



Partial Reprogramming: Implications for Aging & Cancer

NYSE American: AGE

June 8, 2023

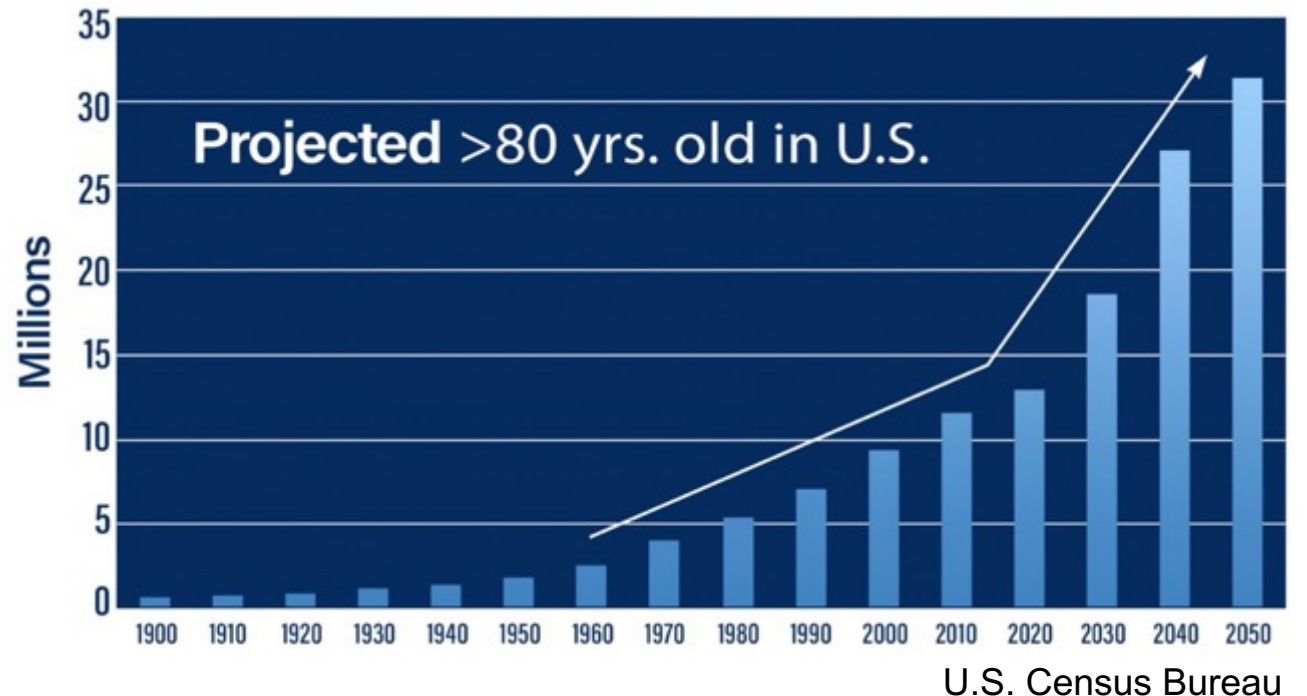
Forward Looking Statements

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 Reverse Bioengineering and its parent company AgeX Therapeutics and its affiliates in developing new stem cell-based products and technologies; results of clinical trials of such products; the ability of Reverse and 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 Reverse and AgeX and its subsidiaries to maintain patent and other intellectual property rights; and the ability of Reverse and 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 Reverse and AgeX and its other subsidiaries, particularly those mentioned in the cautionary statements found in AgeX's Securities and Exchange Commission filings. Reverse and AgeX disclaims any intent or obligation to update these forward-looking statements.

Aging: The Demographic Trend of Our Time

Opportunity: A powerful new technology addressing the demand

- ~80% of \$2.5T health care costs in U.S. associated with chronic disease
- The elderly commonly have two or more chronic degenerative diseases
- Induced Tissue Regeneration (iTR™) technology has the potential to reverse developmental aging and induce regeneration in numerous tissues of the body
- iTR research uncovers pan-cancer applications for both Tx and Dx

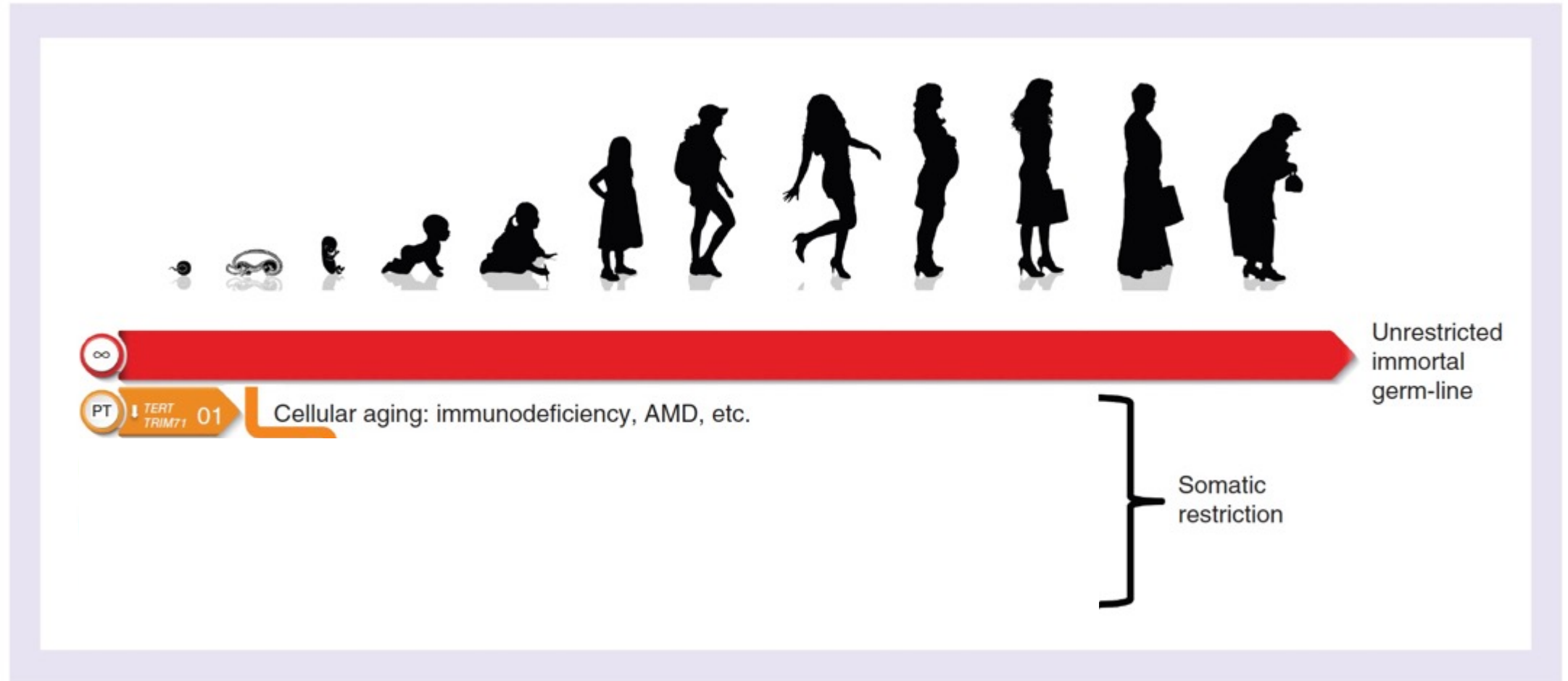


The Evolution of Aging: Antagonistic Pleiotropy

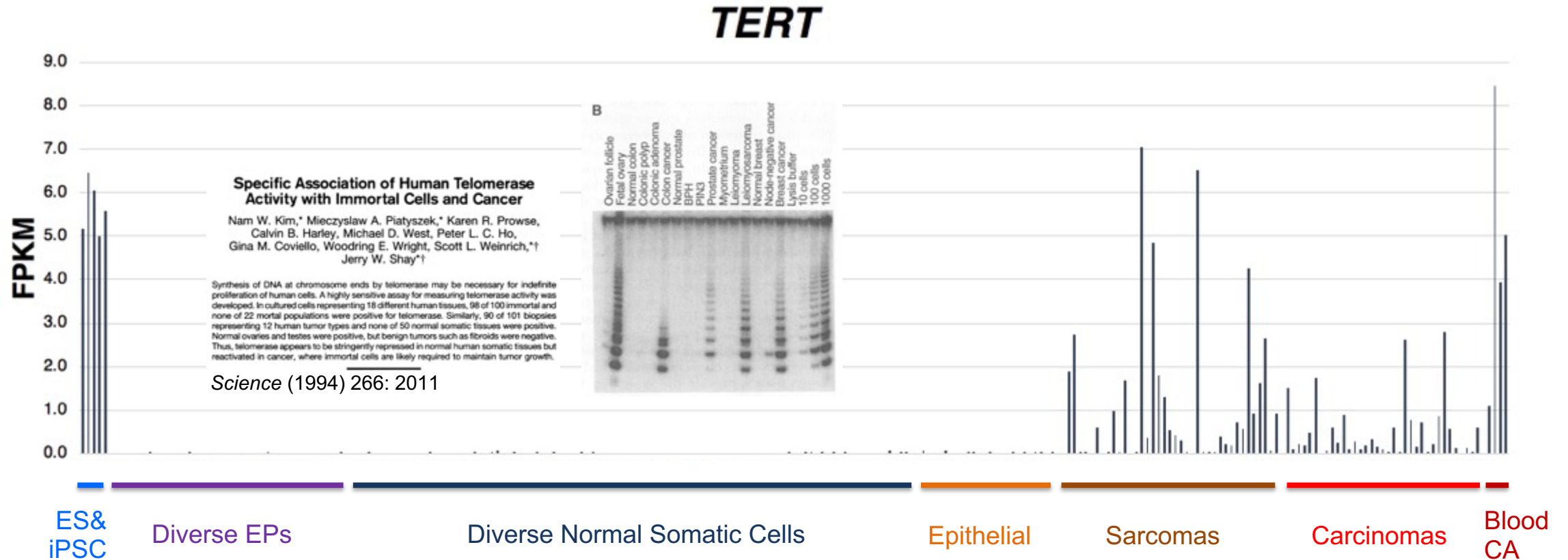
Concept is that nature selected for gene expression that confers a survival benefit early in life, but late in life results in aging and mortality of the soma



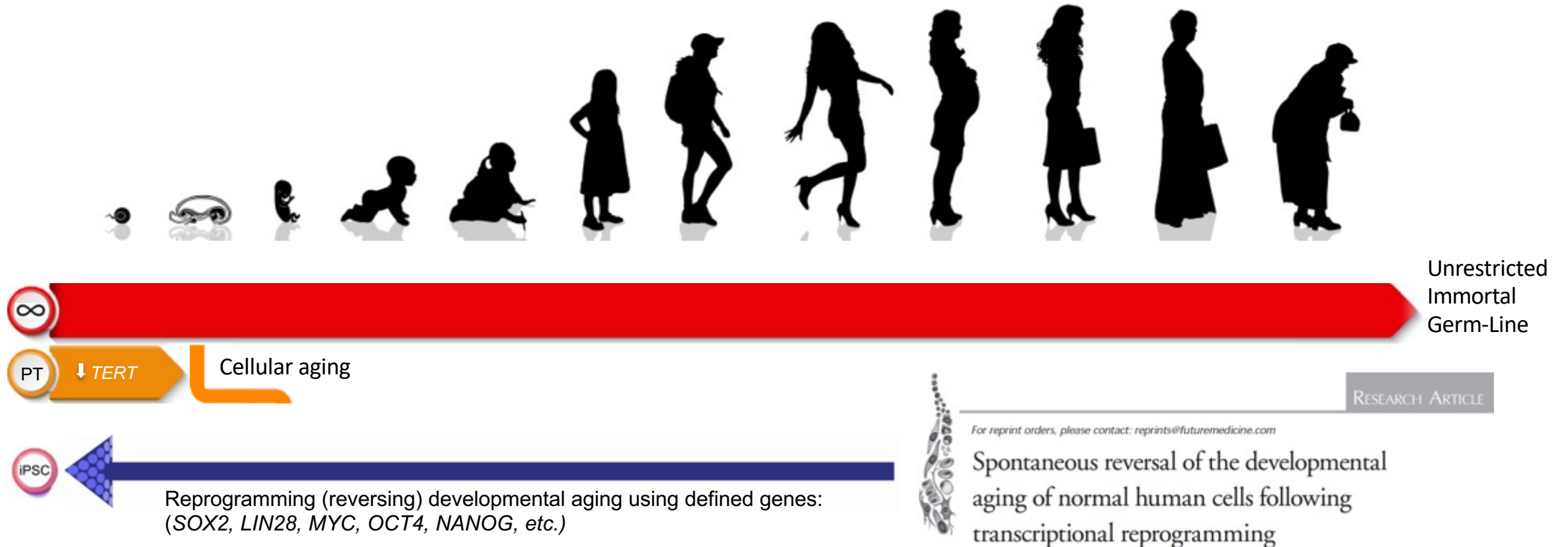
Somatic Restriction



Expression of Telomerase in Normal Somatic Cells & Cancer



Reprogramming Cellular Aging



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RESEARCH ARTICLE

Spontaneous reversal of the developmental aging of normal human cells following transcriptional reprogramming

Regen. Med. (2010) 5(3)

Tissue Regeneration

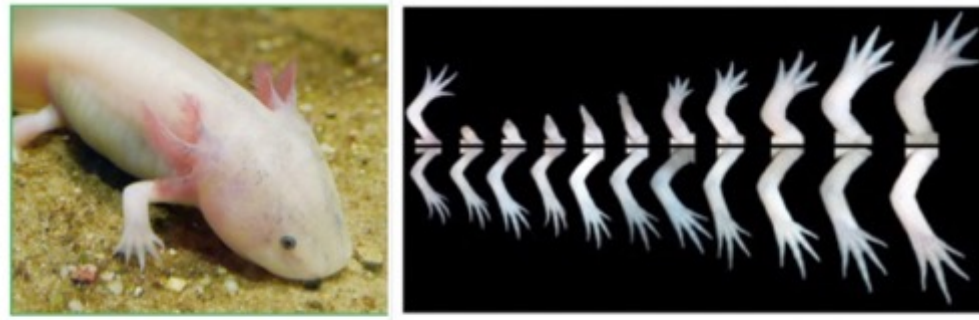


Immortality

Cellular aging

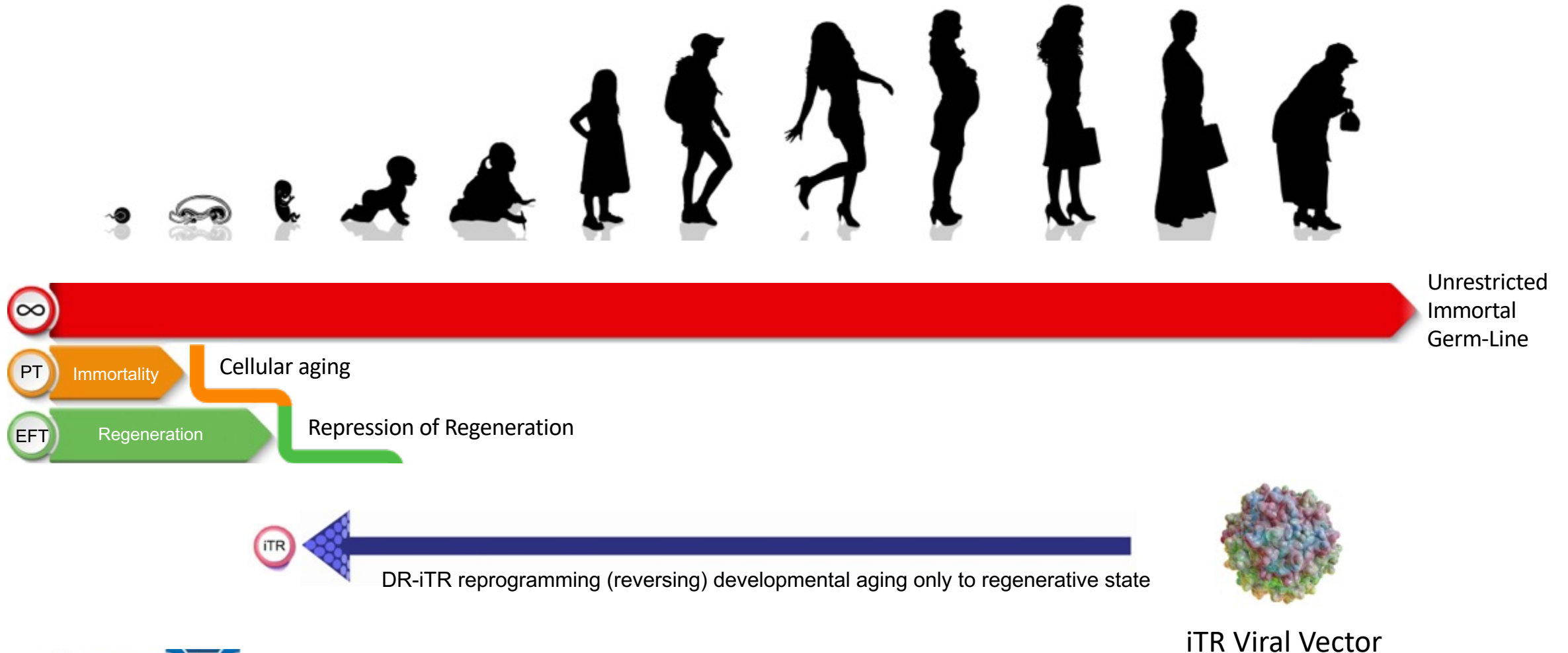
Regeneration

Unrestricted
Immortal
Germ-Line



Example of regeneration
remaining on in somatic cells

Induced Tissue Regeneration (iTR™)



Timing of Mouse Emb-> Fetal Transition (EFT)

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-

Timing of Mouse Emb-> Fetal Transition (EFT)

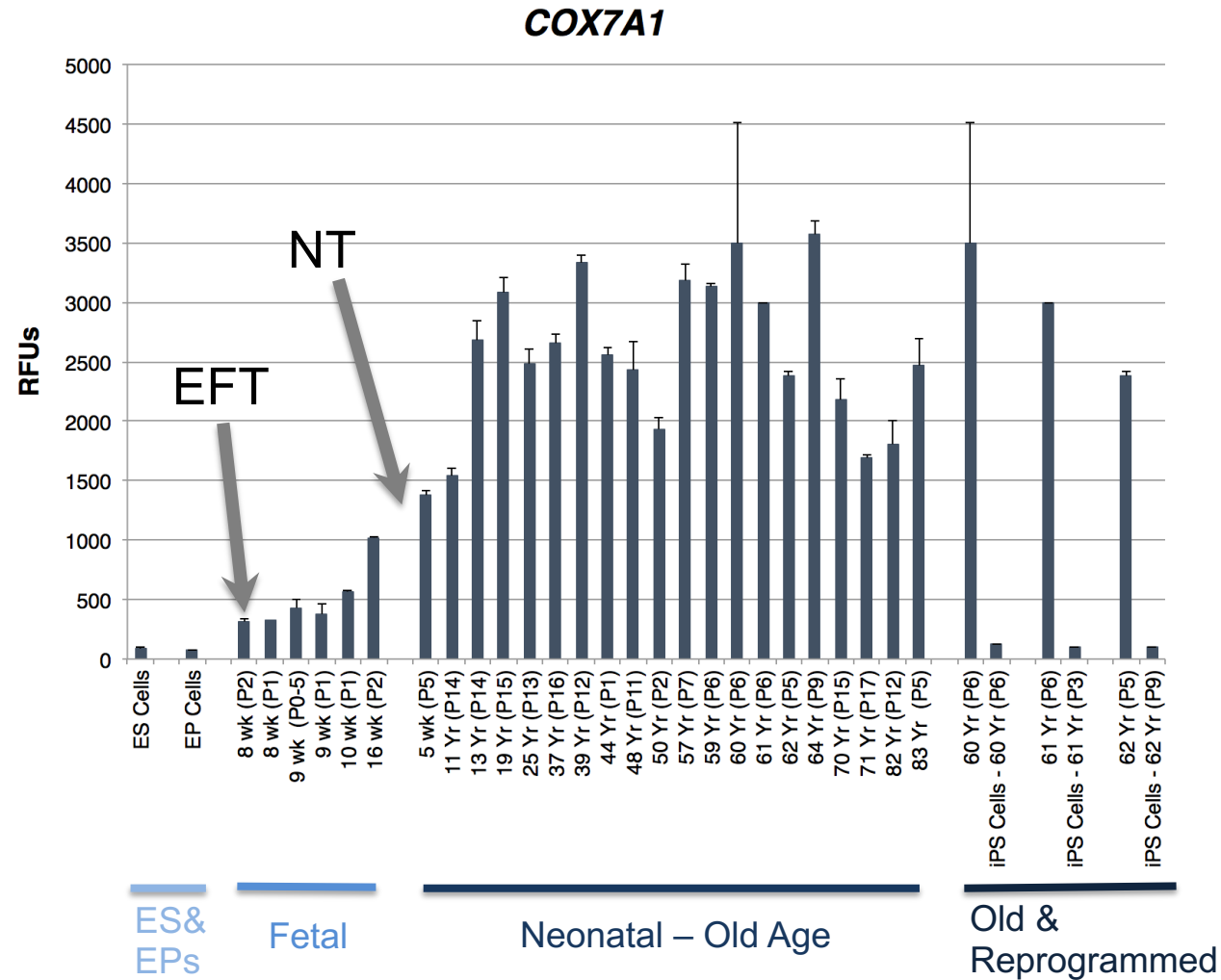


Data For Carnegie Stages Comparison Graph (Species/Days)

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	

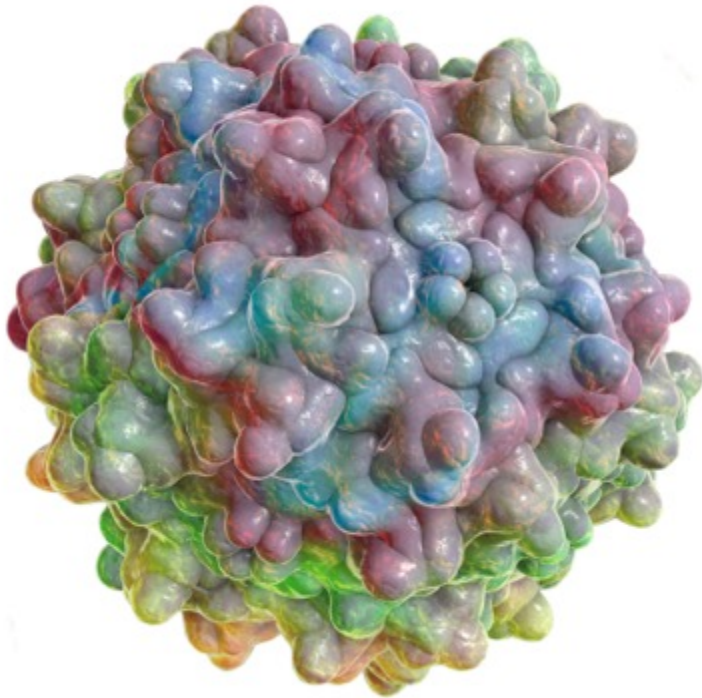
Rat Transition in skin:
(16.5-18.5 days)

COX7A1 in Fibroblasts Throughout Development & Aging

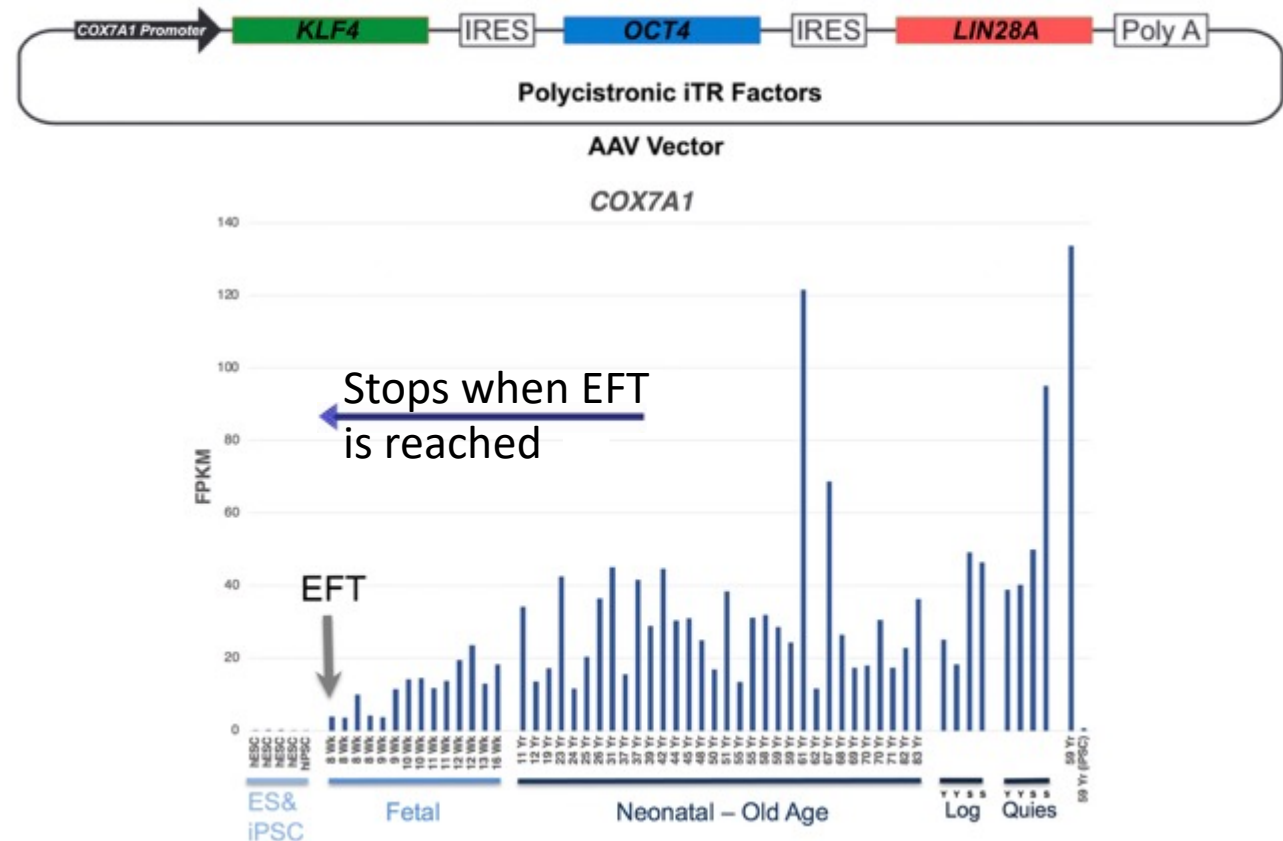


Precise Regulation: DR-iTR

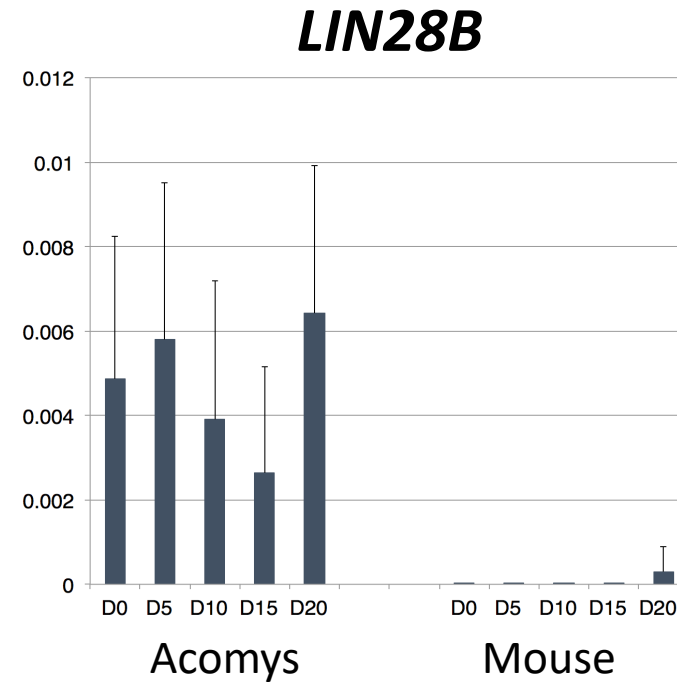
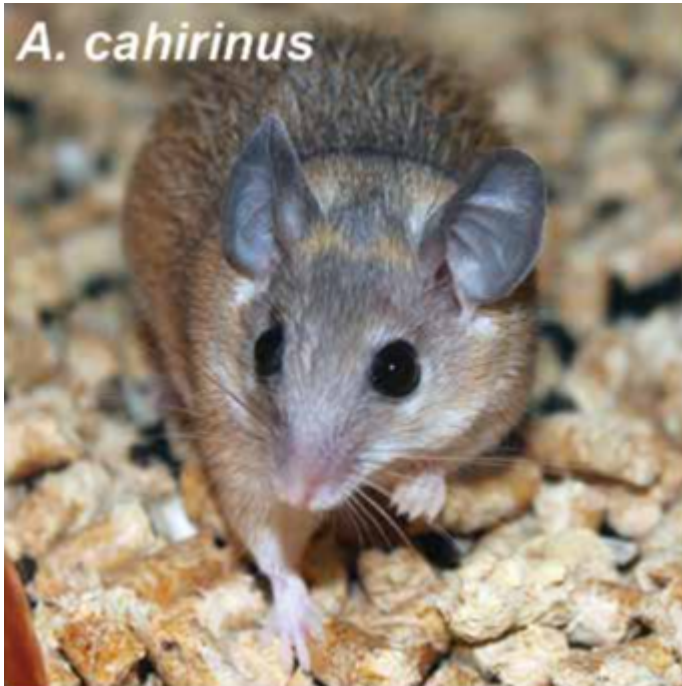
Our proprietary Developmentally-Regulated (DR-iTR) precisely regulates reprogramming genes off with cellular resolution after iTR is reached



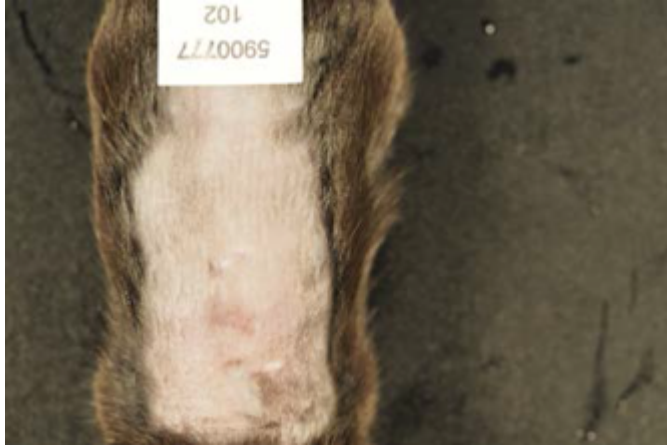
iTR Viral Vector



iTR – Segmental Example



Segmental Reprogramming of Hair Regeneration



WT Control



Cox7a1 -/-



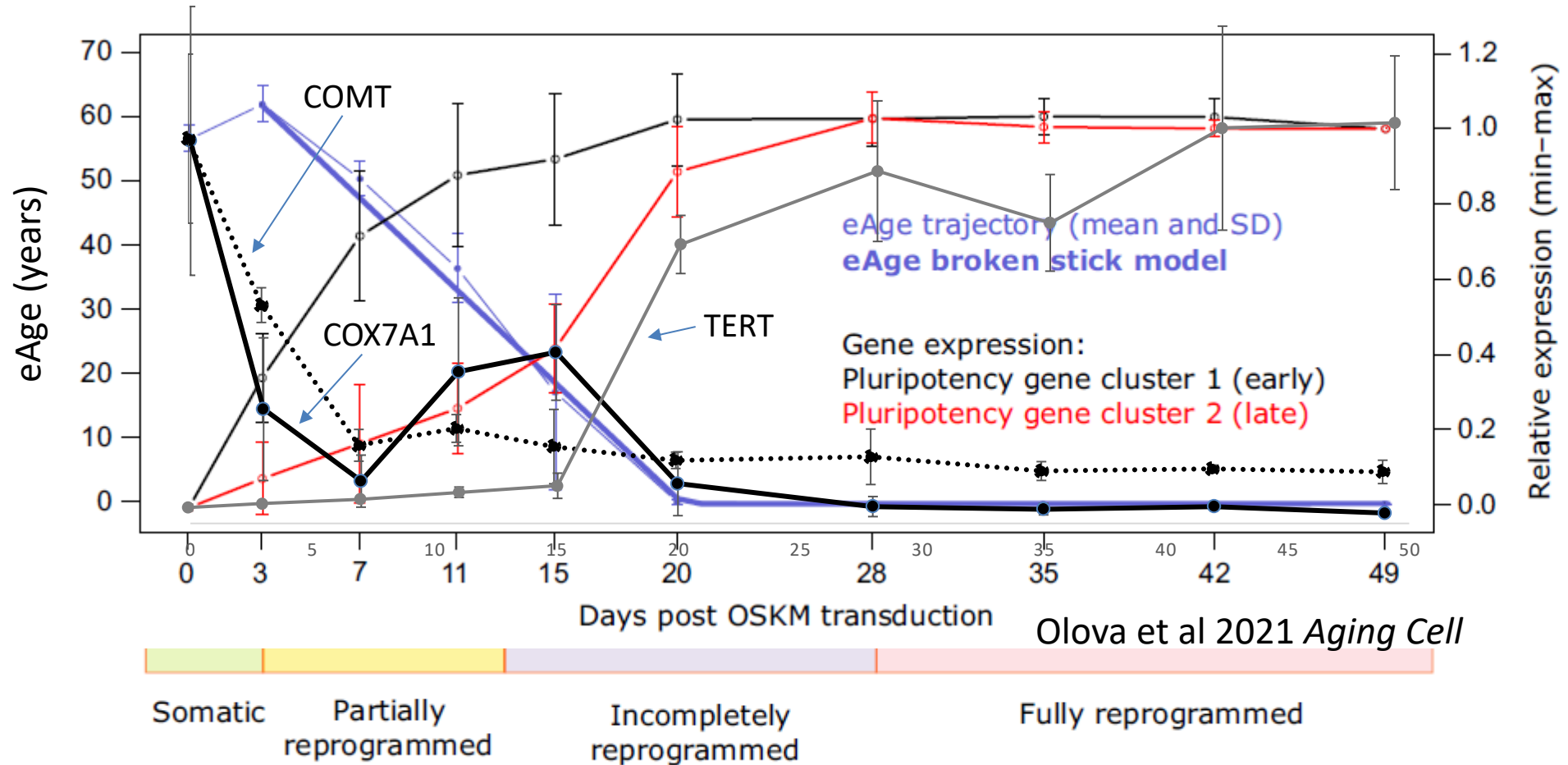
Lin28a +



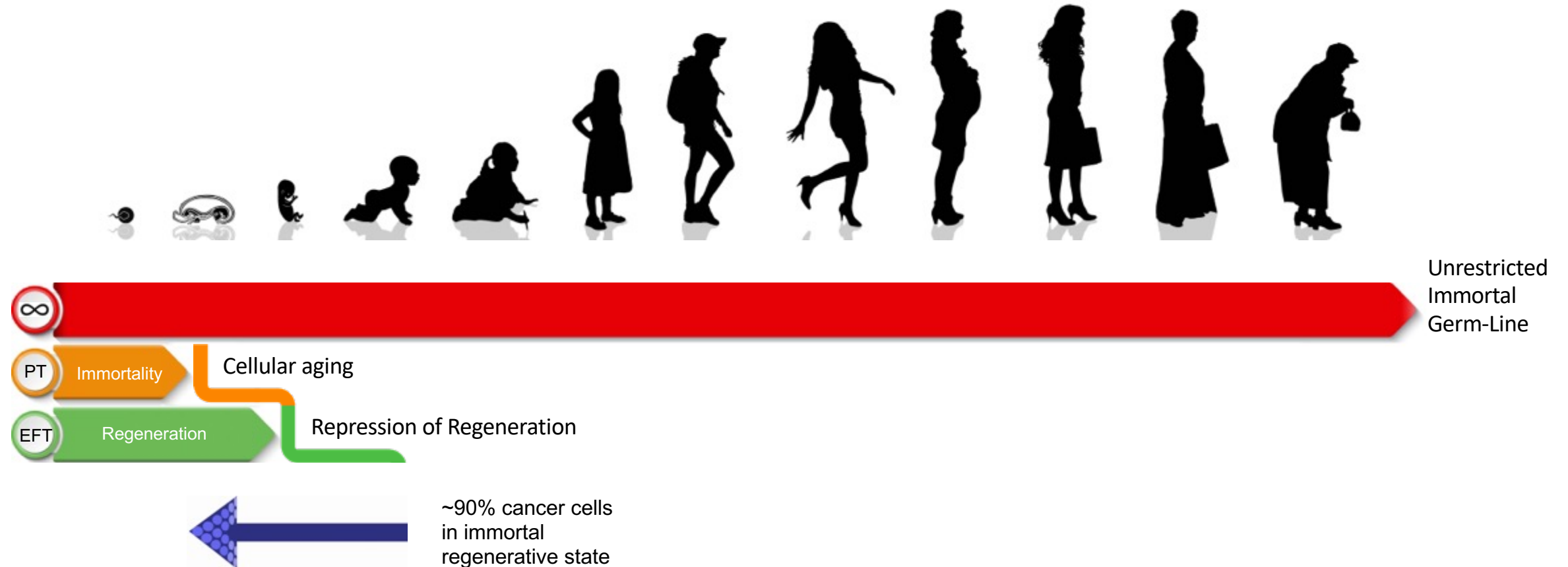
Cox7a1 -/- and *Lin28a* +

**TESTING
FACILITY:**
Charles River
Laboratories

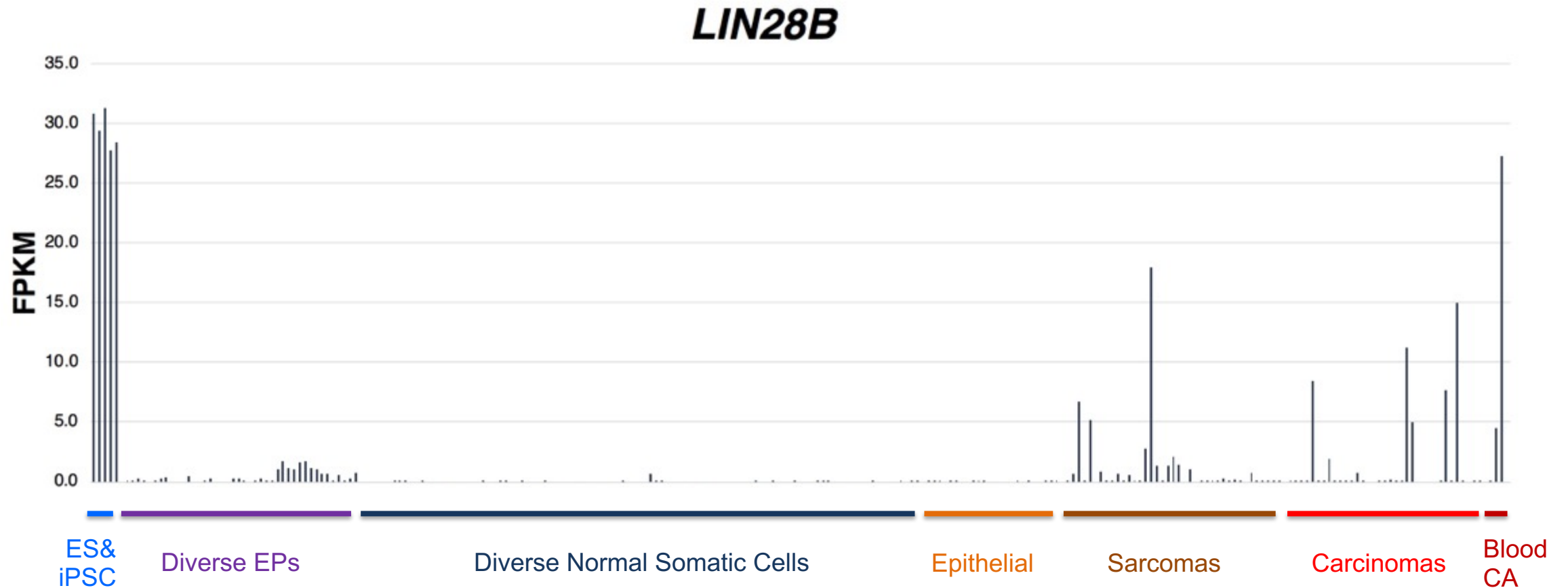
iTR without iPSCs



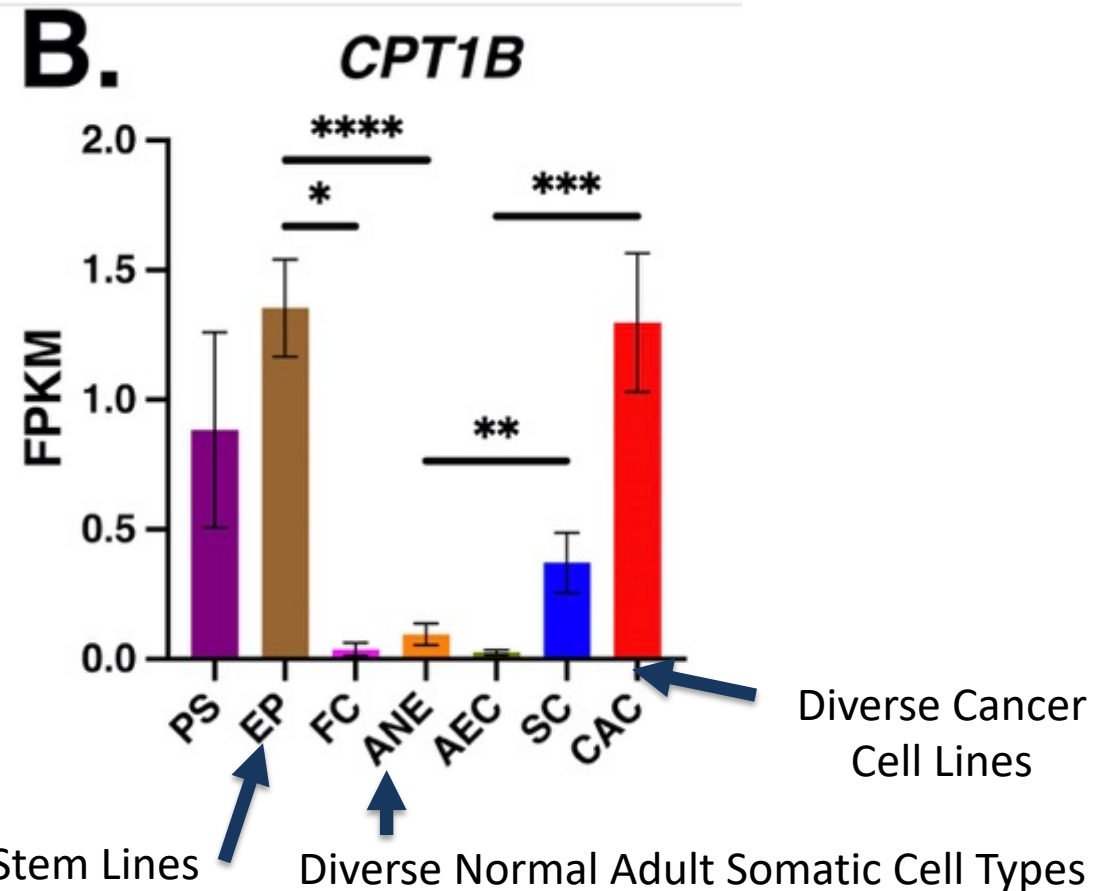
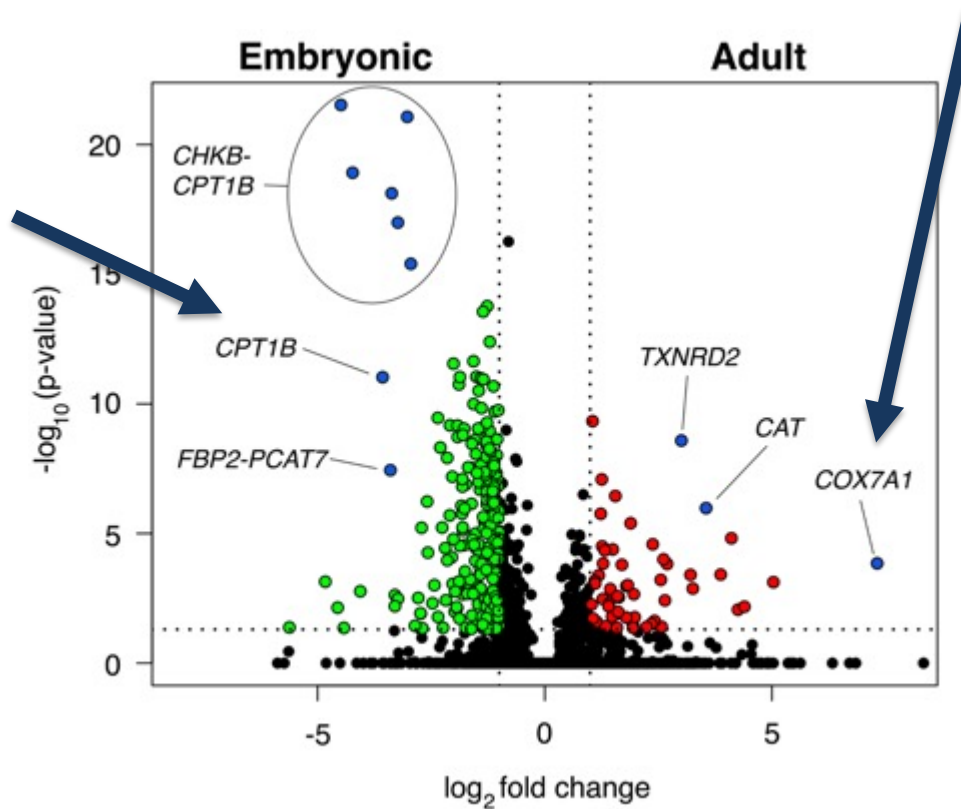
The Immortal & Regenerative Hallmarks of Cancer



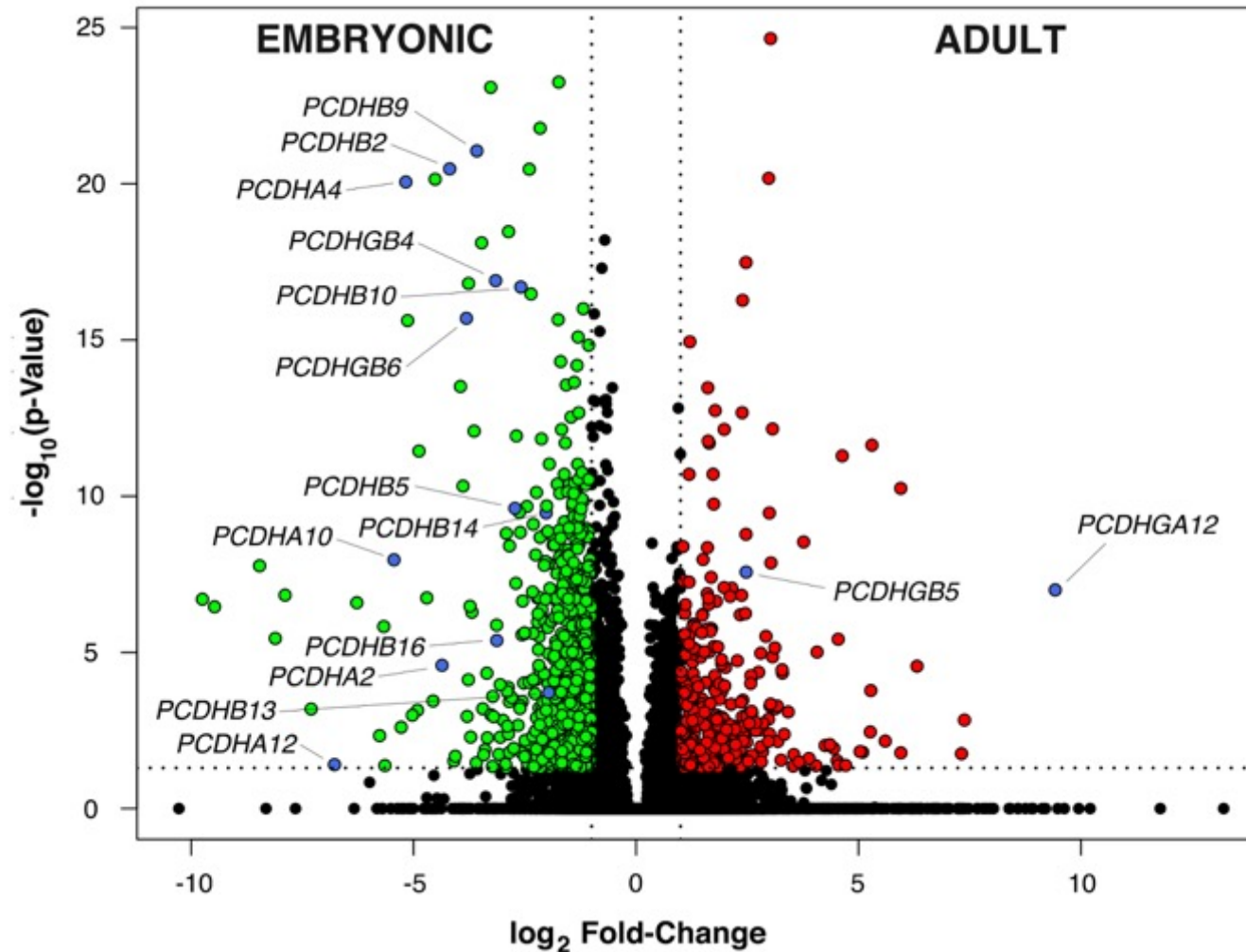
The Regenerative Hallmarks of Cancer: *LIN28B*



Examples of EFT Genes



Taking Lessons from the PCDH Locus



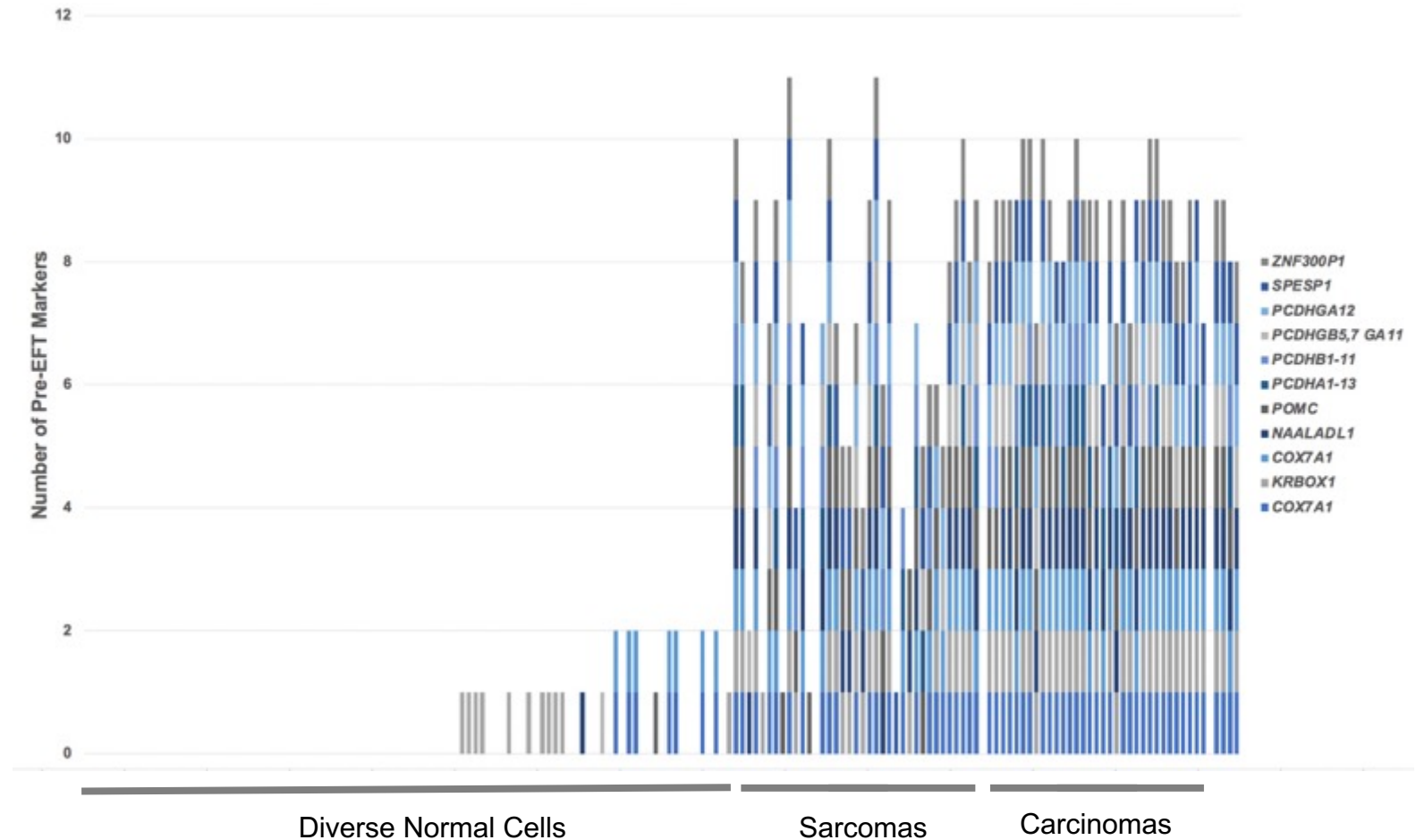
Pre-EFT Pan-Cancer Markers

Newly-discovered hallmark of cancer seen in:

82% Sarcomas

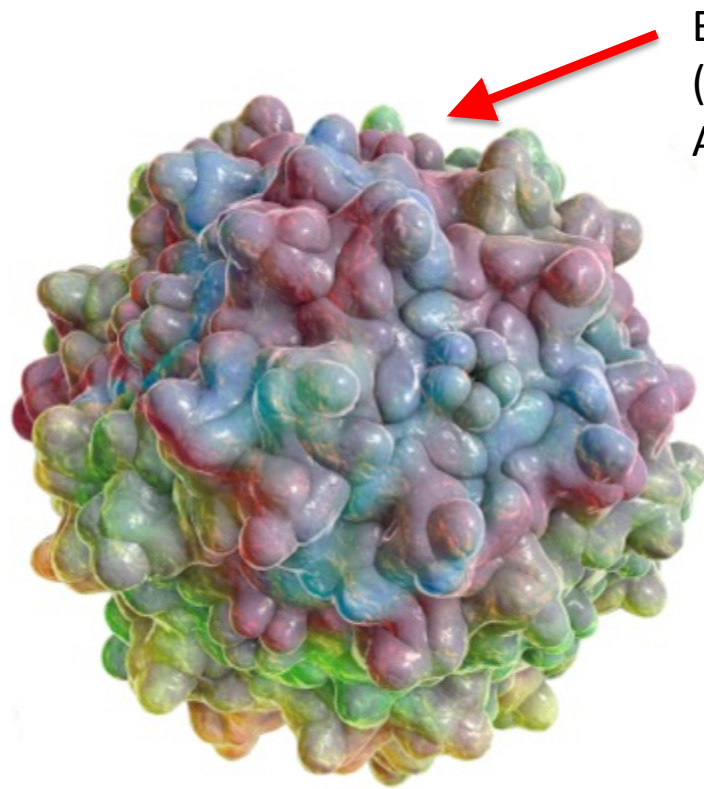
100% Carcinomas including:

- Breast Cancer
- Lung Cancer
- Brain Cancer
- Prostate Cancer
- Colon Cancer
- Liver Cancer
- Kidney Cancer



Cancer Therapeutics -*EPRO*

Vector to Precisely Target and Destroy Pre-EFT Cancer



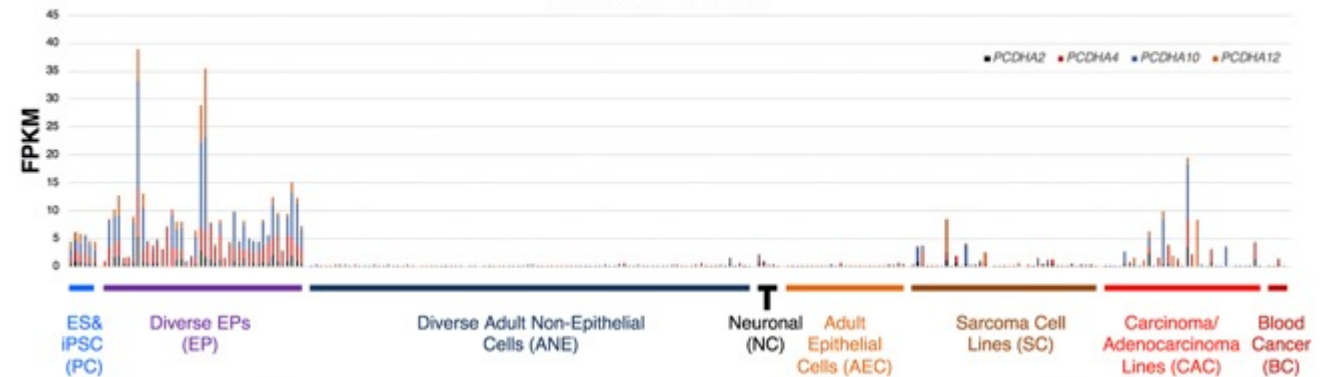
EPRO Oncolytic Viral Vector

Binding Site for Proprietary
(Patent Pending) Embryonic
Antigens



AAV Vector

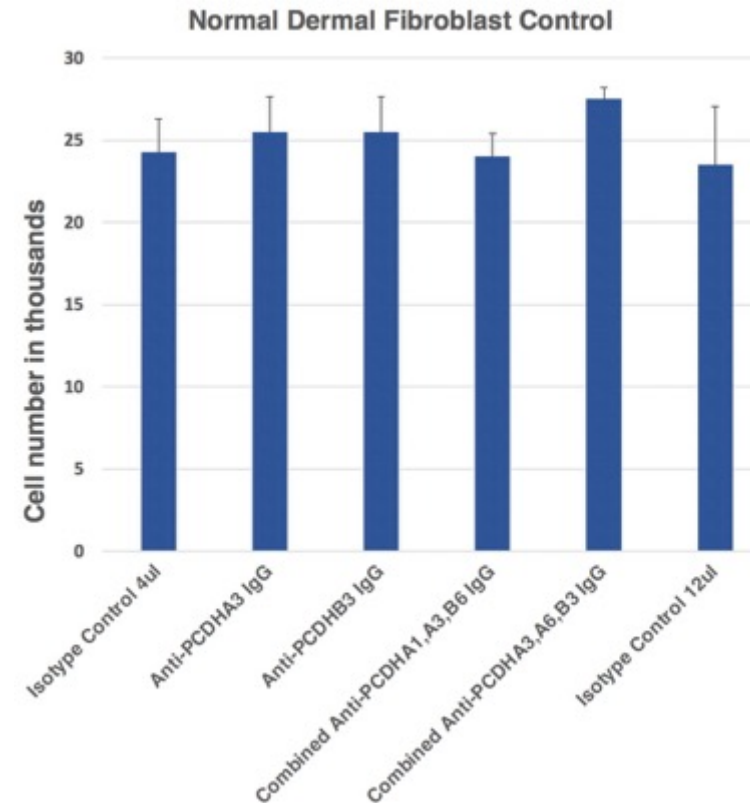
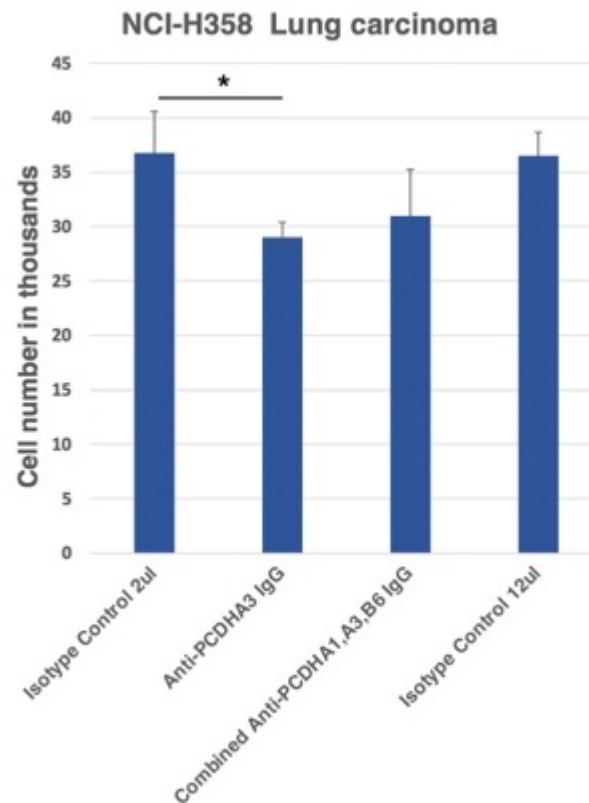
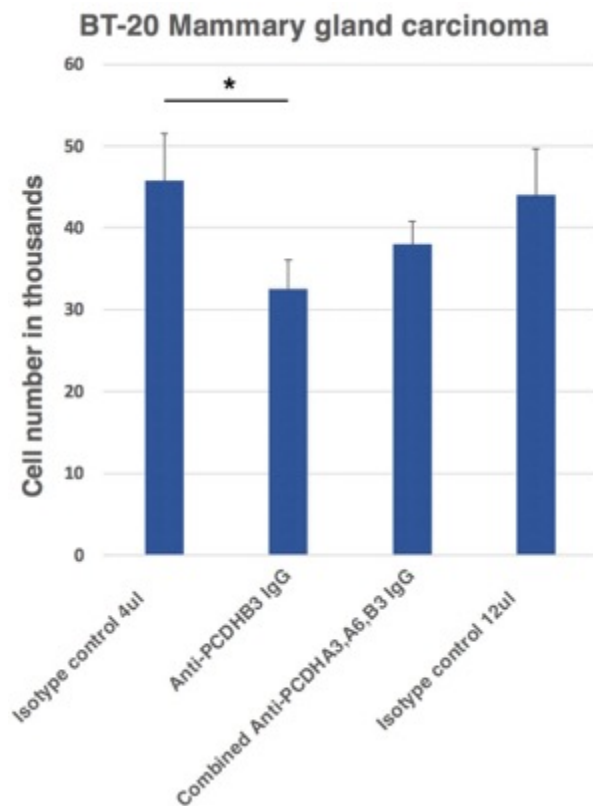
PCDHA Locus



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

Cancer Therapeutics

Early Proof of Concept: Specific Targeting in Breast and Lung Cancer using antibody alone

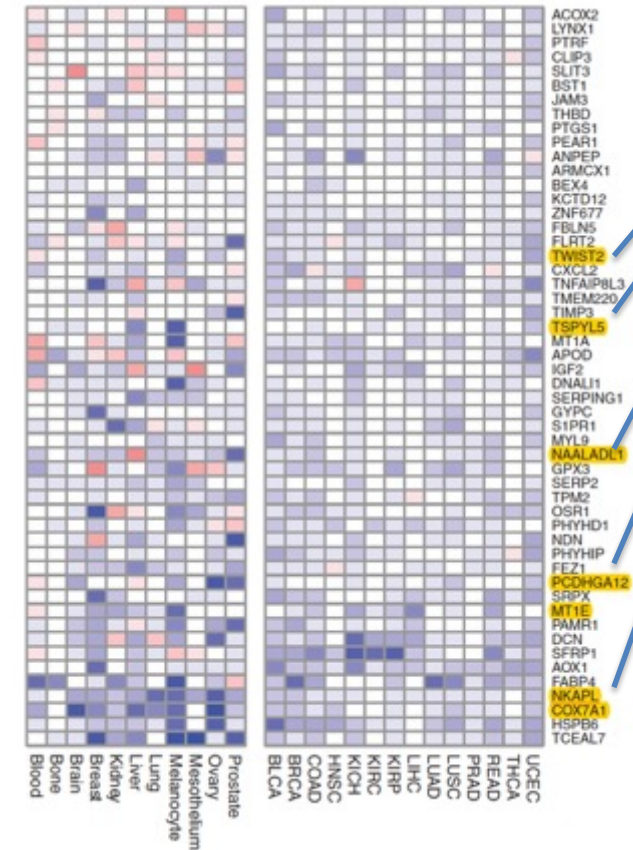


Embryonic Markers and Pan-Cancer Dx

Transcriptome Analysis of Recurrently Deregulated Genes across Multiple Cancers Identifies New Pan-Cancer Biomarkers

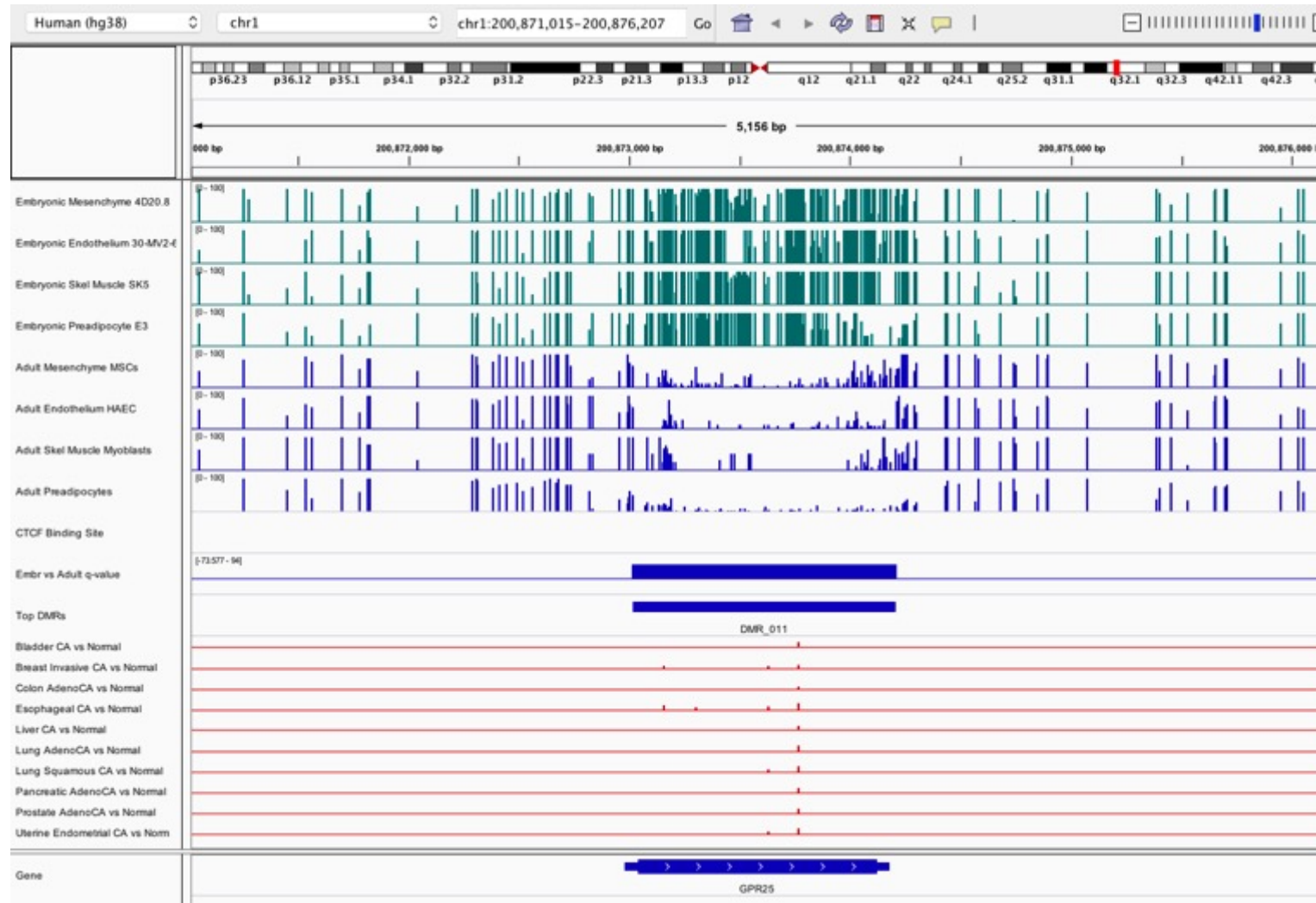
Bogumil Kaczkowski¹, Yuji Tanaka^{1,2}, Hideya Kawaji^{1,2,3}, Albin Sandelin⁴, Robin Andersson⁴, Masayoshi Itoh^{1,3}, Timo Lassmann^{1,5}, the FANTOM5 consortium, Yoshihide Hayashizaki³, Piero Carninci¹, and Alistair R.R. Forrest^{1,6}

Cancer Res; 76(2); 1–11.

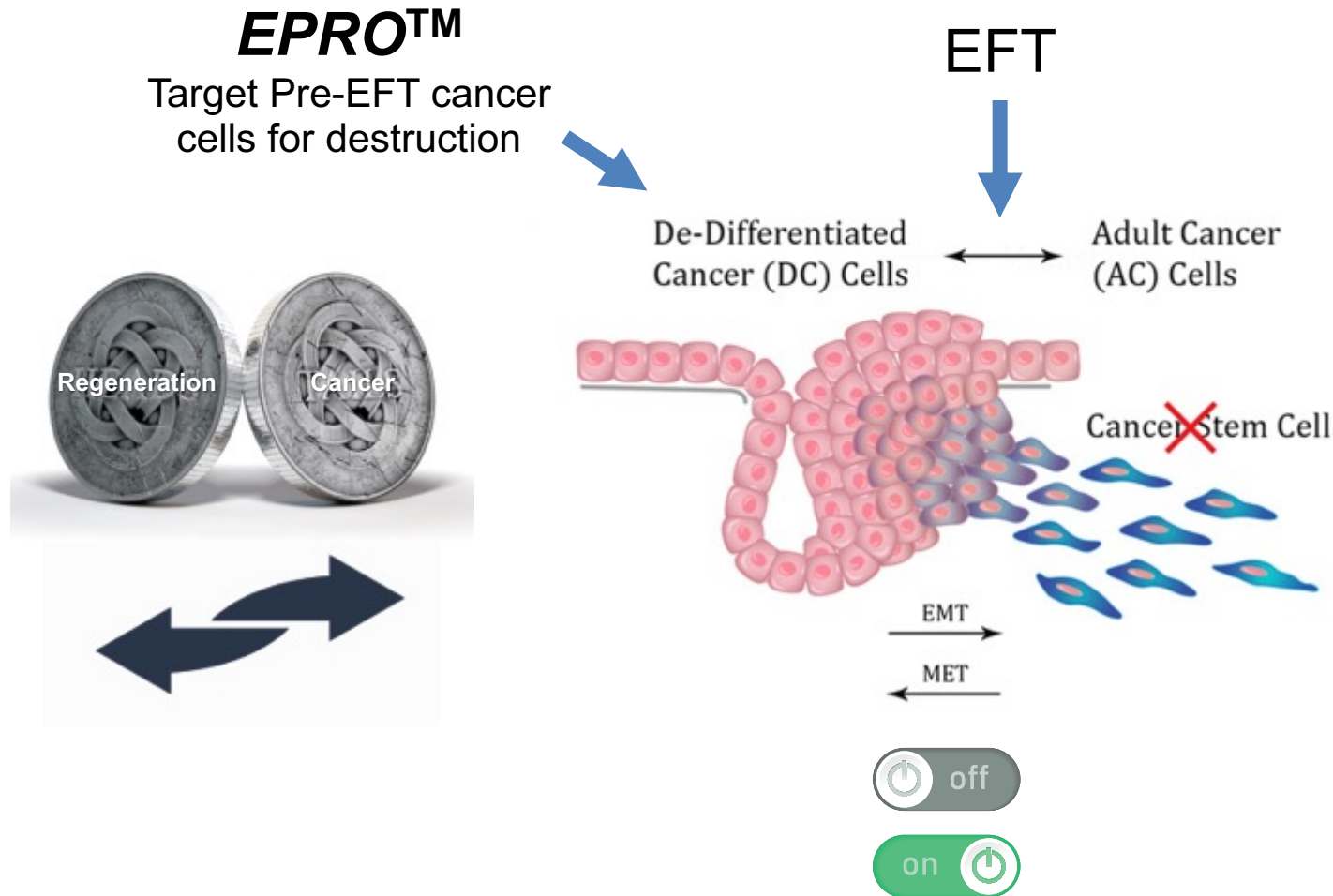


Pre-EFT
Markers

Robust Markers of Embryonic Cancer Cells for Diagnosis



EFT & Novel Pan-Cancer Therapeutic Strategy

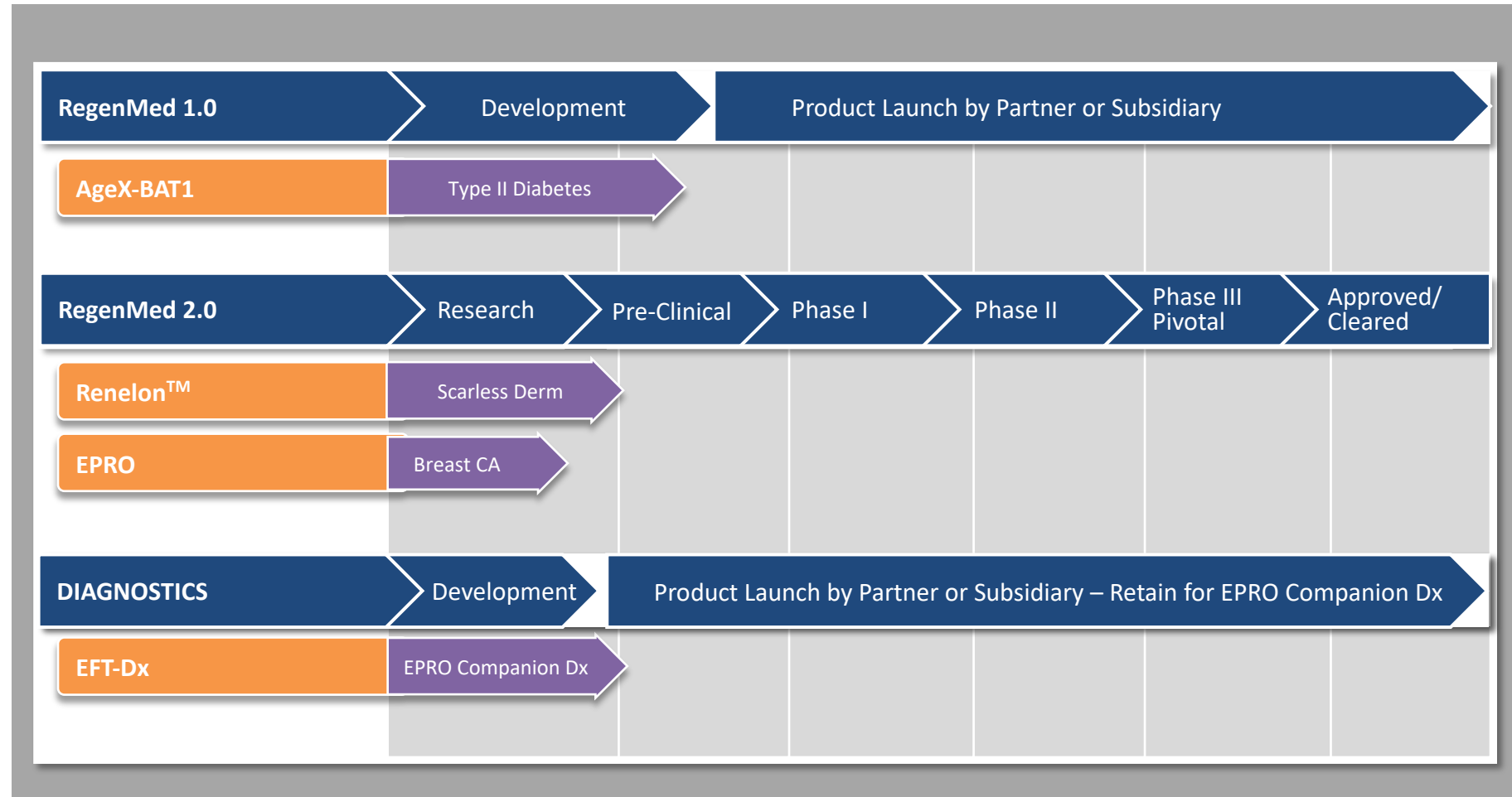


The concept of antagonistic pleiotropy led to:

- 1) [Telomerase as a pan-cancer hallmark.](#)
- 2) More recently, the Pre-EFT hallmark of cancer and that cancer stem cells are not the more primitive cell.

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



Product Pipeline



Significant Biotechnology Revolutions

Recombinant DNA Technology	Monoclonal Antibodies	Regenerative Medicine 1.0
		
<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• 1975 - Hybridoma technology developed• 1997- First \$B Product Rituximab• Advances in Mab Engineering• Today, eight of the 20 best-selling biotechnology drugs in therapeutic monoclonal antibodies• > 200 clinical trials• Current Global Market \$44 B	<ul style="list-style-type: none">• 1998 – First Pluripotent Stem Cells (PSCs) isolated• 2001 – U.S. Federal funding restriction (reversed in 2009)• 2010 – 1st PSC Clinical trial• 2015 – Fuji acquires Cell. Dyn.• 2015 – Astellas acquires Ocata• 2019 – Bayer acquires BlueRock• 2019 – Vertex acquires Semma• 2021 – SANA IPO \$6B M. Cap.• 2022 – LCTX \$670M Roche• Future – 1st \$B product

Significant Biotechnology Revolutions

Recombinant DNA Technology	Monoclonal Antibodies	Regenerative Medicine 1.0	Regenerative Medicine 2.0
			
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Summary

Therapeutic & Dx Opportunities Stemming from Partial Reprogramming

- Induction of Tissue Regeneration (iTR) 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
- *Pan-Cancer Dx*– Detection of most cancer types. By liquid biopsy, determination of embryonic vs adult phenotypes, companion Dx to EPRO