	28	30	33	36	40	42	44	48	52	54	55	58
baboon[3]	Days	23	25	27	28	29	30	31	33	35	37	39	41	43	45	47
monkey[4]	Days	21	22	25	28	29	30	32	34	36	37	38	40	42	44	46
marmoset[5]	Days	57		60		64		67				74				
mouse[6]	Days	9	9.5	10	10.5	11	11.5	12	12.5	13	13.5	14	14.5	15	15.5	16
rat[7]	Days	10.5	11	11.5	12	12.5	13	13.5	14	14.5	15	15.5	16	16.5	17	17.5
hamster[8]	Days	10	10.5	11	11.5	12	12.5	13	13.5	14	14.5	15	15.5	16	16.5	17
guinea pig[9][10]	Days	14.5	15	15.5	17	18	19	20	21	22	23	24	25	26	27	29
rabbit[11]	Days	8	8.5	9.5	10.5	11	12	12.5	13.5	14	14.5	15.5	16	16.5	17	18
sheep[12]	Days	15	16	17.5	18.5	19.5	20.5	22	23	24.5	25.5	27.5	29.5	30	33	
pig[13]	Days	14	15	16	17	18	19	20.5	21.5	23	24	25.5	27.5	29	30.5	32.5
chicken[14]	Days	1	1.5	2	2.25	2.5	3	3.25	3.75	4.75	5.5	6.25	7.25	7.75	8.5	10
dog	Days						27	28	29	30	34	36	37			
bat[15]	Days				40		44	46	50	54	60		70		80	

Rat Transition in skin:
(16.5-18.5 days)

AGEX THERAPEUTICS

Reprogramming the Aging of Somatic Cells



Science 288: 665 (2000)

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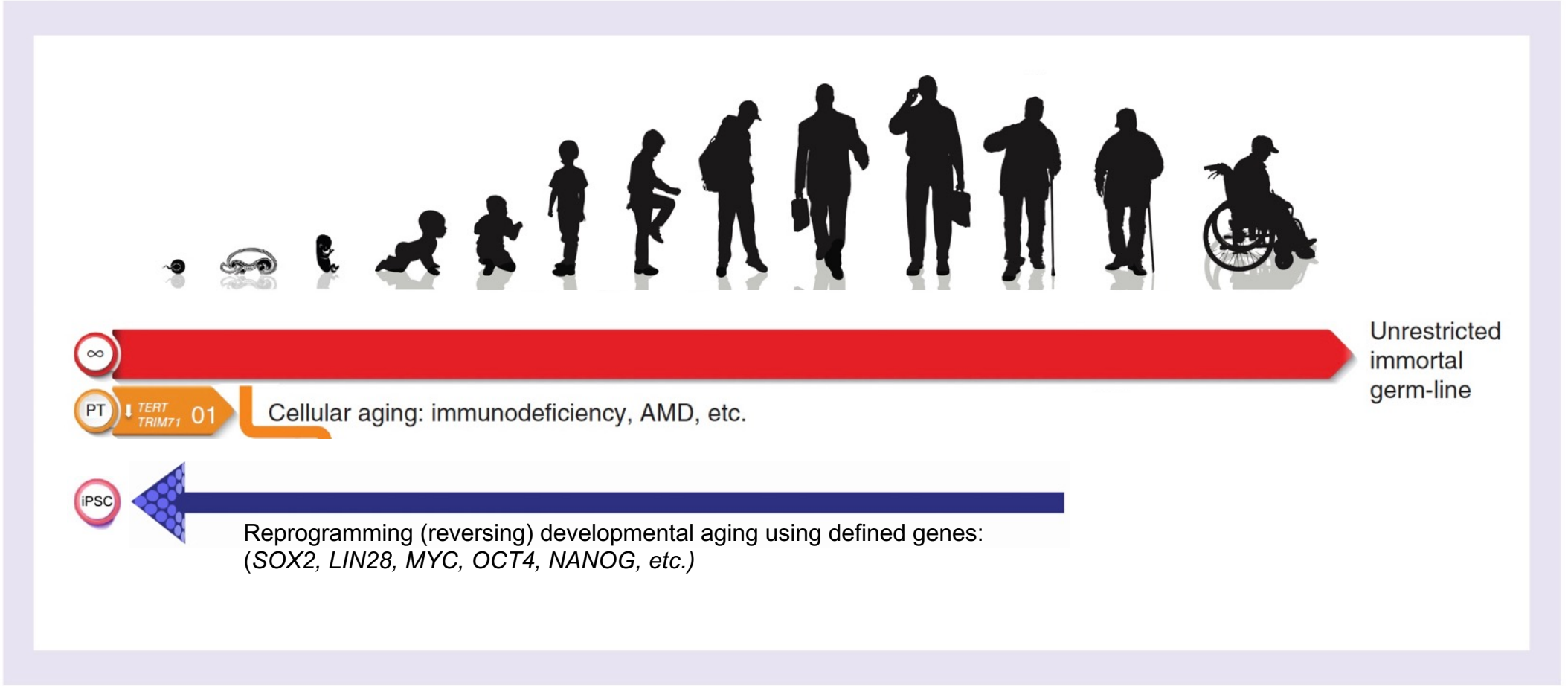
How it Works: Reprogramming to Pluripotency

First came the ability to reprogram aging back to the beginning of life



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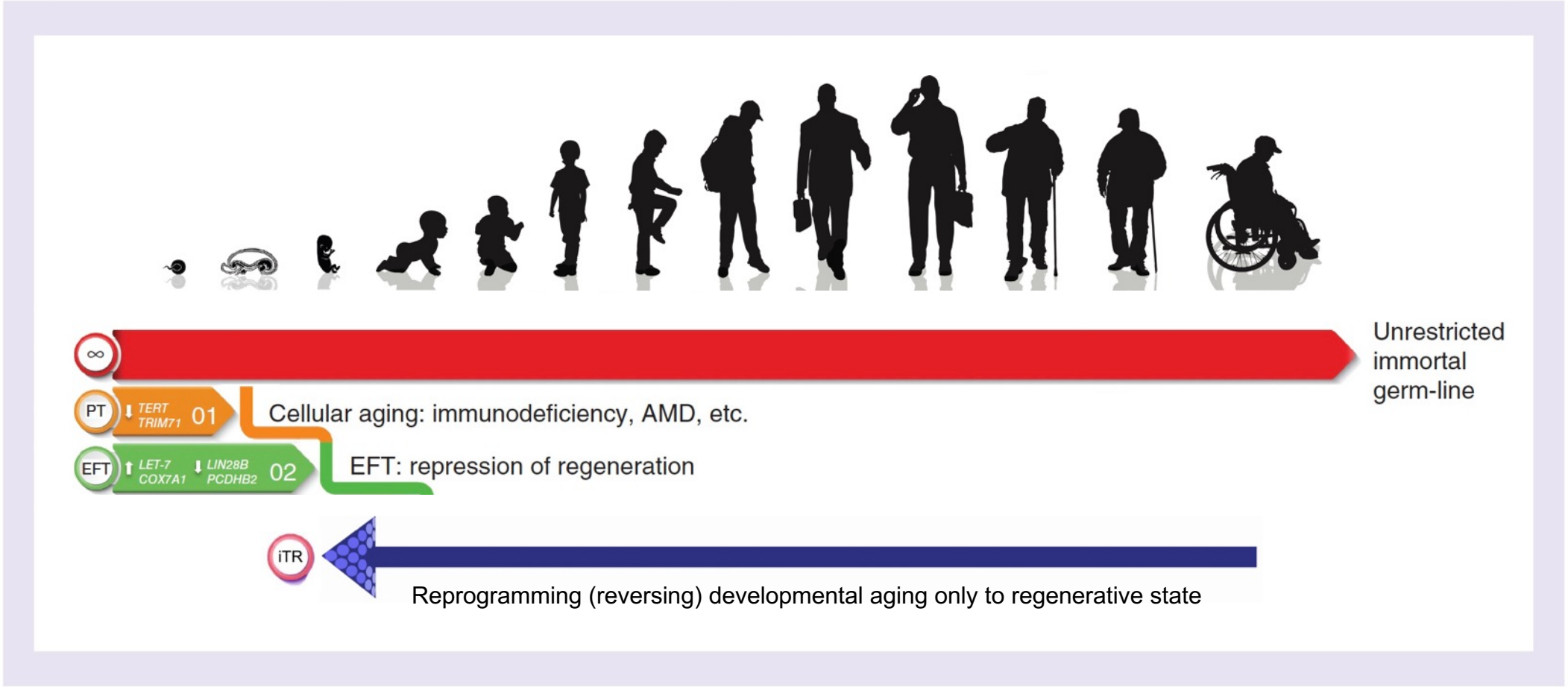
How it Works: Induced Tissue Regeneration (iTR)

iTR™ or "partial reprogramming' induces the regenerative state



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- The powerful platform of pluripotency-based regenerative medicine (RegenMed 1.0)
- Allows the manufacture of young regenerative cells of any kind on an industrial scale for cell-based therapy
- Now technologies for inducing regeneration in the body without cell transplantation (iTR™ – induced Tissue Regeneration (RegenMed 2.0)

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- 2019 – Vertex acquires Semma
- 2021 – SANA IPO $6B M. Cap.
- Future – 1st $B product

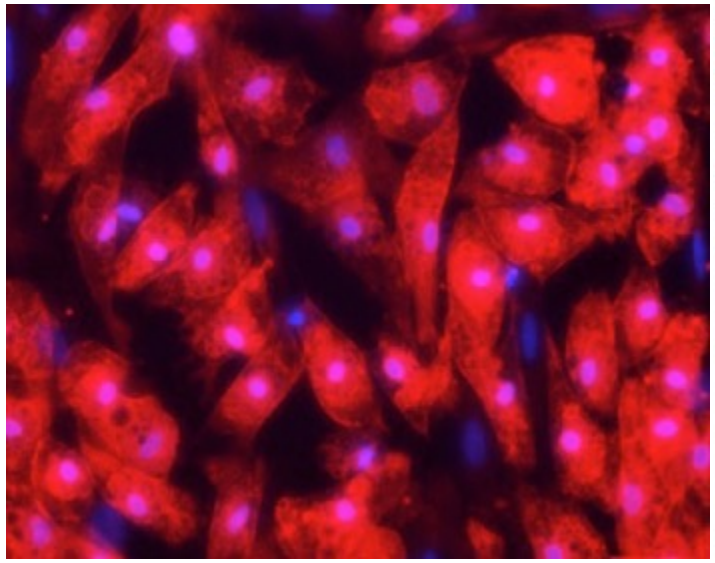
Regenerative Medicine 2.0

- Induced tissue regeneration (iTR) in the body without cell transplantation. Works by reversing developmental aging
- 2010 – While at BioTime we publish evidence technology reverses developmental aging.
- 2013-Present first patents filed and owned by AgeX
- 2022 – Altos >$3B financing
- 2022 – Retro $180M financing

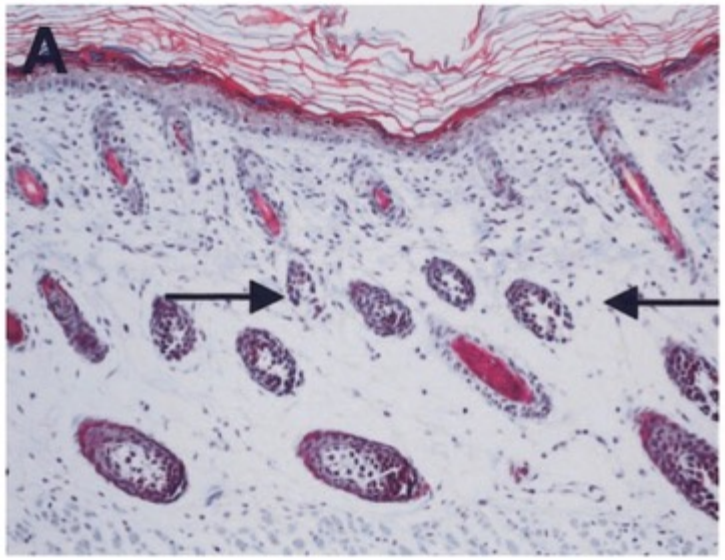
AGEX THERAPEUTICS

Product Development

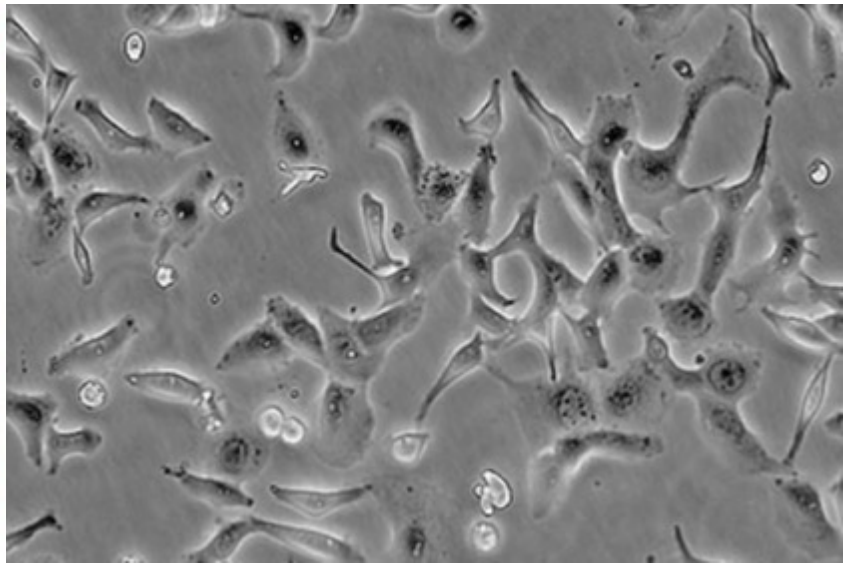
Three initial products in development:



AgeX-BAT1
(Type II Diabetes)



Renelon™
(Skin Regeneration)



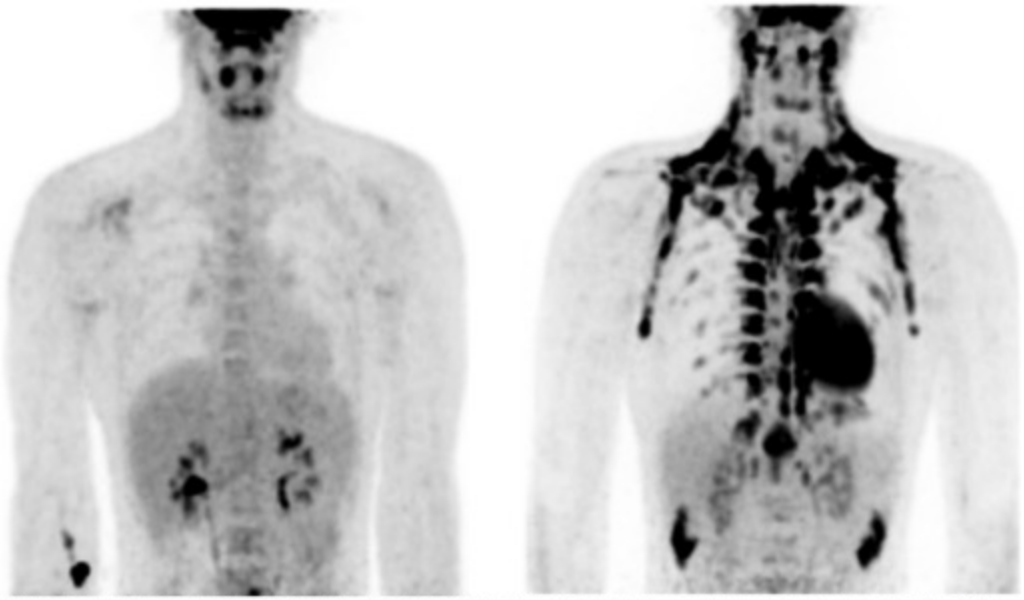
EPRO
(Breast Cancer)

AGEX THERAPEUTICS

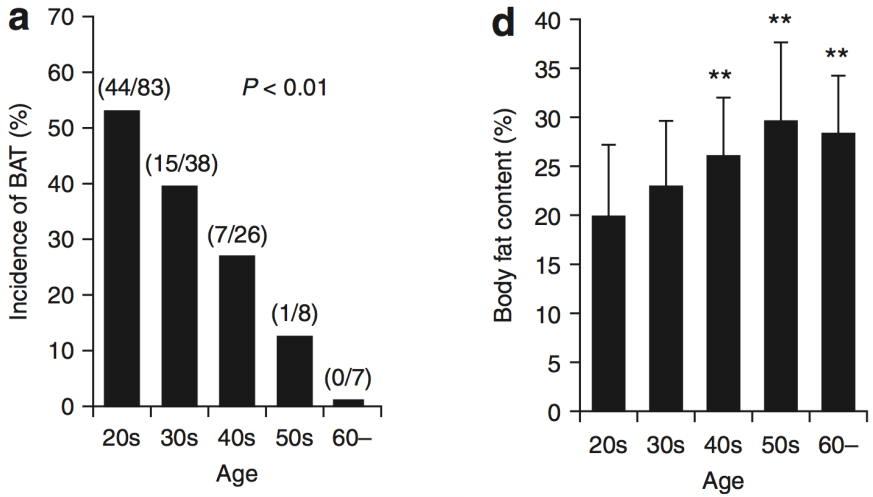
Our Patents & Type II Diabetes (>10X Type I Market)

Transplanted brown-fat-like cells hold promise for obesity and diabetes

Joslin Diabetes Center | 08-26-2020



PET/CT scanning images showing location of brown adipose tissue (brown fat). In a warm environment, brown fat is not active (left). During exposure to mild cold, active heat production takes place in the brown fat (right). Credit: CC BY-SA 3.0 – Mjw.hanssen



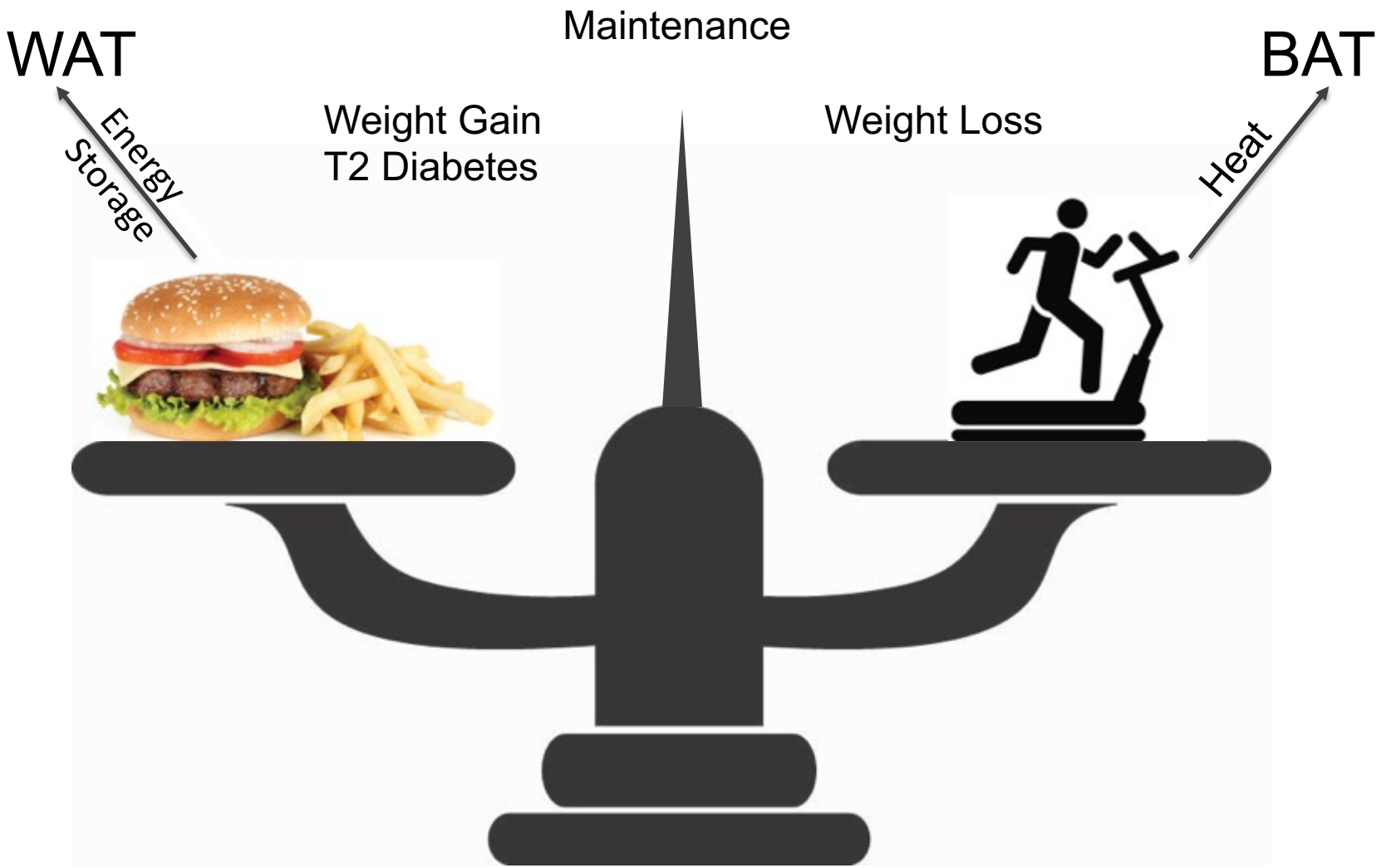
LETTERS
https://doi.org/10.1038/s41591-020-1126-7
nature medicine
Check for updates

Brown adipose tissue is associated with cardiometabolic health

Tobias Becher[1,2,3], Srikanth Palanisamy[1,4], Daniel J. Kramer[1,4,5], Mahmoud Eljalby[1,4], Sarah J. Marx[1], Andreas G. Wibmer[6], Scott D. Butler[7], Caroline S. Jiang[8], Roger Vaughan[4,8], Heiko Schöder[6], Allyn Mark[9] and Paul Cohen[1]✉

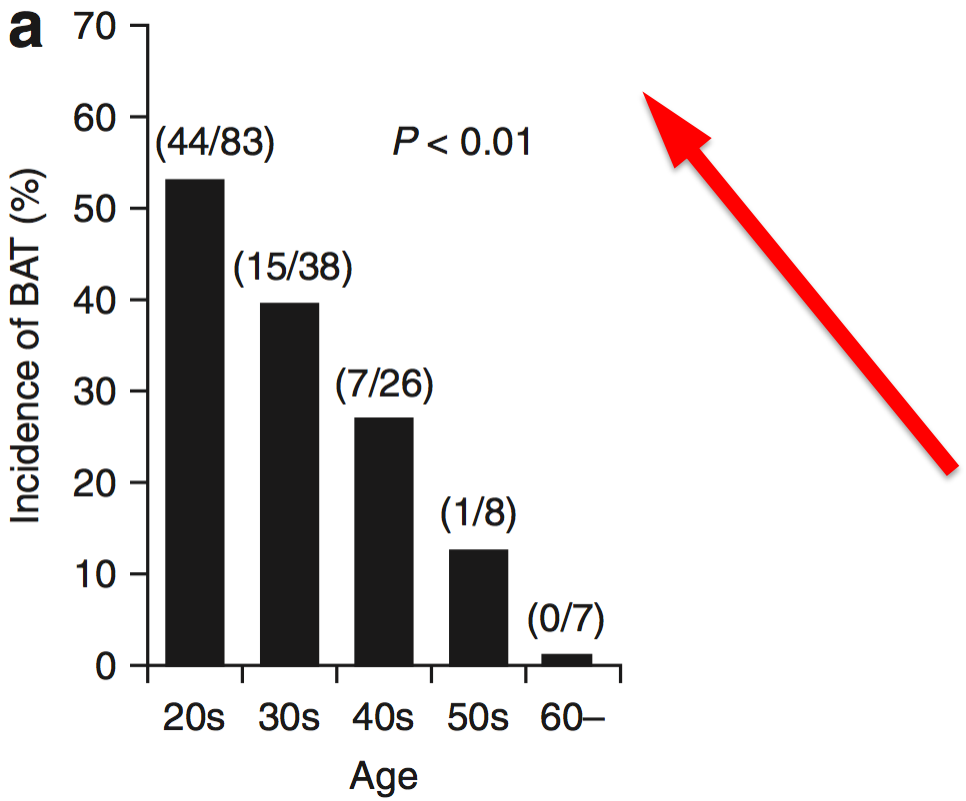
AGEX THERAPEUTICS

Brown Adipose Cells Regulate Metabolism



AGEX THERAPEUTICS

AgeX-BAT1 Transplantation to Restore Youthful BAT Levels

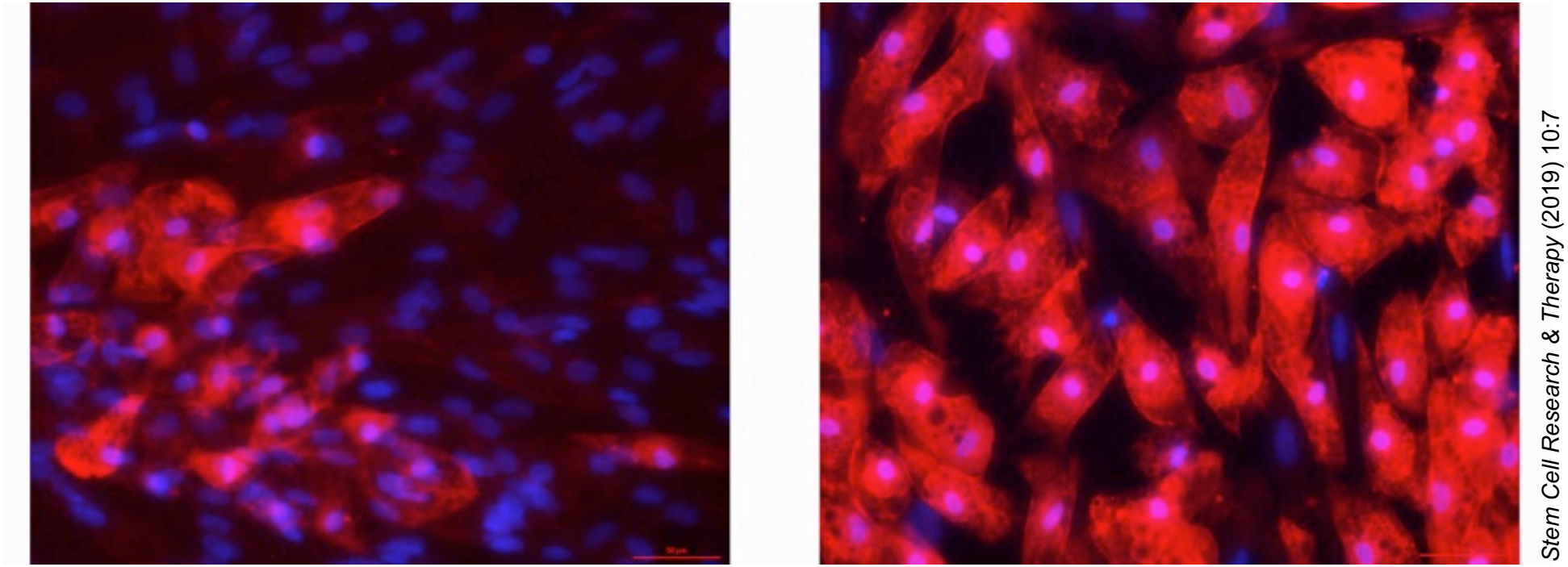


- AgeX-BAT1 significantly improves glucose tolerance and metabolic dysfunction in animals
- Clonal progenitors facilitate process development (purity and scalability)

AGEX THERAPEUTICS

AgeX-BAT1 Purity

Stained for Brown Adipocyte Marker UCP1



Stem Cell Research & Therapy (2019) 10:7

Tissue-Sourced Brown Adipocytes

PureStem Brown Adipocytes

AGEX THERAPEUTICS

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 in 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.

AGEX THERAPEUTICS

iTR Technology is Transformational (Age Reversal)

Jeff Bezos backs anti-aging startup Altos Labs

Calico® Google

Partial reprogramming restores youthful gene expression through transient suppression of cell identity

Antoine Roux Chunlian Zhang Jonathan Paw José Zavala-Solorio Twaritha Vijay

Ganesh Kolumam Cynthia Kenyon Jacob C. Kimmel
Calico Life Sciences LLC

AGEX THERAPEUTICS

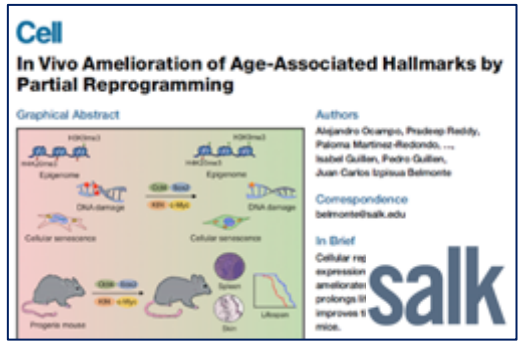
Reprogramming to recover youthful epigenetic information and restore vision

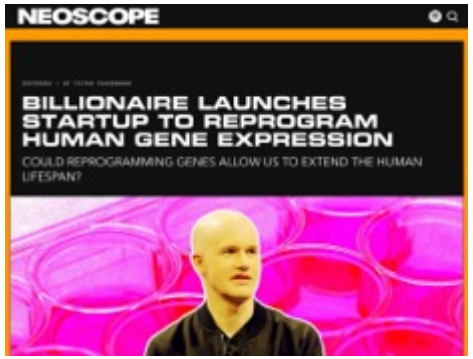
https://doi.org/10.1038/s41586-020-2975-4
Received: 31 July 2019
Accepted: 22 October 2020
Published online: 2 December 2020
Check for updates

Yuancheng Lu, Benedikt Brommer, Xiao Tian, Anitha Krishnan, Chen Wang, Daniel L. Vera, Qiurui Zeng, Doudou Yu, Michael S. Bo, Jae-Hyun Yang, Songlin Zhou, Emma M. Hoffmann, Margarete M. Karg, B. Schultz, Alice E. Kane, Noah Davidsohn, Ekaterina Korobkina, Karolina Chwalek, A. Rajman, George M. Church, Ko, Morgan E. Levine, Mer, David A. Sinclair

iduna THERAPEUTICS

HARVARD MEDICAL SCHOOL





nature COMMUNICATIONS

ARTICLE
https://doi.org/10.1038/s41467-020-15174-3 OPEN

turn.bio

STANFORD SCHOOL OF MEDICINE

Transient non-integrative expression of nuclear reprogramming factors promotes multifaceted amelioration of aging in human cells

Tapash Jay Sarkar, Marco Quarta, Shravani Mukherjee, Alex Colville, Patrick Paine, Linda Doan, Christopher M. Tran, Constance R. Chu, Steve Horvath, Lei S. Qi, Nidhi Bhutani, Thomas A. Rando & Vittorio Sebastiano

Renelon: How it Works:

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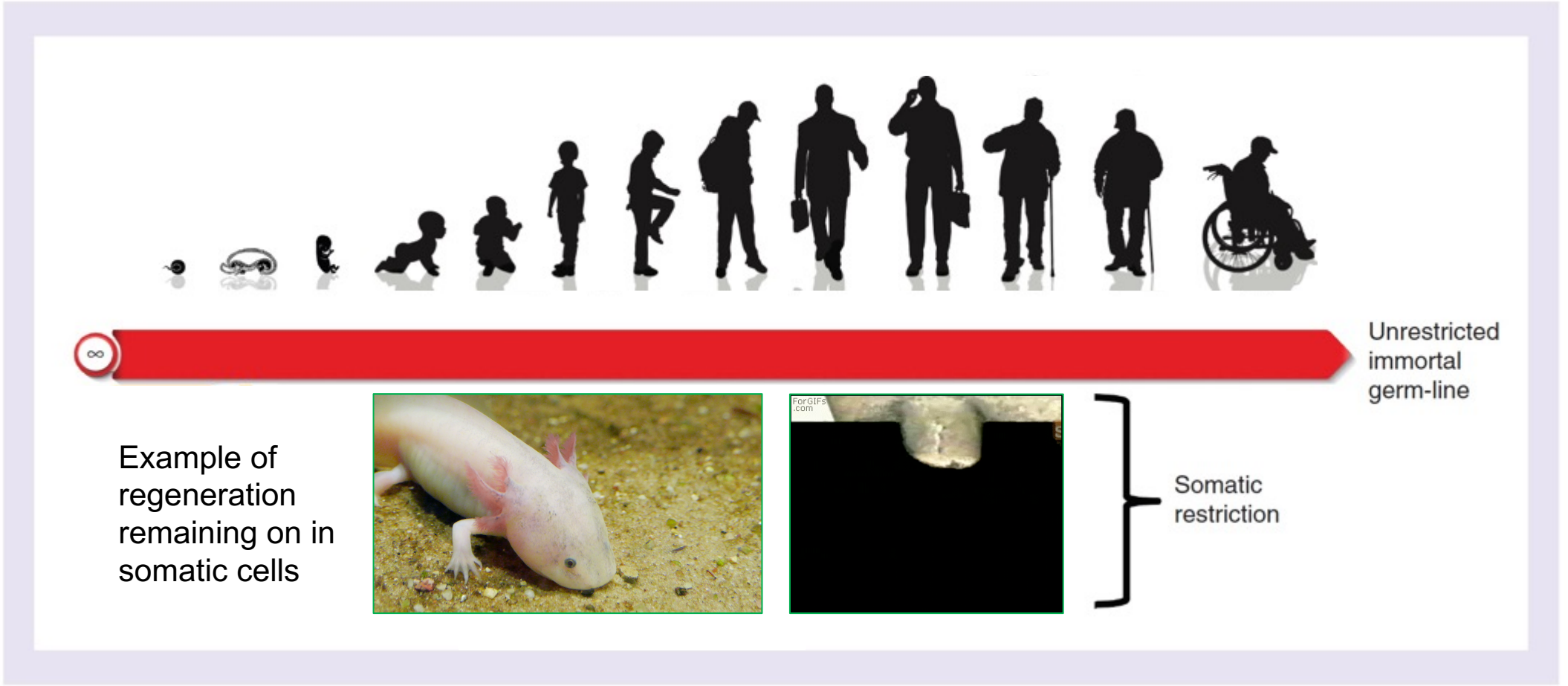
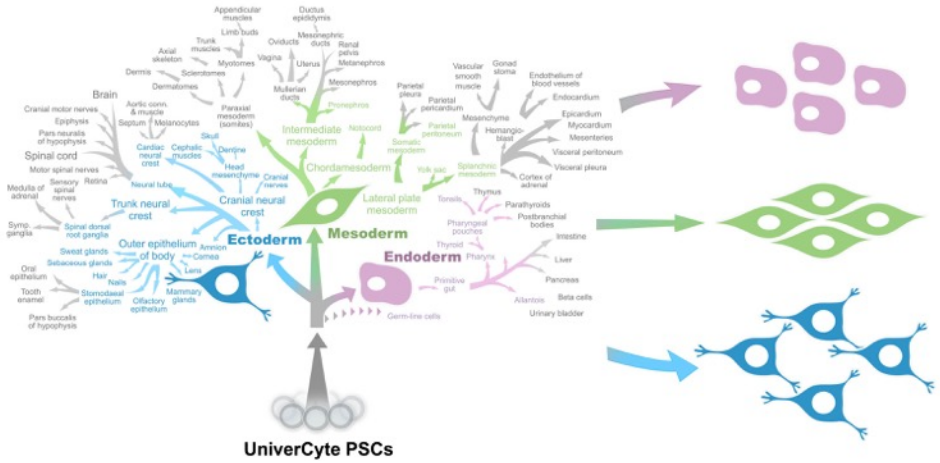


Regen Med. 2019 Sep;14(9):867-886.

AGEX THERAPEUTICS

Embryonic vs Adult Counterpart Analysis

Embryonic (Pre-Fetal)



UniverCyte PSCs

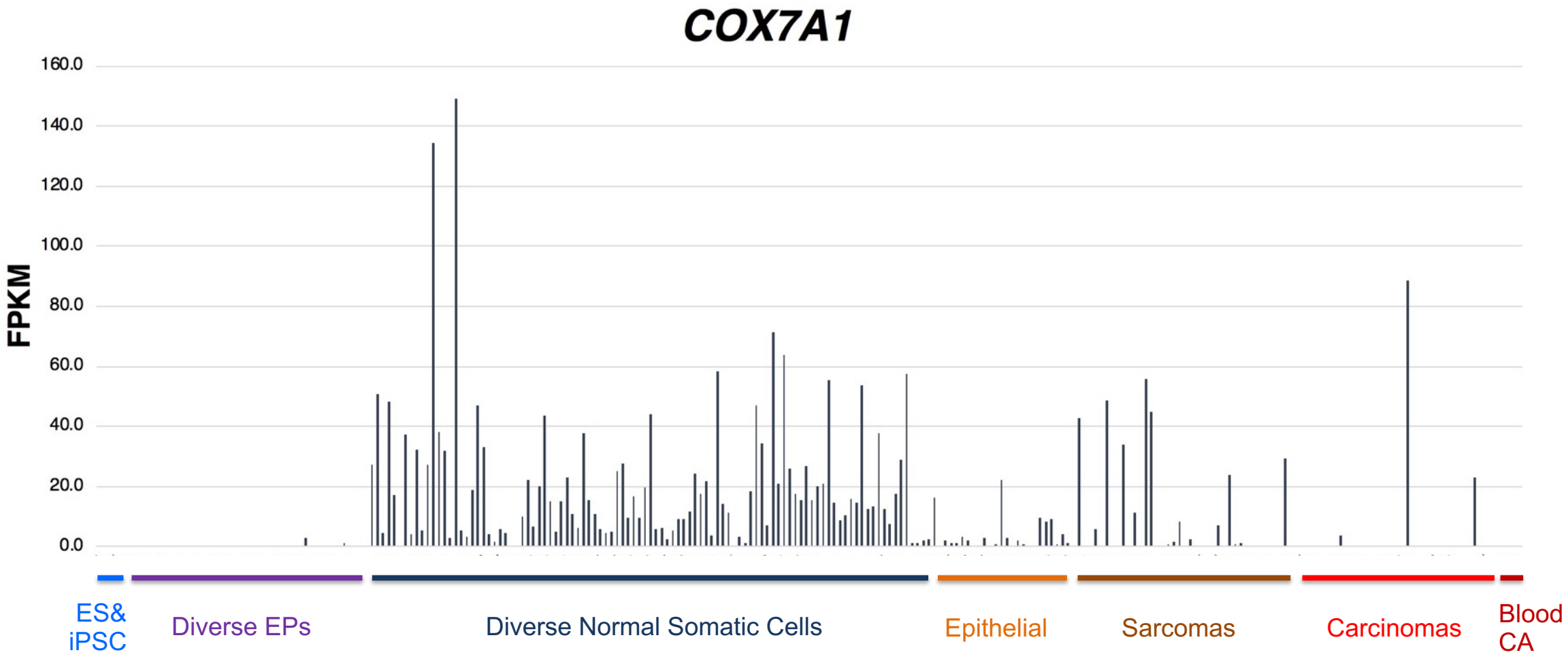
Adult-Derived

Compare:

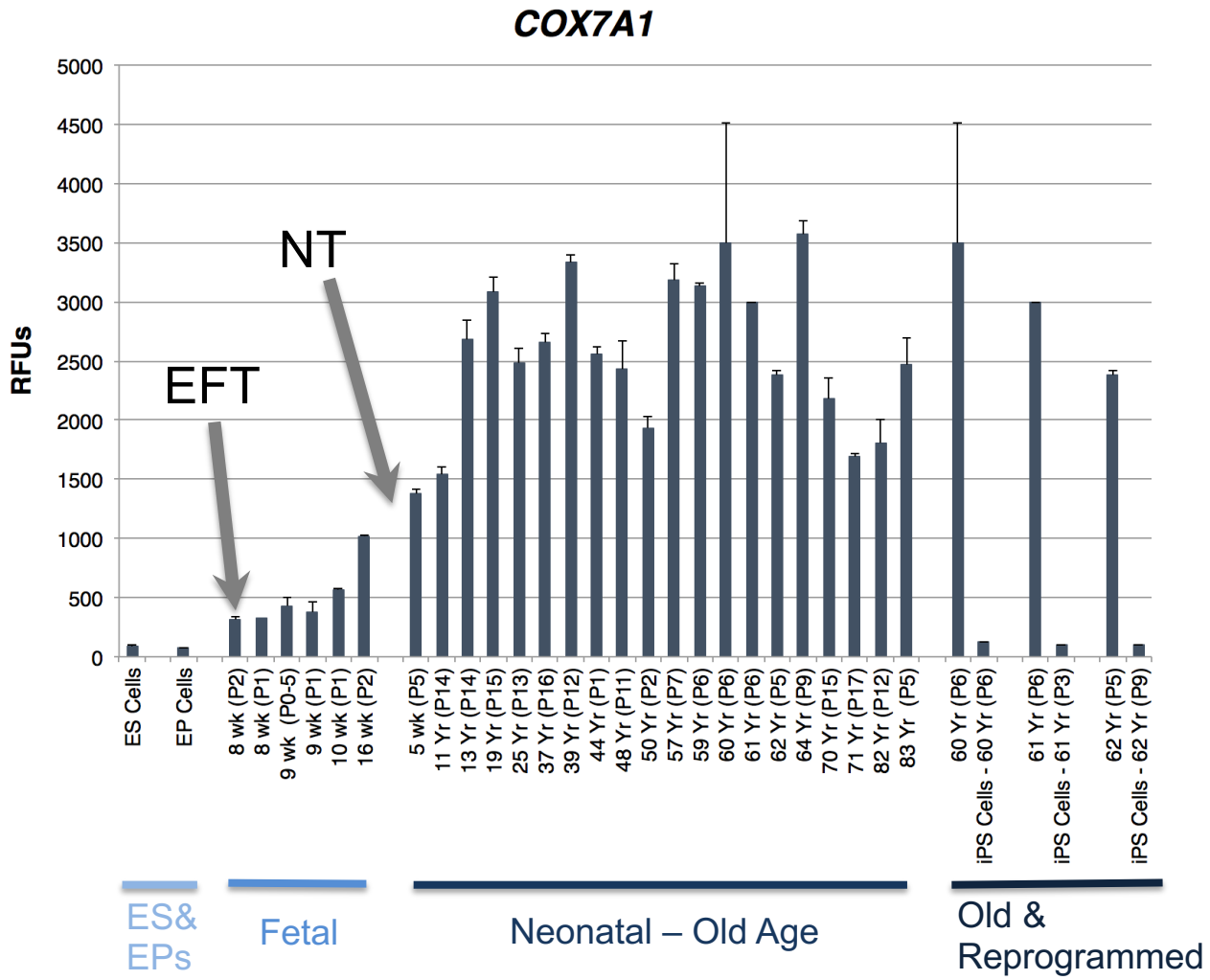
1) Osteochondral Mesenchyme
2) Vascular Endothelium
3) Skeletal Myoblasts
4) White Preadipocytes
5) etc

AGEX THERAPEUTICS

COX7A1


COX7A1
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
FPKM
ES& iPSC
Diverse EPs
Diverse Normal Somatic Cells
Epithelial
Sarcomas
Carcinomas
Blood CA

Unified Theory of Aging



Lin28/LET-7/MIR-4458/HMGA2 Axis

The 21-nucleotide *let-7* RNA regulates developmental timing in *Caenorhabditis elegans*

Brenda J. Reinhart*†, Frank J. Slack*†‡, Michael Basson‡§, Amy E. Pasquinelli*, Jill C. Bettinger‡#, Ann E. Rougvie#, H. Robert Horvitz§ & Gary Ruvkun*

* *Department of Molecular Biology, Massachusetts General Hospital, and Department of Genetics, Harvard Medical School, Boston, Massachusetts 02114, USA*
§ *Howard Hughes Medical Institute, Department of Biology, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139, USA*
# *Department of Genetics, Cell Biology and Development, University of Minnesota, St Paul, Minnesota 55108, USA*
† *These authors contributed equally to this work*

The *C. elegans* heterochronic gene pathway consists of a cascade of regulatory genes that are temporally controlled to specify the timing of developmental events[1]. Mutations in heterochronic genes cause temporal transformations in cell fates in which stage-specific events are omitted or reiterated[2]. Here we show

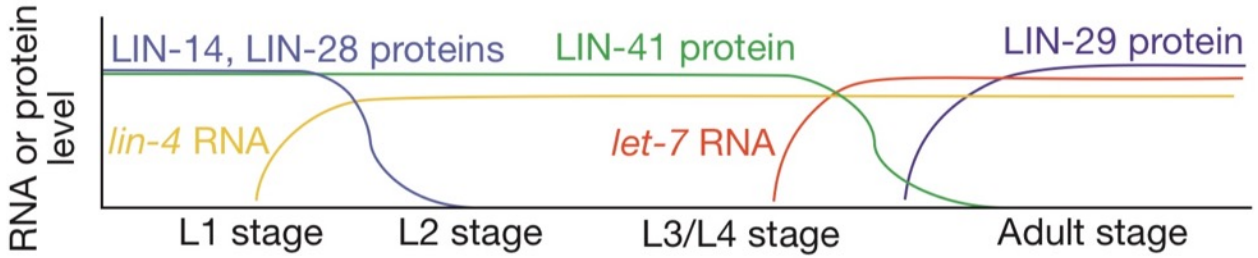
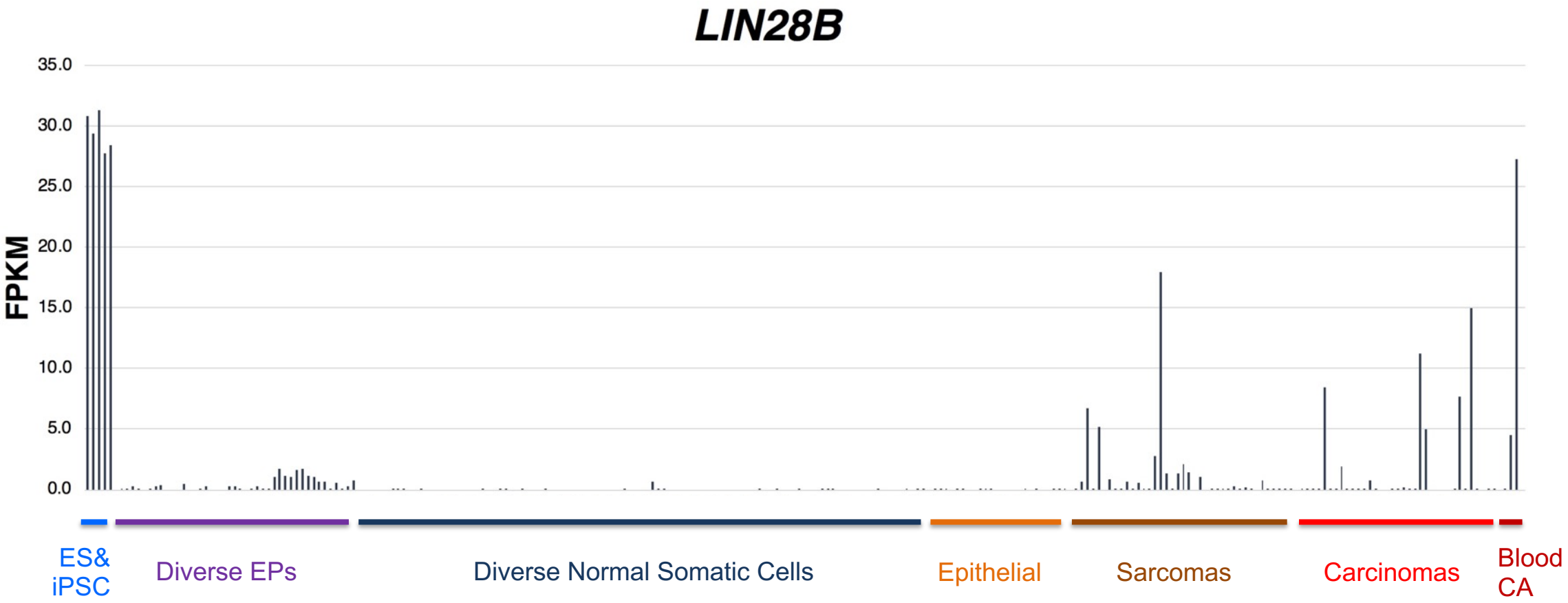


Figure 5 A model for the successive regulation of heterochronic gene activities by the *lin-4* and *let-7* RNAs. LIN-14 and LIN-28 expression levels are decreased by *lin-4* RNA expression at the end of the first larval stage to allow progression to late larval stages. In late larval stages, the expression of LIN-41 and other genes may be similarly downregulated by the *let-7* RNA, relieving their repression of LIN-29 protein expression and allowing progression to the adult stage. Because the *lin-29* mRNA does not contain sites complementary to the *let-7* RNA, *lin-29* is not likely to be a direct target of *let-7*.

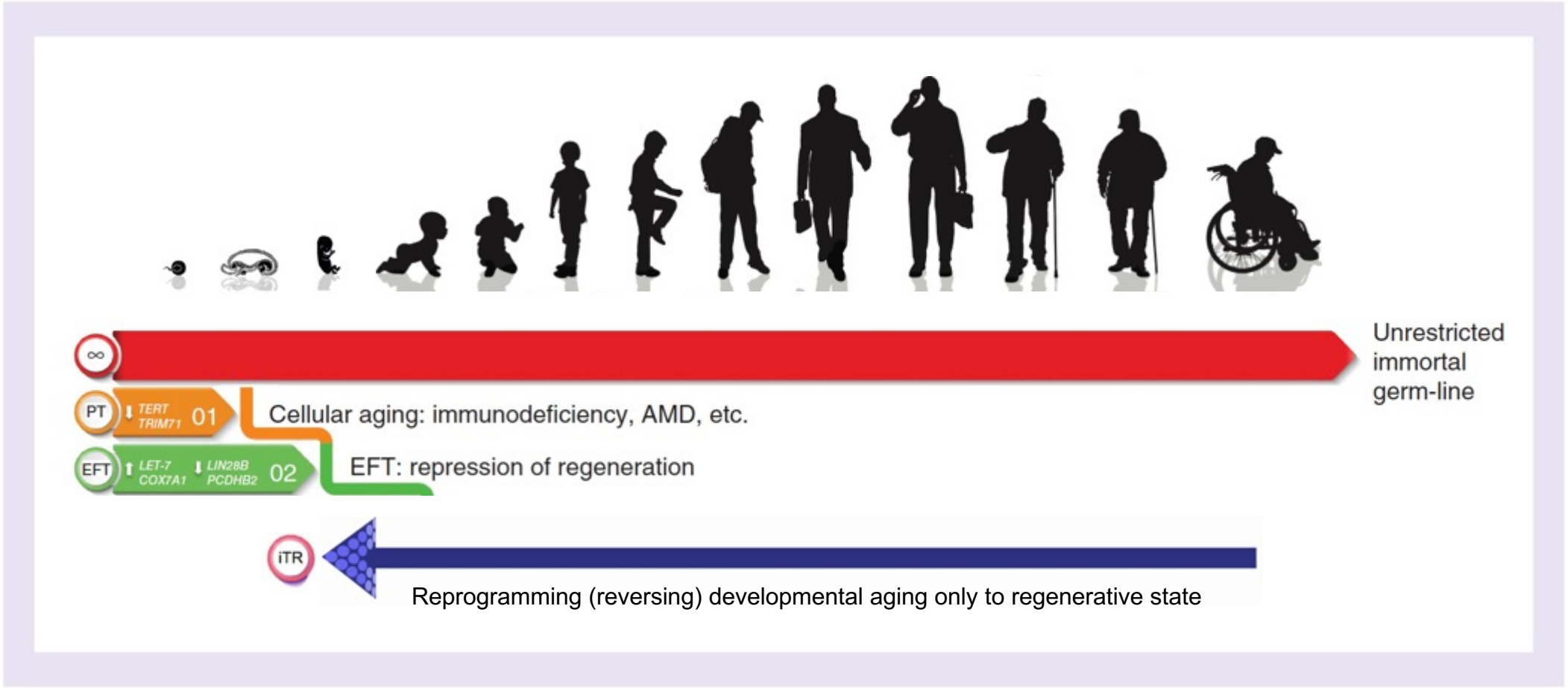
AGEX THERAPEUTICS

LIN28B


LIN28B
FPKM
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
ES& iPSC
Diverse EPs
Diverse Normal Somatic Cells
Epithelial
Sarcomas
Carcinomas
Blood CA

Renelon: How it Works:

iTR™ or "partial reprogramming' to the regenerative state



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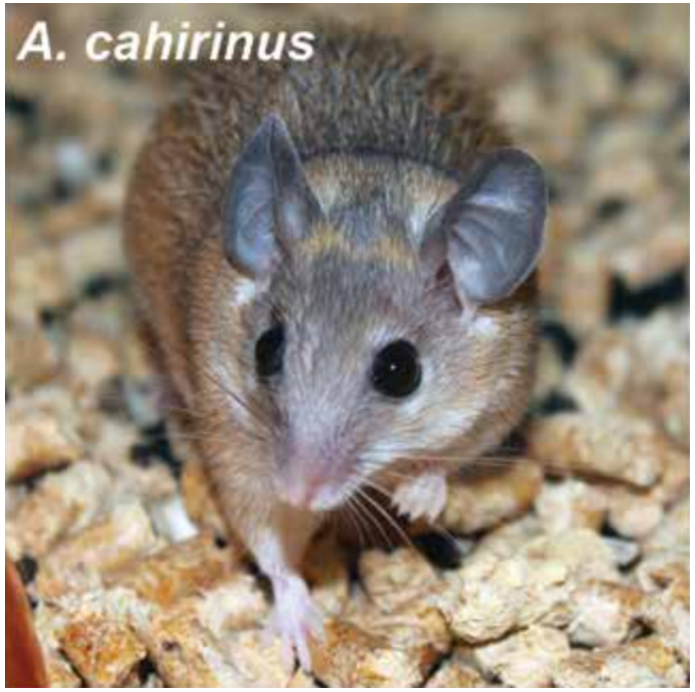
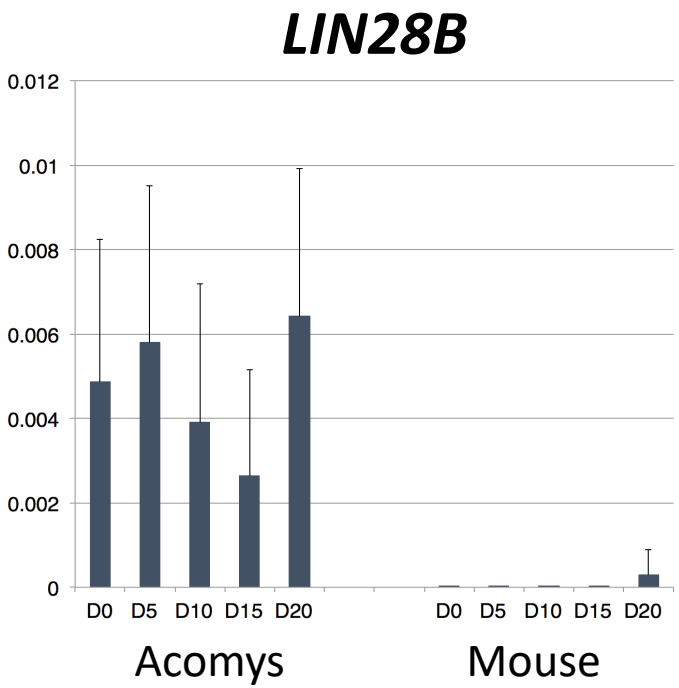
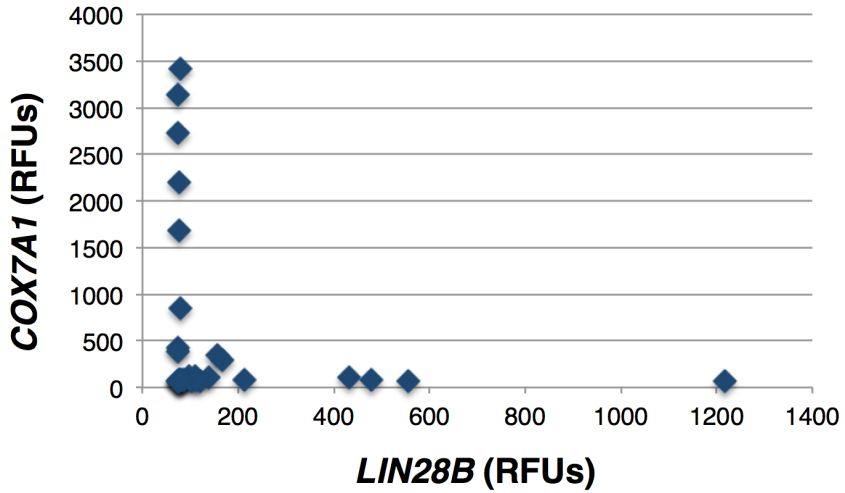
AGEX THERAPEUTICS

iTR – Segmental Example

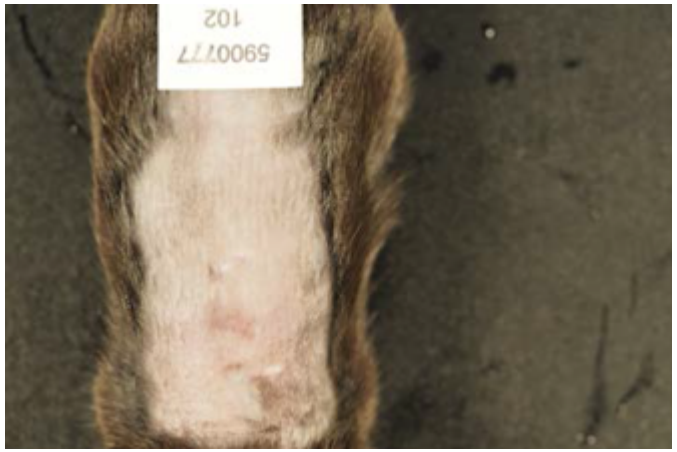






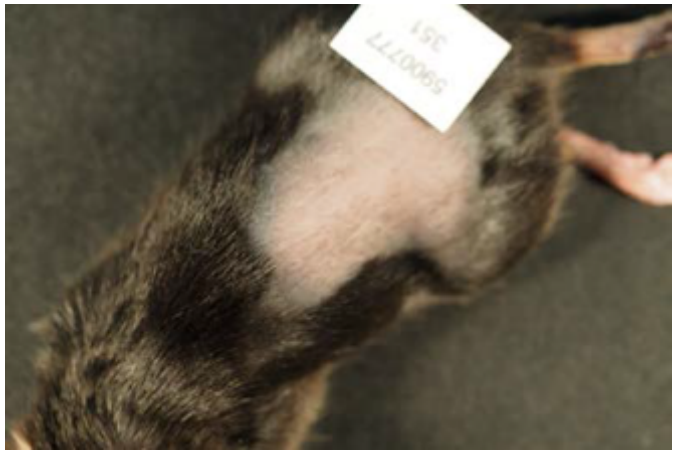
AGEX THERAPEUTICS

Reprogramming of Skin & Hair Regeneration



WT Control

***Cox7a1* -/-**



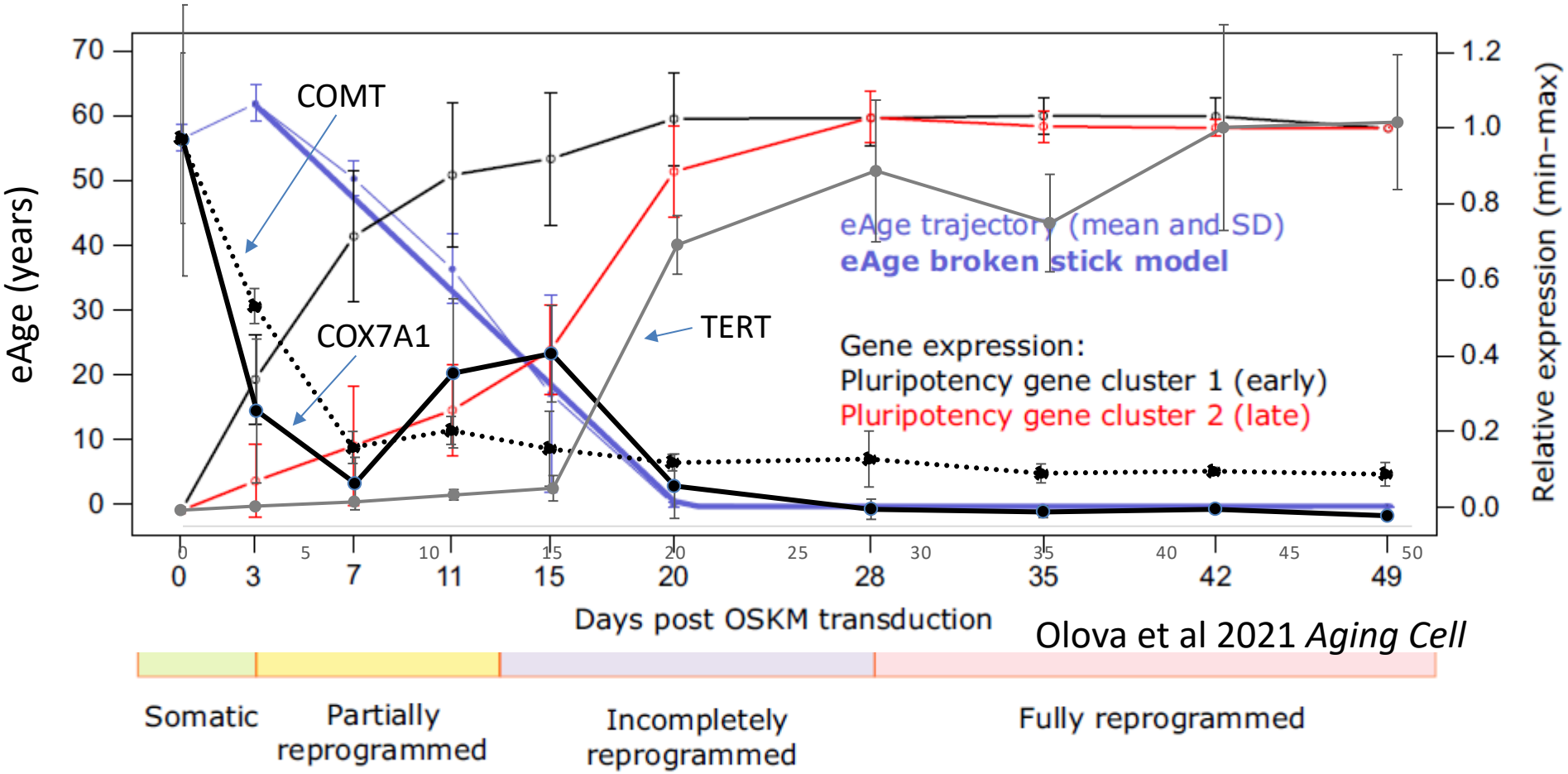
***Lin28a* +**

***Cox7a1* -/- and *Lin28a* +**

TESTING FACILITY:
Charles River Laboratories

AGEX THERAPEUTICS

iTR without iPSCs

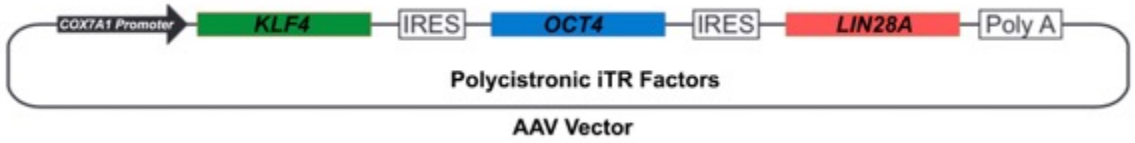


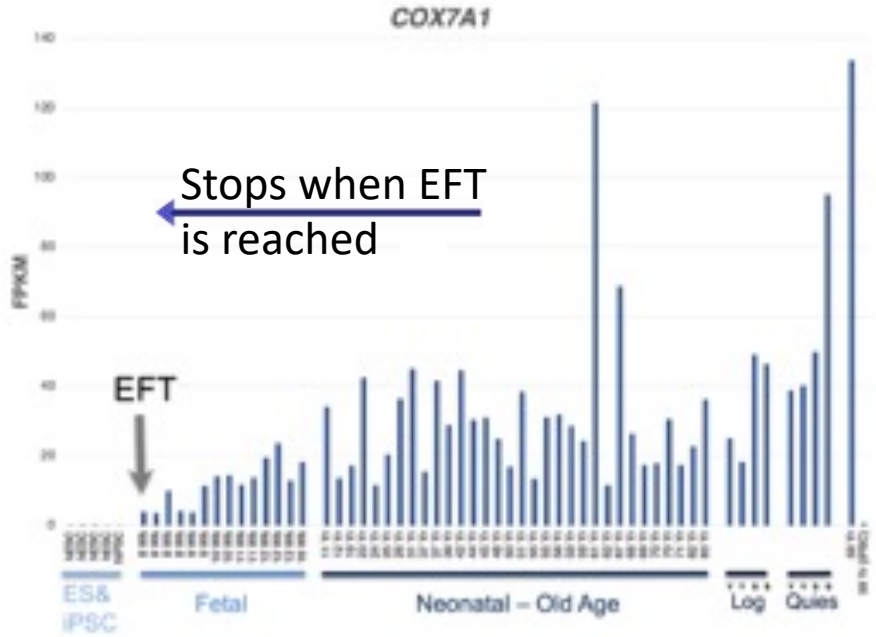
Olova et al 2021 *Aging Cell*

Renelon: Precise Regulation: DR-iTR

Our proprietary Developmentally-Regulated (DR-iTR) precisely regulates reprogramming genes off with cellular resolution after iTR is reached

iTR Viral Vector





AGEX THERAPEUTICS

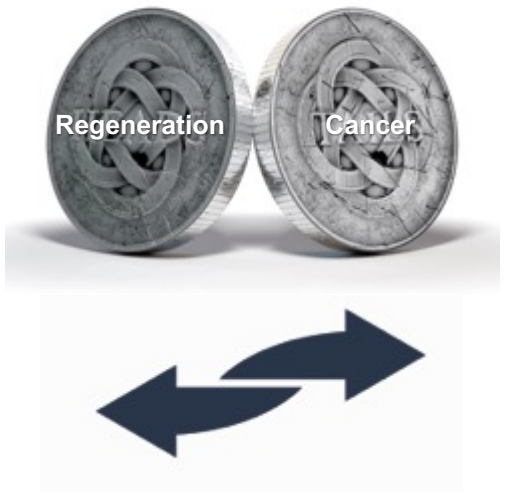
COX7A1 Chromatin Embryonic, Adult, Cancer

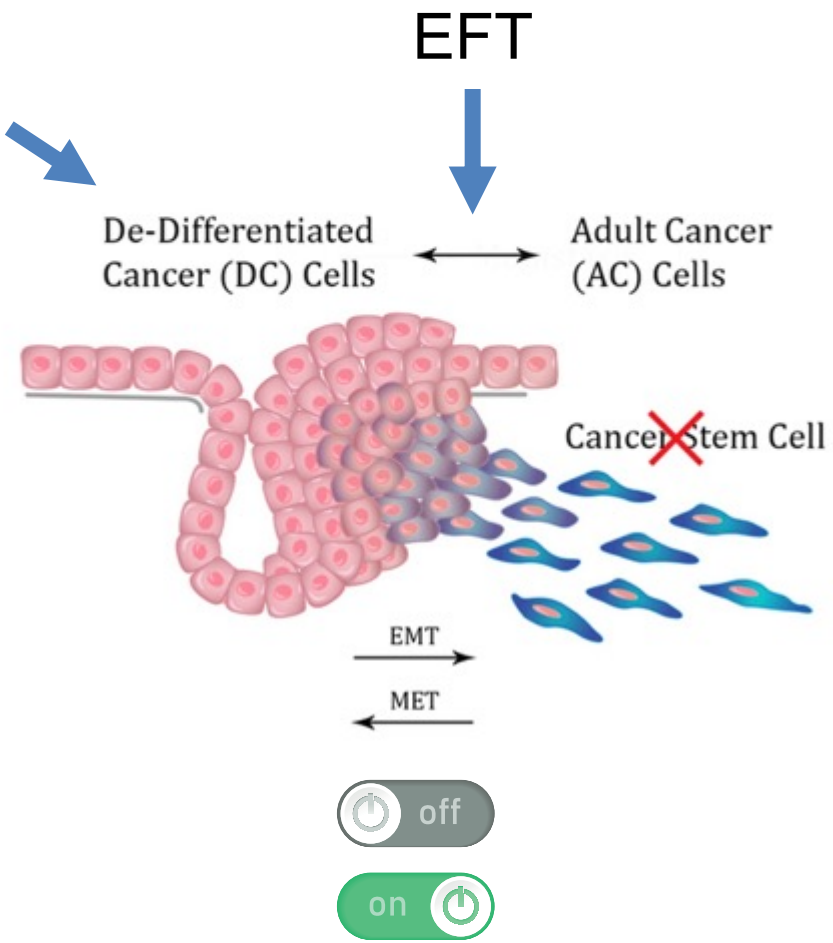
Expression by RNAseq (FPKM)

	COX7A1	*PCDHGA12*
EE - ATAC	0.0	
EM - ATAC	0.0	
AE - ATAC	15.36	
AM - ATAC	28.04	
OSTEOSARCOMAS		
U-2	0.14	0.0
SJSA	0.16	0.0
KHOS/240S	**1.6**	**1.6**
KHOS/NP	**9.5**	**1.9**
EMyo	0.0	
AMyo	106.74	
RHABDOMYOSARCOMAS		
CCL-136	?	
HTB-82	0.07	0.24
CRL-7774	0.16	0.23
CRL-2061	0.13	0.0
EA	0.32	
AA	23.36	
LIPOSARCOMAS		
CRL-3044 Lipo-Sarcoma	0.15	3.89

EFT & Novel Pan-Cancer Therapeutic Strategy

EPRO™
Target Pre-EFT cancer cells for destruction





Our scientists discovered two hallmarks of cancer:

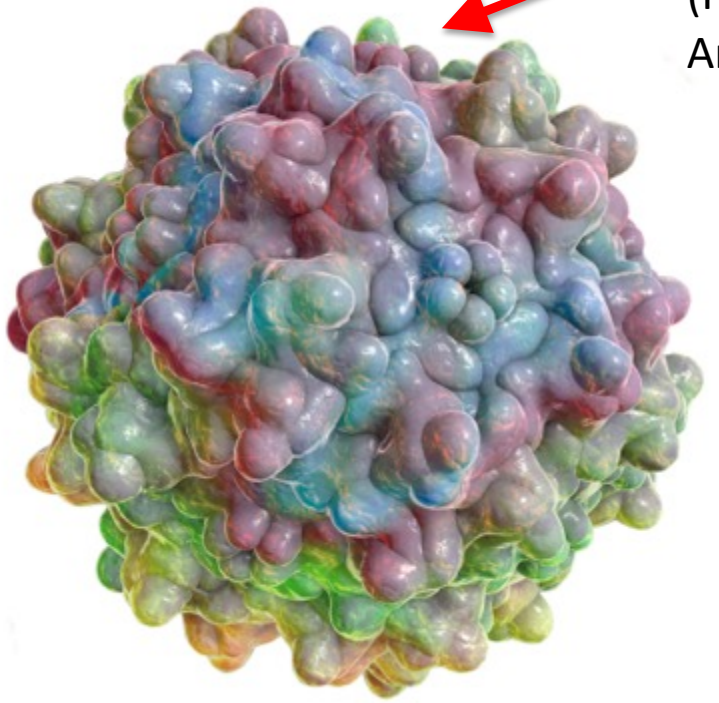
1) previously, telomerase as a pan-cancer hallmark.
2) More recently, the EFT hallmark of cancer and that cancer stem cells are not the more primitive cell.

These discoveries lead to novel pan-cancer therapeutic and diagnostic strategies.

AGEX THERAPEUTICS

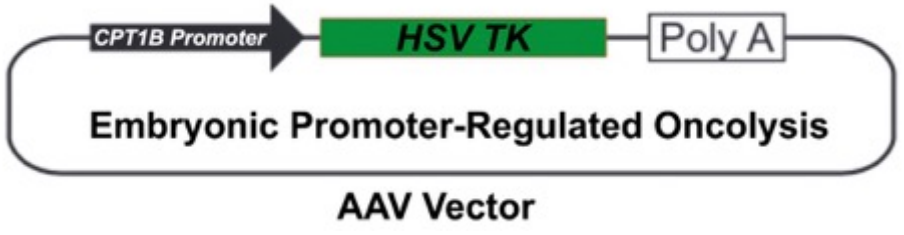
Cancer Therapeutics -*EPRO*

Vector to Precisely Target and Destroy Pre-EFT Cancer

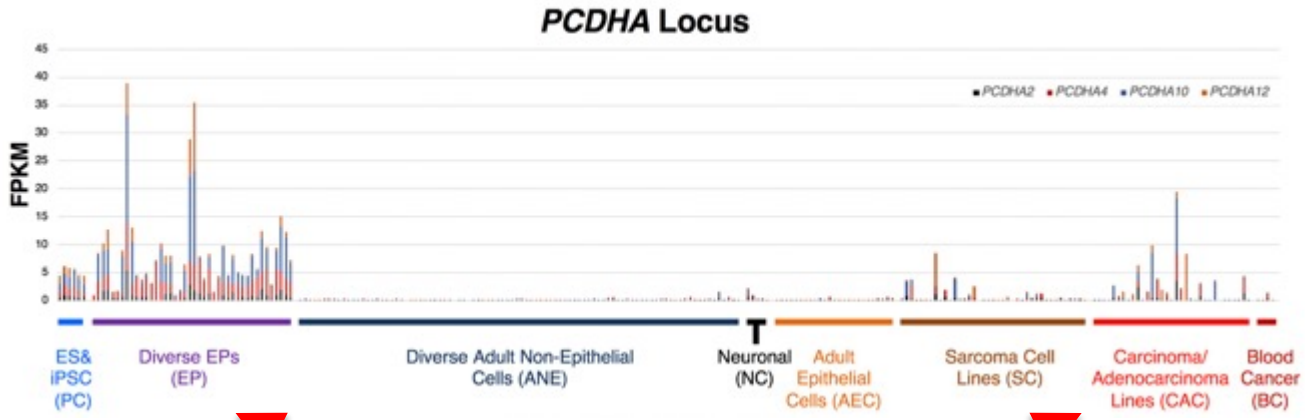


Binding Site for Proprietary (Patent Pending) Embryonic Antigens

EPRO Oncolytic Viral Vector

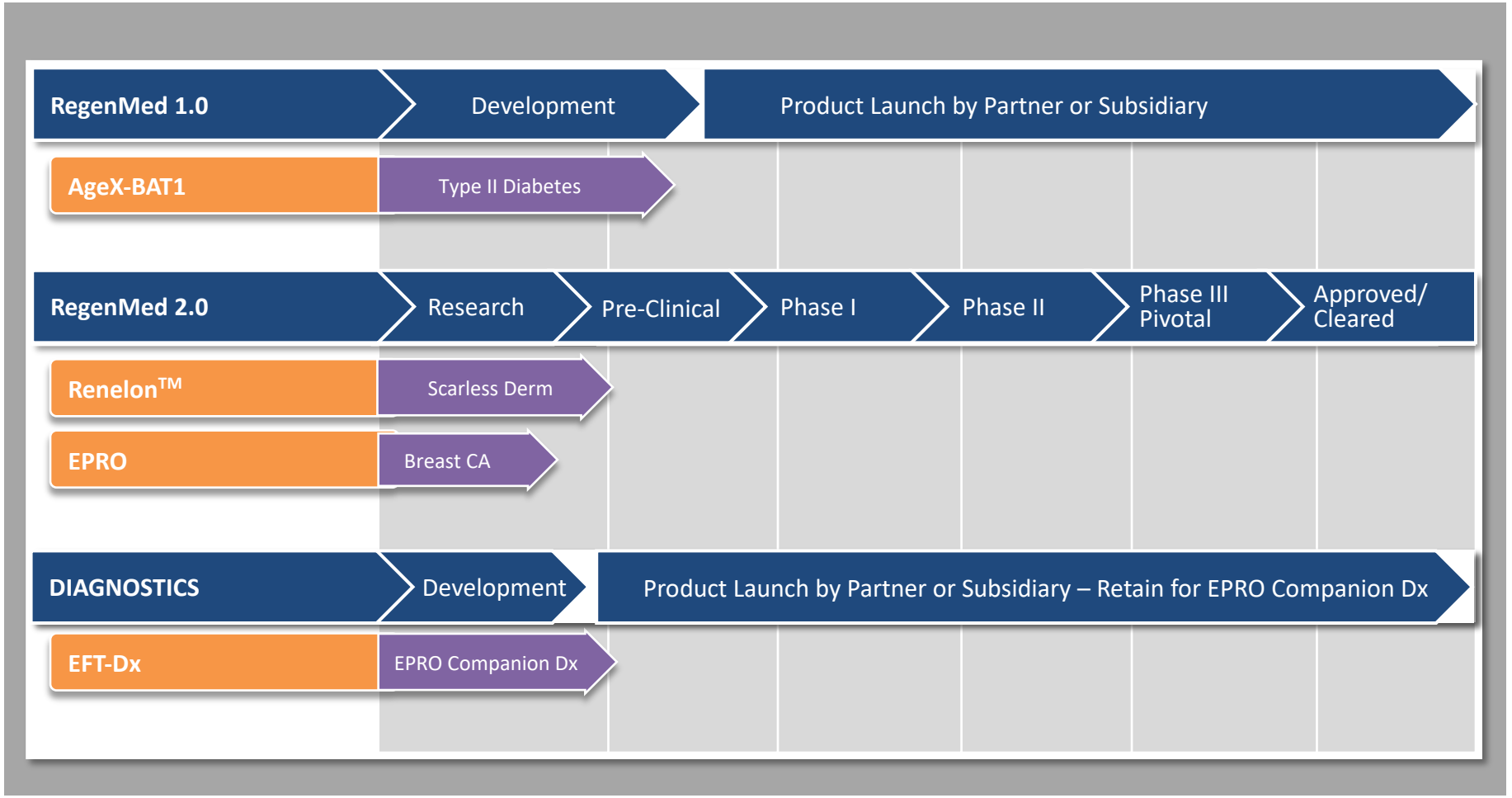


AAV Vector



Example of Proprietary Antigens not Expressed in Most Adult Cells, but Expressed in Cancer

Product Pipeline



AGEX THERAPEUTICS

Summary

Therapeutic Opportunities Stemming from the Immortal Germ-Line

- *AgeX-BAT1* – Brown adipocytes formulated in HyStem matrix for Type II diabetes
- *Renelon*™ – Induction of Tissue Regeneration and reversal of age markers in tissues afflicted with age-related degenerative disease
  - Initial development of *ex vivo* therapy in dermatology
- *EPRO*– Immuno-oncological targeting the destruction of numerous cancer cell types
  - Initial POC in breast cancer

AGEX THERAPEUTICS