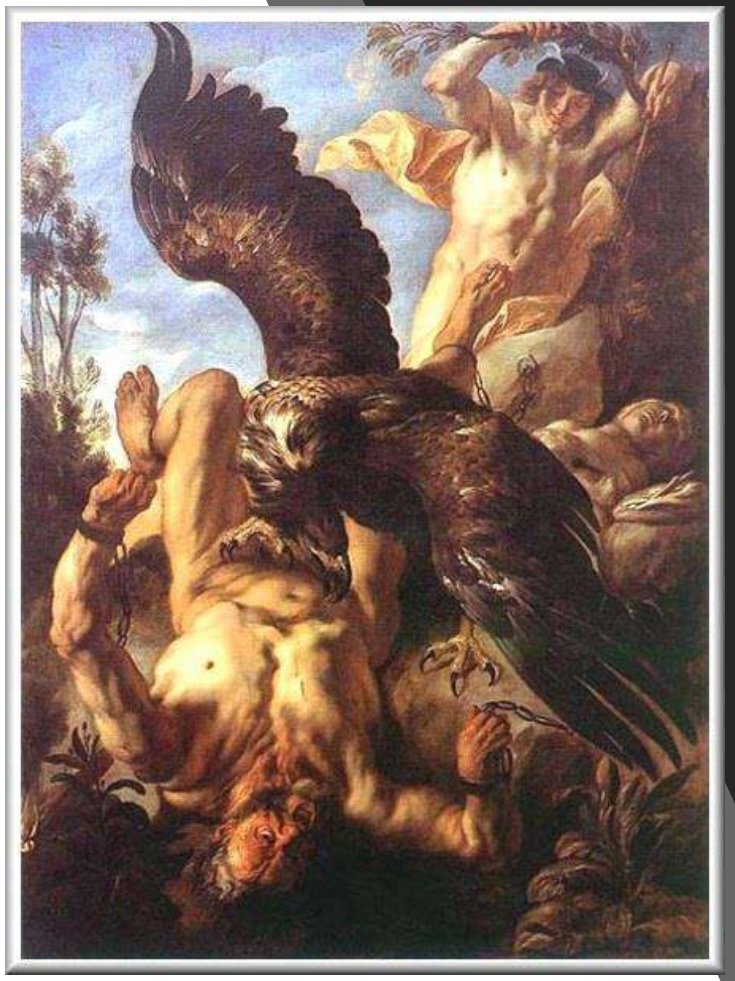
ABRM Regenerative Medicine Board Certification Review Course

Module I – The History of Regenerative Medicine

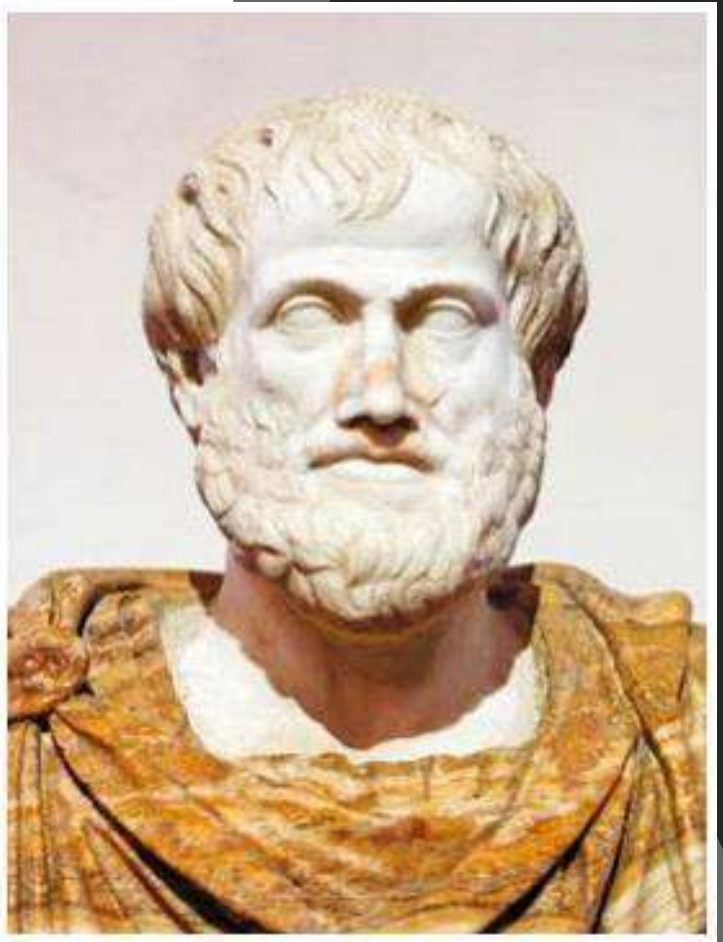
ABRM – History of Regenerative Medicine



Greek Mythology (Heroid)

- Prometheus stole fire from Olympus, thereby offending Zeus
- Prometheus was banished and chained; an eagle came each night to pick at his liver
- Prometheus' liver would regenerate each day

ABRM – History of Regenerative Medicine



300 BC: Aristotle

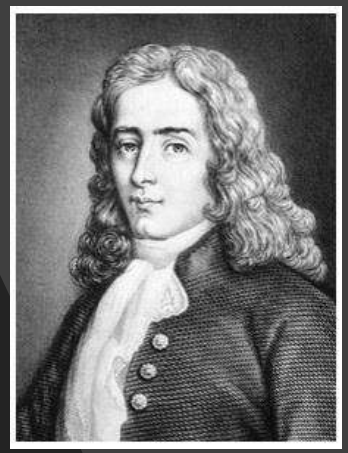
- Wrote two major works on regeneration in the animal realm based on observations of the regrowth of animal tails
- Hypothesized that biological form originates from undifferentiated matter

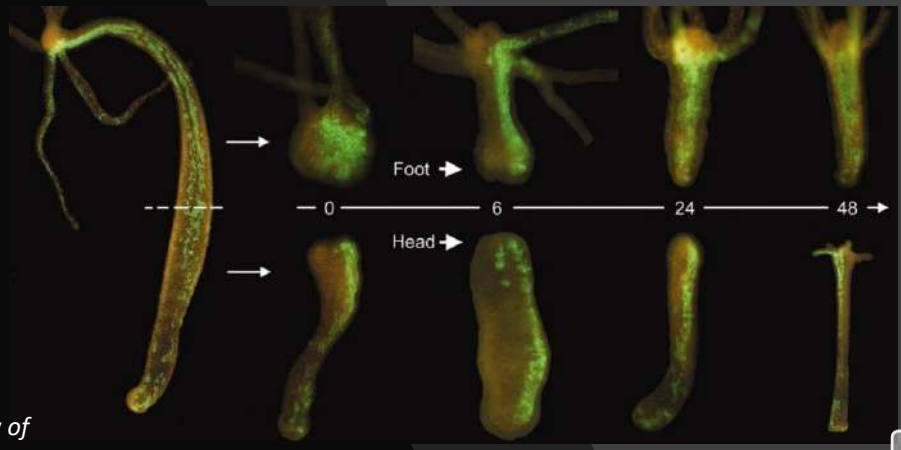
Mayenschein J. **Regenerative medicine's historical roots in regeneration, transplantation, and translation.** Develop Biol. Volume 358, Issue 2, 15 October 2011, Pages 278–284

ABRM – History of Regenerative Medicine

1700s: Abraham Trembley

- Regeneration in freshwater polyps (hydra)
- First cloning experiment
- Cloned 50 polyps from single organism
- Plant vs. animal



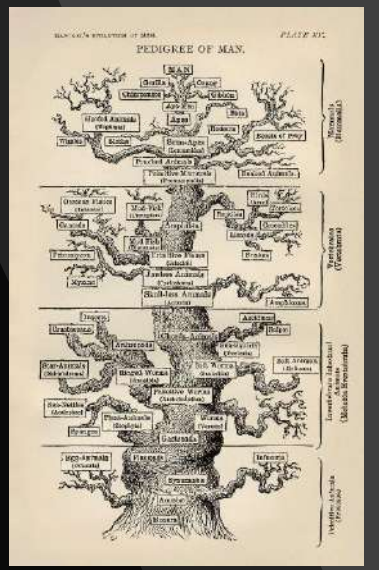


Lenhoff, Howard M., and Sylvia G. Lenhoff. "Abraham Trembley and the Origins of Research on Regeneration in Animals." in *A History of Regeneration Research: Milestones in the Evolution of a Science*, ed. C. E. Dinsmore, 47–66. Cambridge: Cambridge University Press, 1991.

ABRM – History of Regenerative Medicine

1868: Ernst Haeckel (German Biologist)

- Darwinist
- Used transitions from evolution to embryology
- Used term "Stem Cell" to describe:
  - Unicellular organism as ancestor of multicellular organisms
  - Example: fertilized egg becomes a whole organism



Haeckel, E. (1868). Naturliche Schopfungsgeschichte (Berlin: Georg Reimer).

ABRM – History of Regenerative Medicine

1887 Theodor Boveri (German Biologist)

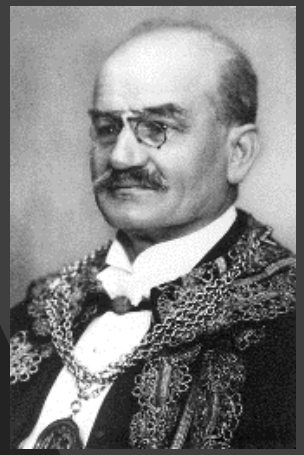
- Identified the earliest embryonic germ cells (roundworm Ascaris)
- Discovered that only the germ cell lineage contains the full complement of chromatin initially present in the fertilized egg
- Concluded that these cells are true Stem Cells since chromatin is not fragmented during cell division

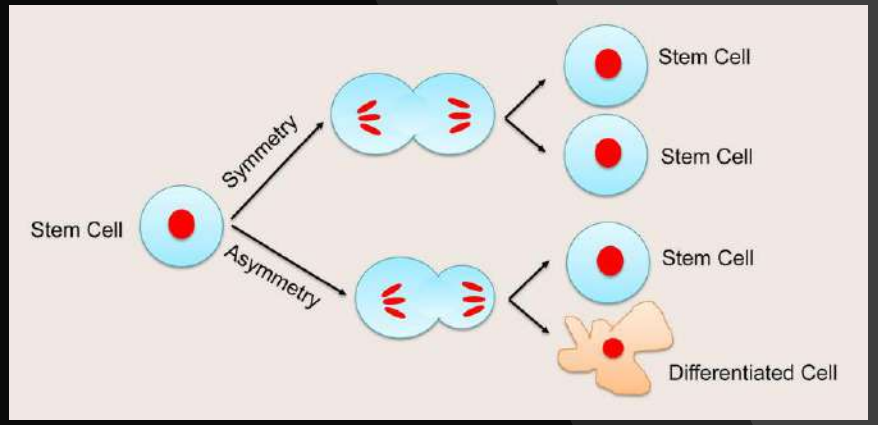
Dietel, M. (2014), Boveri at 100: the life and times of Theodor Boveri. J. Pathol., 234: 135-137. https://doi.org/10.1002/path.4410

ABRM – History of Regenerative Medicine

1892: Valentin Haecker (German Zoologist)

- Studied development of the crustacean *Cyclops*
- Discovered a large cell which became internalized during gastrulation
- Observed that this 'Stem Cell' underwent asymmetric cell division with one daughter cell becoming mesodermal and the other a replica germ cell



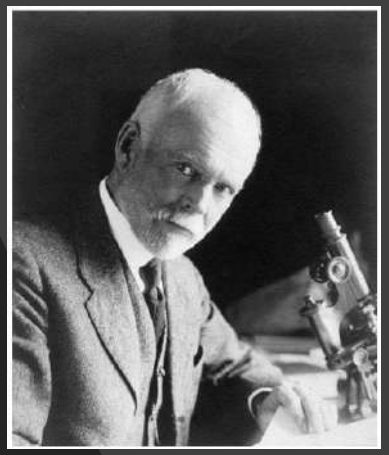


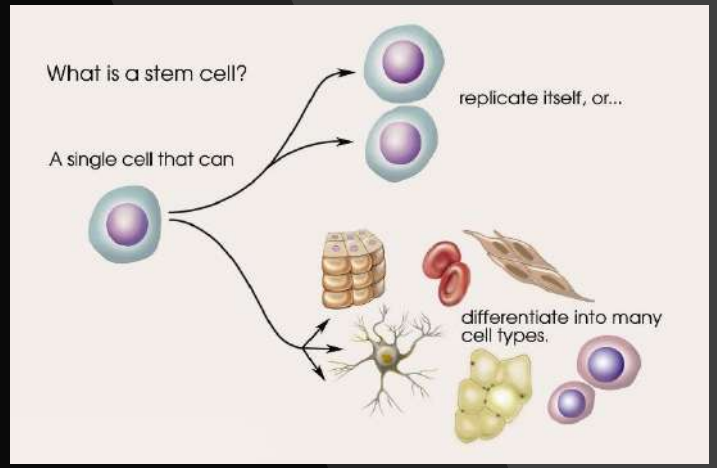
Hoßfeld U, Watts E, Levit GS. Valentin Haecker (1864-1927) as a pioneer of phenogenetics: Building the bridge between genotype and phenotype. Epigenetics. 2017 Apr 3;12(4):247-253.

ABRM – History of Regenerative Medicine

1896: E.B. Wilson (Columbia University)

- First Cell Biologist
- Stem Cells: “special cells able to give rise to specialized cells”
- Created the concept of differentiation



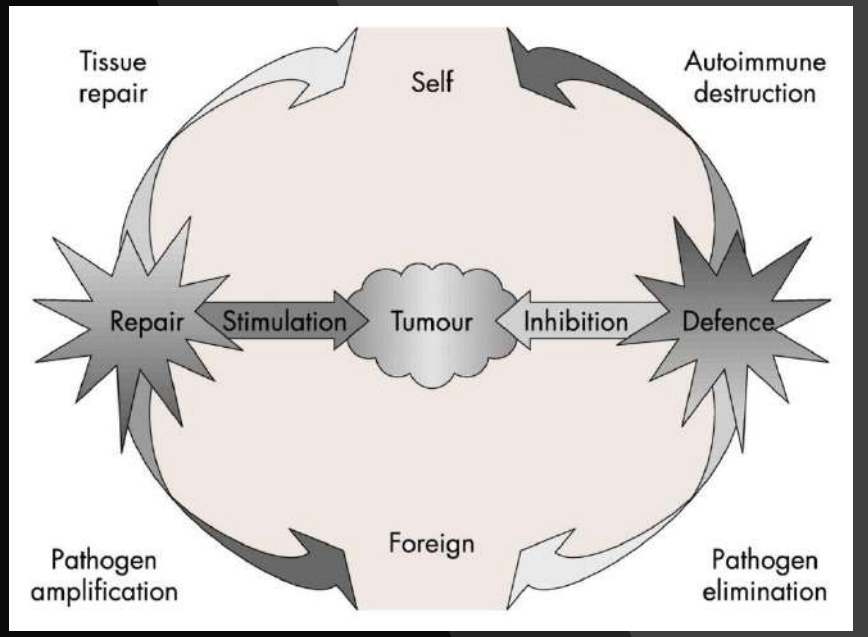


Wilson E.B. 1896; 1900; 1925. *The cell in development and inheritance*. Macmillan.

ABRM – History of Regenerative Medicine

1893: William Coley (New York University)

- Father of Cancer Immunotherapy
  - Used bacteria as immunotherapy agent for sarcoma
  - Streptococcus tumor injections
  - Coley's toxins



McCarthy EF et al. **The Toxins of William B. Coley and the Treatment of Bone and Soft-Tissue Sarcomas.** Iowa Orthop J. 2006; 26: 154–158.

ABRM - History of Regenerative Medicine

1907: Ross Granville Harrison (Johns Hopkins, Yale)

- Nerve cell differentiation in tadpole model
- Neuroblast differentiation in hanging drop of lymph as culture medium
- First stem cell study and tissue culture

Mayenschein J. **Regenerative medicine's historical roots in regeneration, transplantation, and translation.** Develop Biol. Volume 358, Issue 2, 15 October 2011, Pages 278–284

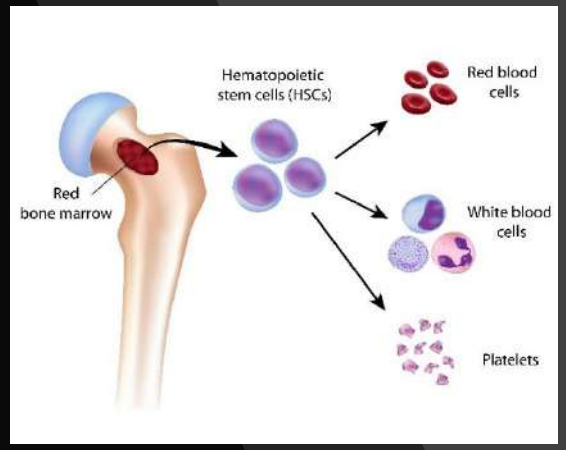
ABRM – History of Regenerative Medicine

1909: Alexander Maximow (St. Petersburg Military Academy)

- Hypothesized on existence of Hematopoietic Stem Cells (HSC) as precursors of blood cells
- Unitarian theory of hematopoiesis

1924: Alexander Maximow

- Identifies single precursor cell within mesenchyme which gives rise all types of blood cells (HSC)

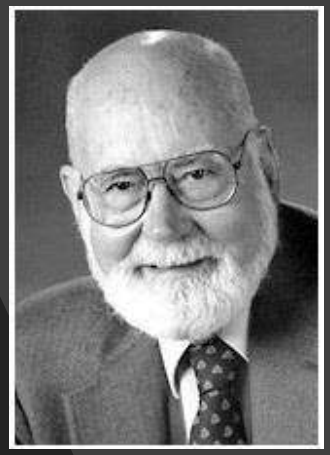


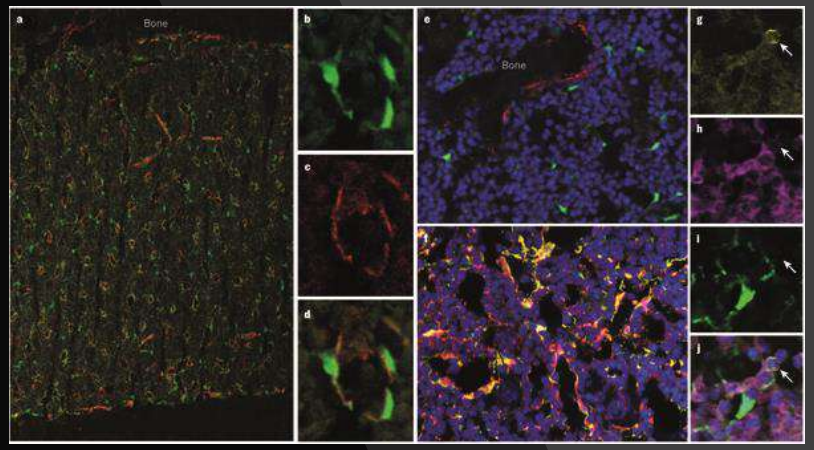
Maximow, Alexander A. (1928). "Cultures of blood leucocytes. From lymphocyte and monocyte to connective tissue". *Arch Exp Zellforsch* **5**: 169-268.

ABRM – History of Regenerative Medicine

1956: E. Donnall Thomas (U. Washington)

- First successful Bone Marrow Transplant due to matched tissue types
- Donor – Recipient: siblings (leukemia)
- First successful unrelated donor-recipient bone marrow transplant (1977)
- Nobel Prize in 1990



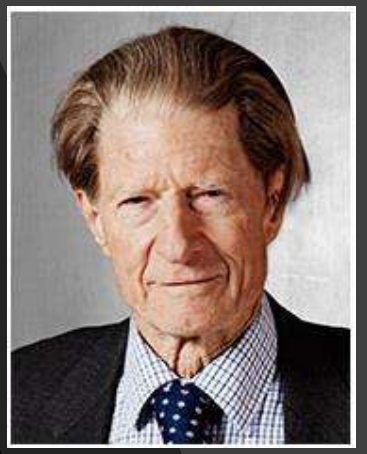


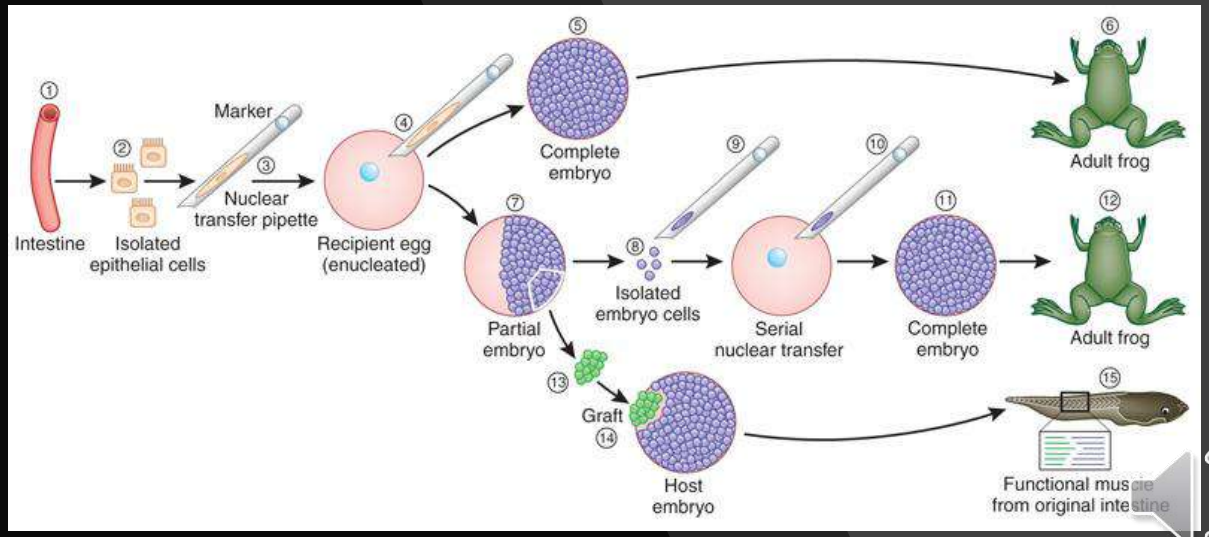
Thomas ED, et al. **Bone-Marrow Transplantation.** N Engl J Med 1975; 292:832-843

ABRM – History of Regenerative Medicine

1958: Sir John B. Gurdon (University of Oxford)

- Removed somatic cell nucleus from tadpole and implanted in tadpole egg
- Successful frog cloning
- Nobel Prize 2012





*Gurdon, J. B.; Elsdale, T. R.; Fischberg, M. (1958). "Sexually Mature Individuals of Xenopus laevis from the Transplantation of Single Somatic Nuclei". Nature. **182** (4627): 64–65.*

ABRM – History of Regenerative Medicine

1961-63: Ernest McCulloch and James Till (Ontario Cancer Institute)

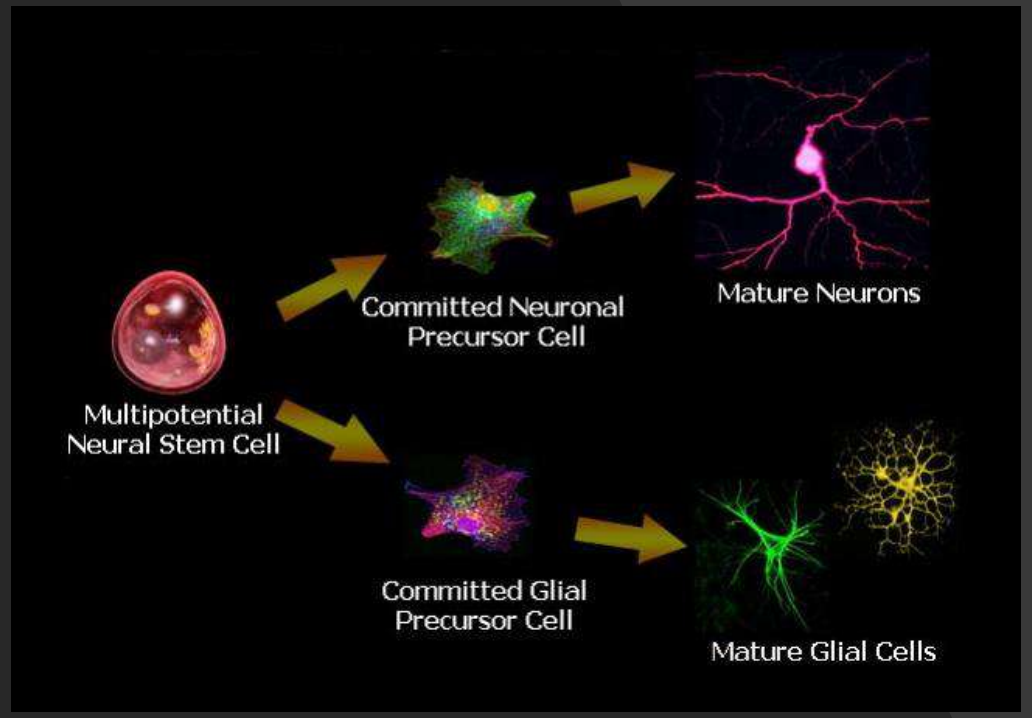
- Irradiated recipient BM in mice
- Transplanted donor BM cells caused spleen nodules in recipient
- Demonstrated that each nodule originated from singular cell
- Nodules contained cells of all 3 different blood cell lines
- Each nodule originated from single HSC

Becker, A.J.; McCulloch, E.A.; Till, J.E. (1963). "Cytological demonstration of the clonal nature of spleen colonies derived from transplanted mouse marrow cells". *Nature* 197 (4866): 452–4

ABRM – History of Regenerative Medicine

1965: Joseph Altman and Gopal Das (MIT Labs)

- Demonstrated adult neurogenesis in rodent brains: Neural Stem Cells
- Contradicted "no new neurons" dogma

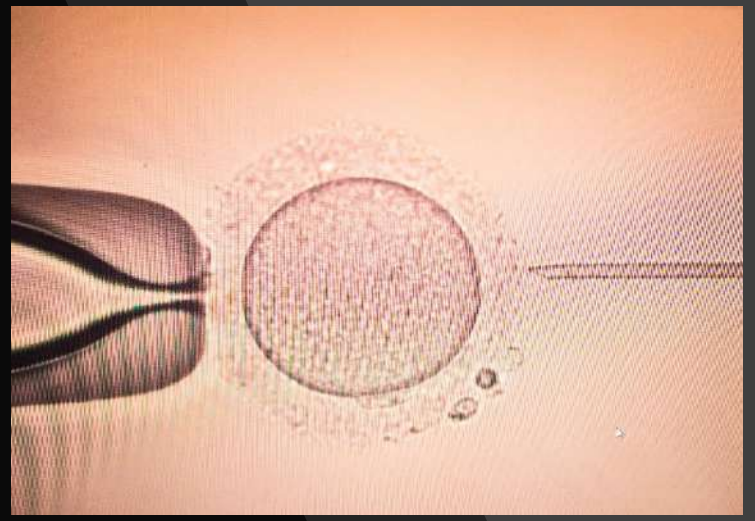


Altman J, Das GD. P**ostnatal neurogenesis in the guinea-pig.** Nature. 1967 Jun 10;214(5093):1098-101

ABRM – History of Regenerative Medicine

1968: Robert Edwards and Barry Bavister (University of Cambridge)

- First in-vitro fertilization of human egg
- Used new bicarbonate-based culture medium containing bovine serum albumin
- Edwards: Nobel Prize 2010



Edwards, Robert G. “The Bumpy Road to Human *in vitro* Fertilization.” *Nature Medicine* 7 (2001): 1091–94.

ABRM – History of Regenerative Medicine

1968: Robert A. Good (University of Minnesota)

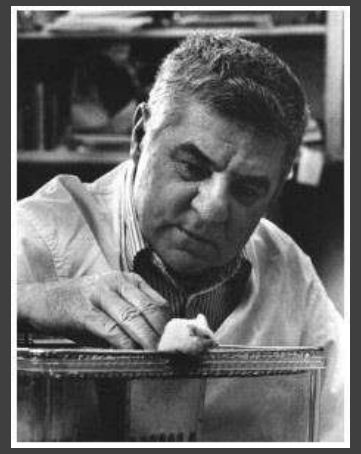
- Father of Immunology
- Performed first successful BM Transplant for Immune Disease
- HLA compatible sibling donor

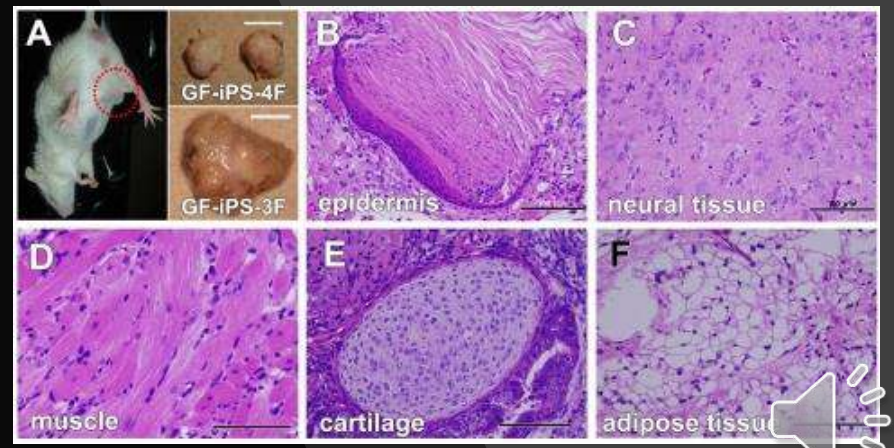
Robert Alan Good MD, PhD." *Biology of Blood and Marrow Transplantation* 9 (2003): 608–09.

ABRM – History of Regenerative Medicine

1970: Leroy Stevens (Jackson Laboratory, Maine)

- Discovered teratoma in mice scrotum
- Teratoma: hair, bone, intestine blood tissue
- Includes mix of differentiated and undifferentiated cells
- Discovered Embryonic Stem Cells in murine blastocysts



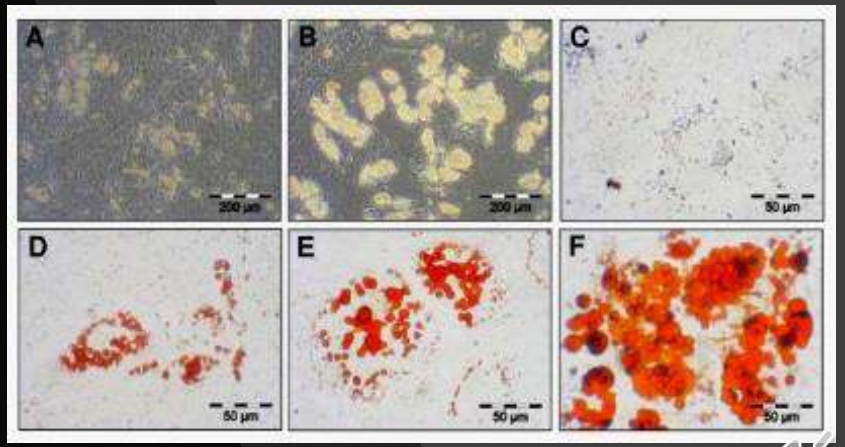


L.C. Stevens, "Studies on transplantable testicular teratomas of strain 129 mice, " *Journal of the National Cancer Institute*, 20:1257-70, June 1958.

ABRM History of Regenerative Medicine

1970: Alexander Friedenstein (Academy of Sciences, Moscow)

- Discovered Mesenchymal Stem Cells in Bone Marrow (stromal MSC)
- In-vitro Colony Forming Units (CFU) of Bone Marrow
- Selected plastic adherent cells
- Final CFU-F growth documented Osteocytes

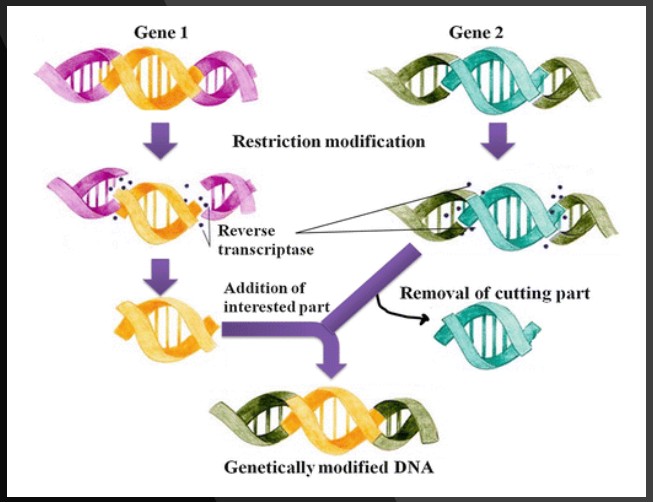


Friedenstein AJ, Piatetzky II S, Petrakova KV. Osteogenesis in transplants of bone marrow cells. J Embryol Exp Morphol. 1966;16(3):381–90

ABRM – History of Regenerative Medicine

1974: Rudolph Jaenisch and Beatrice Mintz (Salk Institute)

- Pioneered Genetically Modified Organisms (GMOs)
- Inserted foreign DNA into mouse embryo (DNA transfection)
- Used retrovirus DNA insertion technique

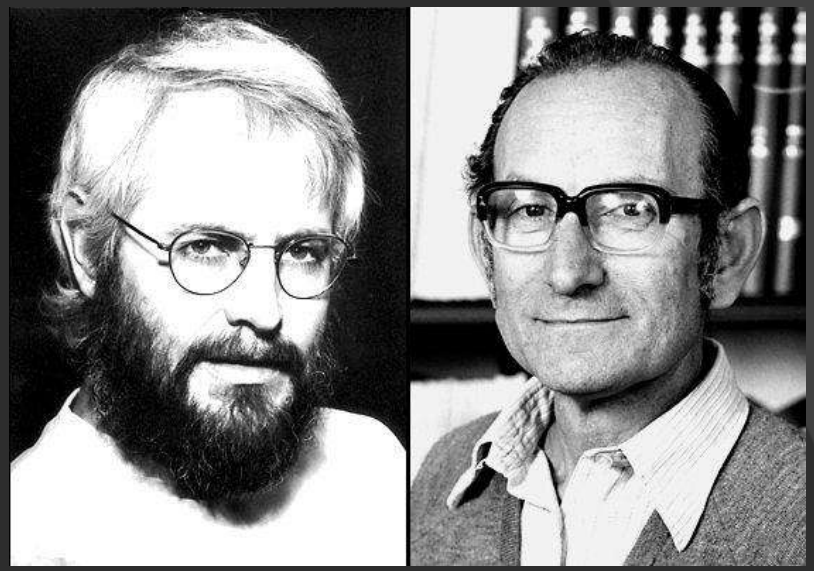


Jaenisch R, Mintz B (1974). "Simian virus 50 DNA sequences in DNA of healthy adult mice derived from preimplantation blastocysts injected with viral DNA". Proc. Natl. Acad. Sci. U.S.A. ***71*** *(4): 1250–1254.*

ABRM – History of Regenerative Medicine

1975: George Kohler and Cesar Milstein (Cambridge)

- Discovery of monoclonal antibodies
  - Revolutionized Immunotherapy
  - Merged myeloma cells with anti-body producing B-Cells
    - B-Cells now divided rapidly
    - Hybridoma technology

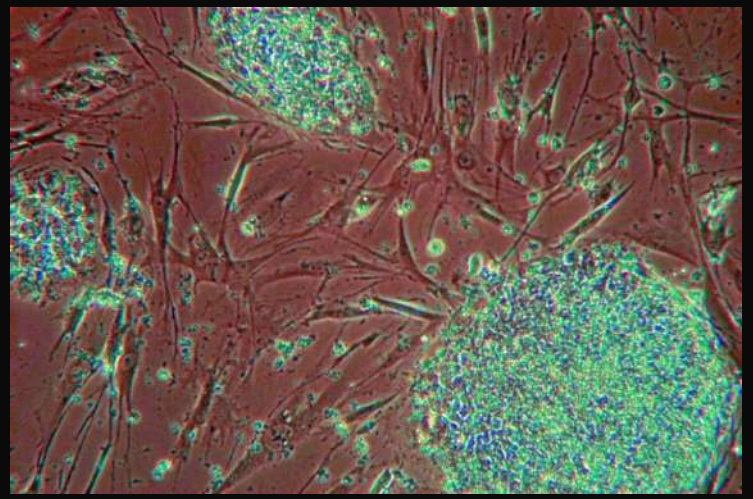


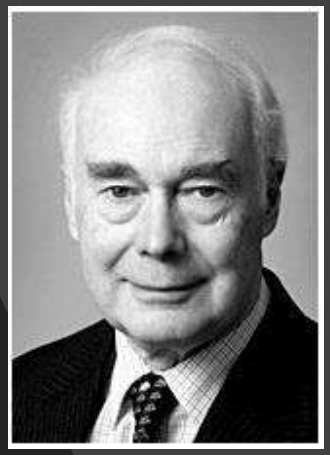
Freysd'ottir J. Production of monoclonal antibodies. Methods Mol Med. 2000;40:267-79. doi: 10.1385/1-59259-076-4:267.

ABRM – History of Regenerative Medicine

1981: Martin Evans and Gail Martin (Cambridge and UCSF)

- Coined the term "Embryonic Stem Cells"
- First Mouse ESC culture



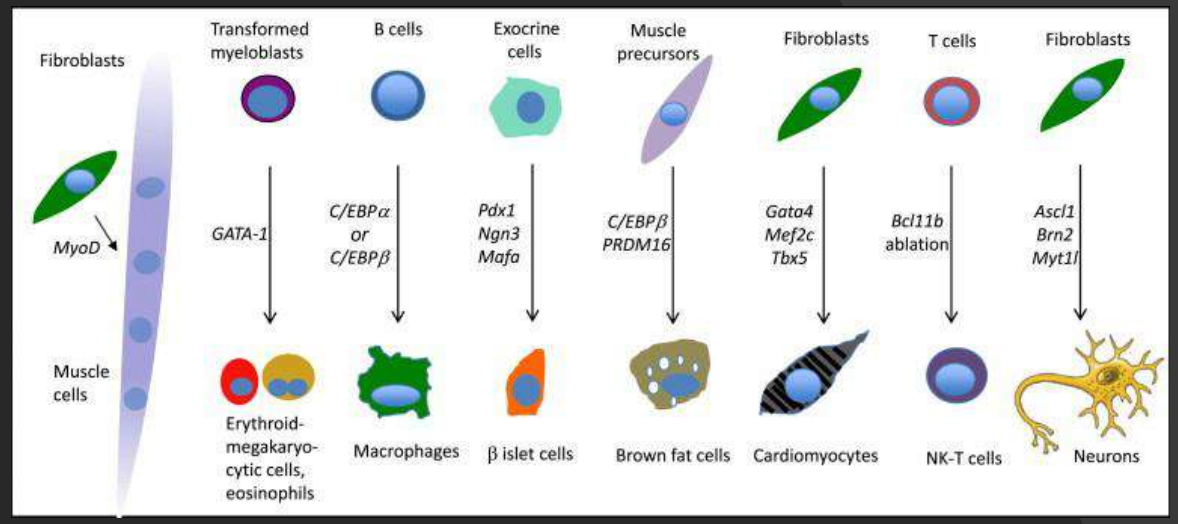


Evans M, Kaufman M (1981). "Establishment in culture of pluripotent cells from mouse embryos". Nature. ***292*** *(5819): 154–6*

ABRM – History of Regenerative Medicine

1987: Andrew Lassar and Harold Weintraub (Hutchinson Cancer Research Institute)

- Fibroblast to myoblast conversion
- Evidence of trans-differentiation



Davis RL, Weintraub H, Lassar AB. **Expression of a single transfected cDNA converts fibroblasts to myoblasts.** Cell. 1987 Dec 24;51(6):987-1000.

ABRM – History of Regenerative Medicine

1987 Arnold Caplan (Case Western University)

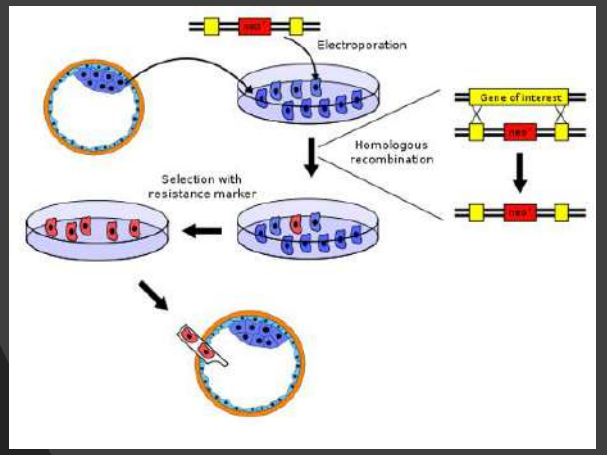
- Formally introduced the term "Mesenchymal Stem Cell" (MSC)
- Delineated specific phenotypic expressions of MSCs
- Broader differentiation potential than previously envisioned
- Popularized the clinical potential of MSCs

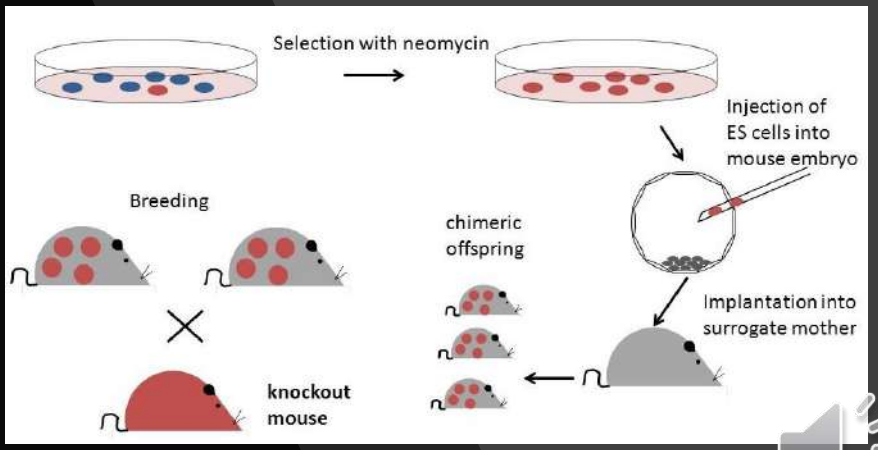
Caplan AI. **Mesenchymal stem cells.** J Orthop Res. 1991 Sep;9(5):641-50.

ABRM – History of Regenerative Medicine

1989: Mario Capecchi, Martin Evans and Oliver Smithies

- Created the first "knock-out mice"
- Mice created from embryonic stem cells
- Homologous gene recombination
- Disruption of gene sequence (genes "knocked out")
- Creates "Chimeric Mouse"
- Nobel Prize 2007





Thomas, K. R.; Capecchi, M. R. (1987). "Site-directed mutagenesis by gene targeting in mouse embryo-derived stem cells". Cell. ***51*** *(3): 503–512.*

ABRM – History of Regenerative Medicine

1989: Joseph and Charles Vacanti and Robert Langer (University of Massachusetts, MIT)

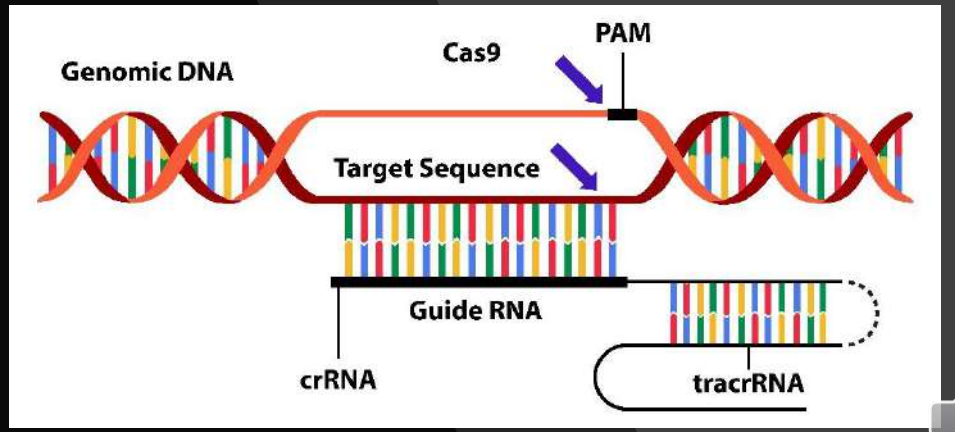
- Coined term "Tissue Engineering"
- Performed first in-vitro cell seeding onto biodegradable scaffold
- Created first xenogenic organ experiment

Langer R, Vacanti JP. Tissue engineering. Science. 1993 May 14;260(5110):920-6.

ABRM – History of Regenerative Medicine

1993: Francisco Mojica (University of Alicante, Spain)

- Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)
  - Powerful gene editing tool
  - Uses nuclease (Cas-9) to “cut” specific DNA location
  - Palindropic repeats: repetitive nucleotide sequence same in both directions

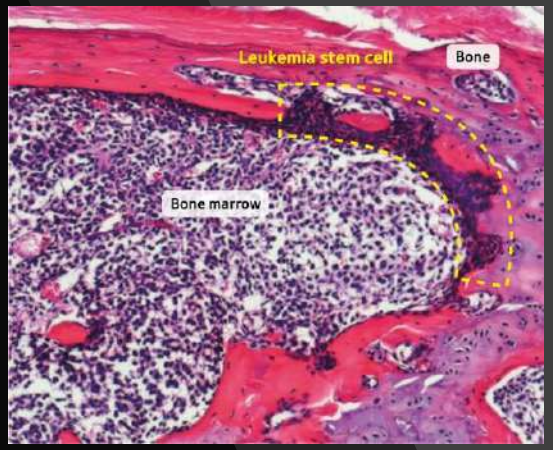


Ledford H et al. **Five big mysteries about CRISPR’s origins. Nature V541, 2017**

ABRM – History of Regenerative Medicine

1997: Dominique Bonnet and John Dick (Hospital for Sick Children, Toronto)

- AML Leukemia caused by cancerous HSCs
- Leukemic transformation
- Concept of "Cancer Stem Cell"
- CD 24, CD44, CD133

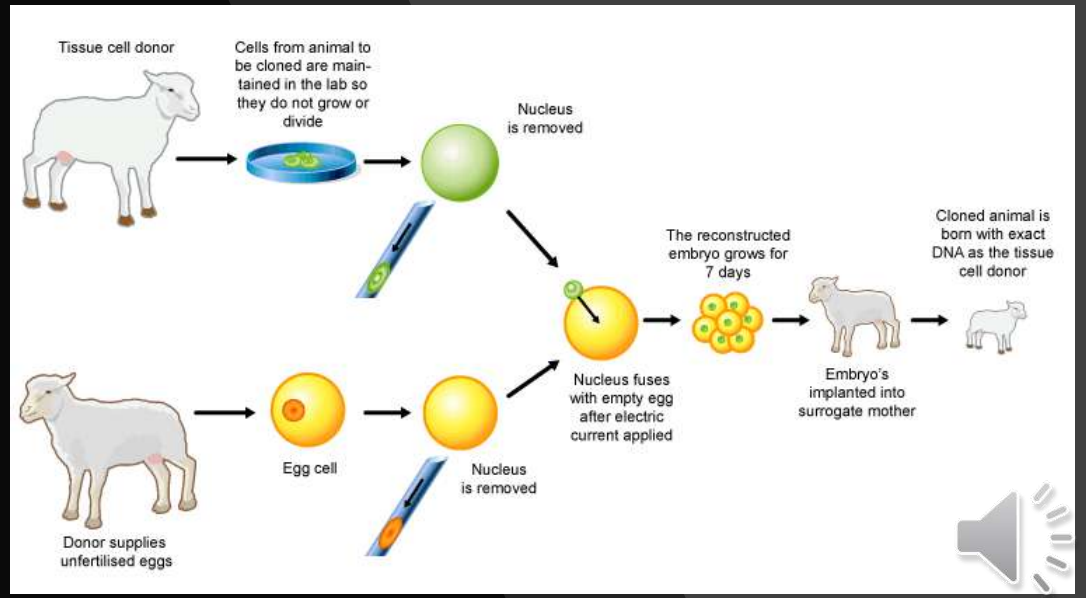


Bonnet D, Dick JE. **Human acute myeloid leukemia is organized as a hierarchy that originates from a primitive hematopoietic cell.** *Nature Medicine* **3**, 730 - 737 (1997)

ABRM – History of Regenerative Medicine

1997: Ian Wilmut and Keith Campbell (Roslin Institute, Scotland)

- Dolly the Sheep
- Somatic Cell Nuclear Transfer (SCNT)
- Adult nucleus implanted in enucleated, fertilized egg

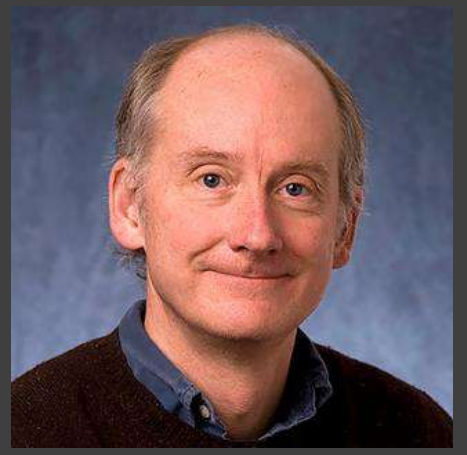


Campbell, K. & Wilmut, I. (1998) "Nuclear Transfer". *Animal Breeding: Technology for the 21st Century*. (ed: A.J. Clark; Harwood Academic Publishers). pp. 47–62

ABRM – History of Regenerative Medicine

1998: James Thomson and Jeffrey Jones (University of Wisconsin)

- First to isolated and culture human embryonic Stem cells from blastocysts
- Utilized embryos from in-vitro fertilization
- Pluripotency of Embryonic Stem Cells



Thomson JA, Itskovitz-Eldor J, Shapiro SS, Waknitz MA, Swiergiel JJ, Marshall VS, Jones JM. **Embryonic stem cell lines derived from human blastocysts.** Science. 1998 Nov 6;282(5391):1145-7.

ABRM – History of Regenerative Medicine

2000: NIH Guidelines on Pluripotent Stem Cells

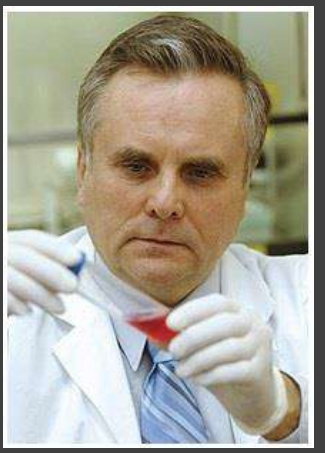
- ESCs must be obtained from private fertility sources
- Excess of Donor's needs only
- Donor consent required

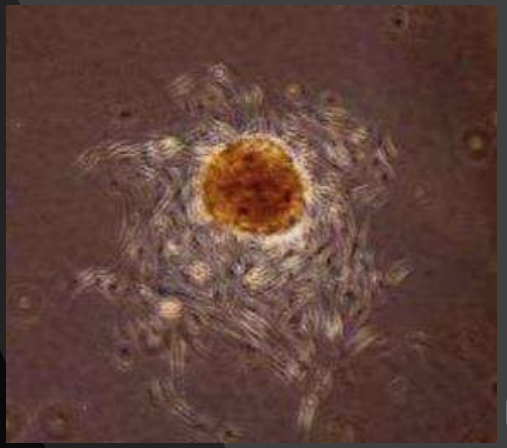
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-050.html

ABRM – History of Regenerative Medicine

2005: Magdalena Kucia and Mariusz Ratajczak (University of Louisville)

- Discovered non-hematopoietic tissue committed Stem Cells, eventually termed 'Very Small Embryonic-Like Stem Cells' (VSEL) in mice
- 2008: VSEL isolation in humans
- Initially thought to be cell debris due to small size (3-5 micron)



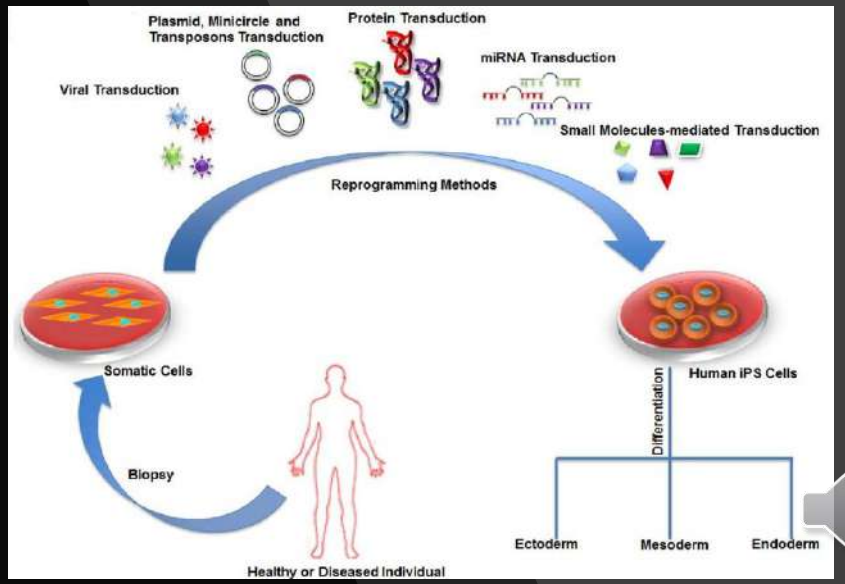


Ratajczak MZ. Very small embryonic-like stem cells: characterization, developmental origin, and biological significance. *Experimental Hematology*,*36*(6), 742-751.

ABRM – History of Regenerative Medicine

2006: Shinya Yamanaka and Kazutoshi Takahashi (Kyoto University, Japan)

- Adult murine fibroblasts converted into embryonic-like Stem Cells
- Used retrovirus to enter genetic code termed "induced pluripotent Stem Cells" (iPSC)
- Nobel Prize 2007 and 2012

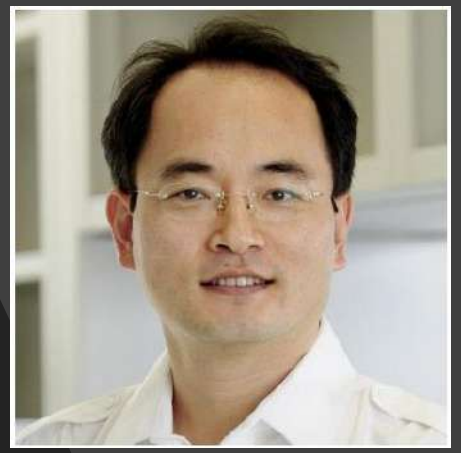


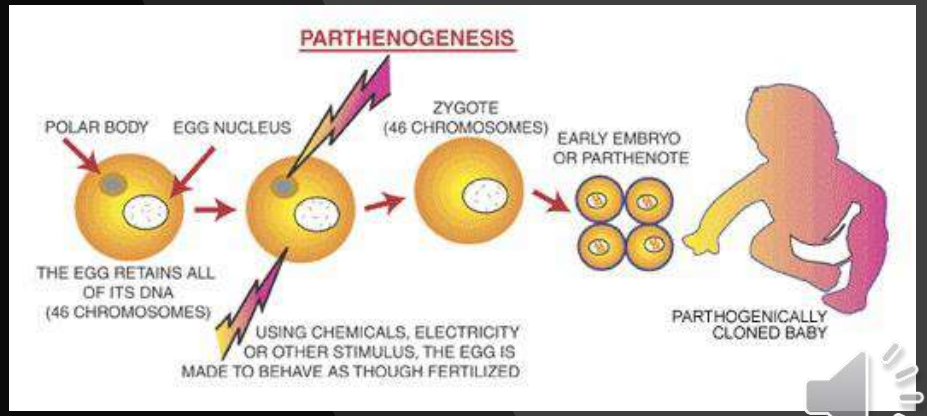
Takahashi K, Yamanaka S. **Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors.** Cell. 2006 Aug 25;126(4):663-76.

ABRM – History of Regenerative Medicine

2006: Kim Kitai and George Daley (Boston Children's Hospital)

- Demonstrated parthenogenesis in mice
- Asexual cell reproduction from unfertilized eggs
- Identical paired chromosomes
- Potential alternative to SCNT

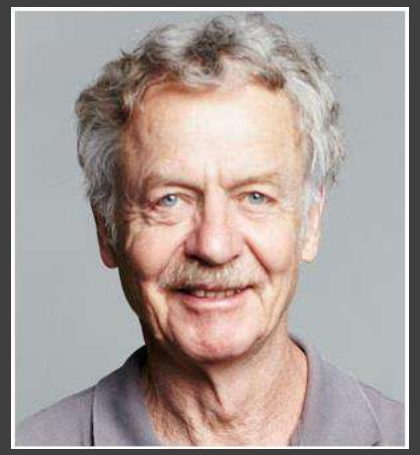




Kitai K et al. Histocompatible Embryonic Stem Cells by Parthenogenesis. *Science* 26 Jan 2007: Vol. 315, Issue 5811, pp. 482-486

ABRM – History of Regenerative Medicine

2007/2008 Rudolf Jaenisch (Whitehead Institute, MIT)



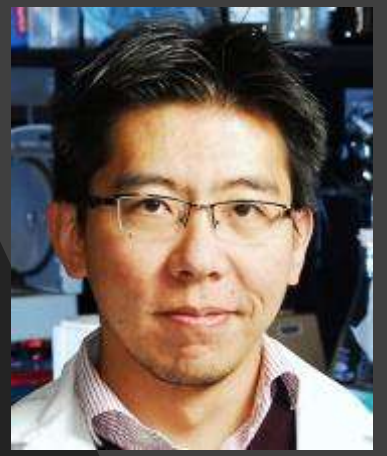
- 2007: Used iPSC method to generate murine hematopoietic precursor cells (HPC)
  - Used HPCs to successfully treat induced Sickle Cell Anemia in mice
- 2008: Used iPSC method to generate neuronal precursor cells (NPC)
  - Used NPCs to successfully treat induced Parkinson's Disease in mice

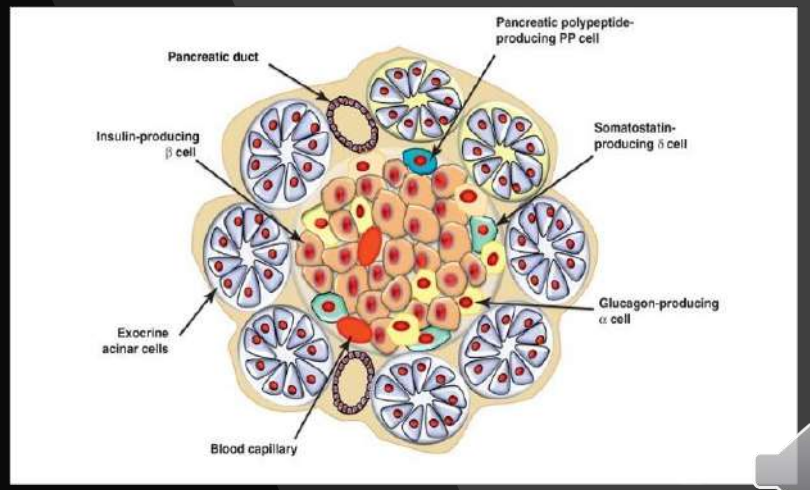
Wernig M, Zhao JP, Pruszak J, Hedlund E, Fu D, Soldner F, Broccoli V, Constantine-Paton M, Isacson O, Jaenisch R. Neurons derived from reprogrammed fibroblasts functionally integrate into the fetal brain and improve symptoms of Parkinson's disease. Proc. Natl. Acad. Sci. USA 105(15): 5856-5861, 2008.

ABRM – History of Regenerative Medicine

2008: Qiao Zhou and Juliana Brown
(Harvard Stem Cell Institute, Boston Children's Hospital)

- Converted rodent pancreatic exocrine cells into insulin-producing cells
- Transcription Factors: Ngn3, Mafa, and Pdx1
- Skips the iPSC step



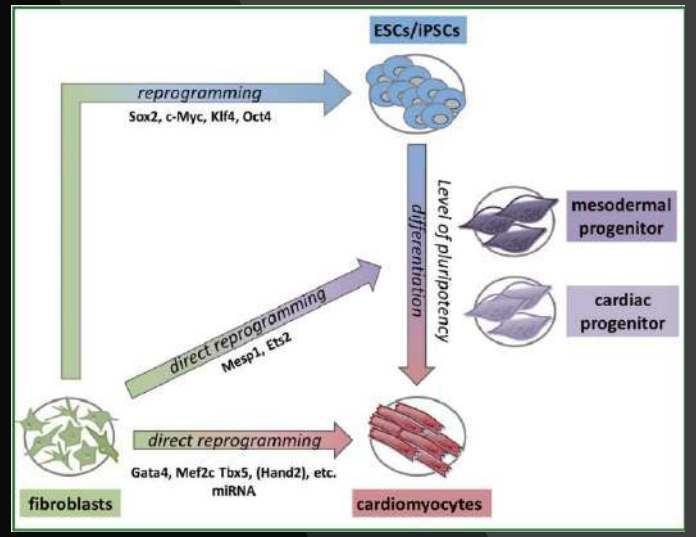


Zhou Q, Brown J. ***In vivo* reprogramming of adult pancreatic exocrine cells to β-cells.** *Nature* **455**, 627-632 (2 October 2008)

ABRM – History of Regenerative Medicine

2010: Deepak Srivastava
(Gladstone Institute, California)

- Direct reprograming of mouse cardiac fibroblasts into functional cardiomyocytes
- Identified specific reprograming transcription factors (Gata4, Mef2c, and Tbx5)

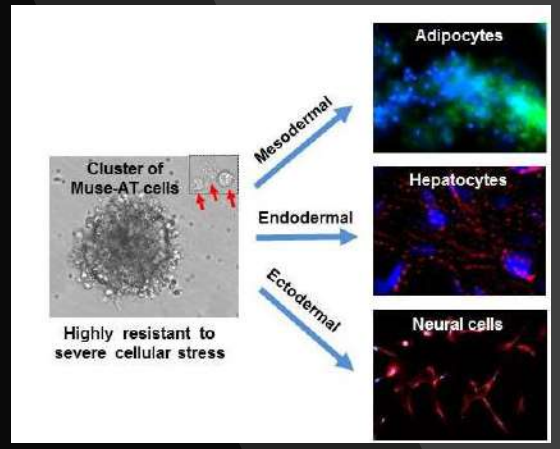


Ieda M, Fu J, Delgado-Olguin P, Vedantham V, Hayashi Y, Bruneau B, Srivastava D. Direct reprogramming of fibroblasts into functional cardiomyocytes by defined factors. Cell 142: 375-386, 2010.

ABRM – History of Regenerative Medicine

2010 Mari Dezawa (Kyoto University)

- Multi-lineage Differentiating Stress Enduring (MUSE) Stem Cell Discovery
  - Sources: Bone Marrow, Skin Fibroblast
  - Inactive Circulating Form
  - Activated by physiological stress
  - Stress Enduring
  - Engrafting

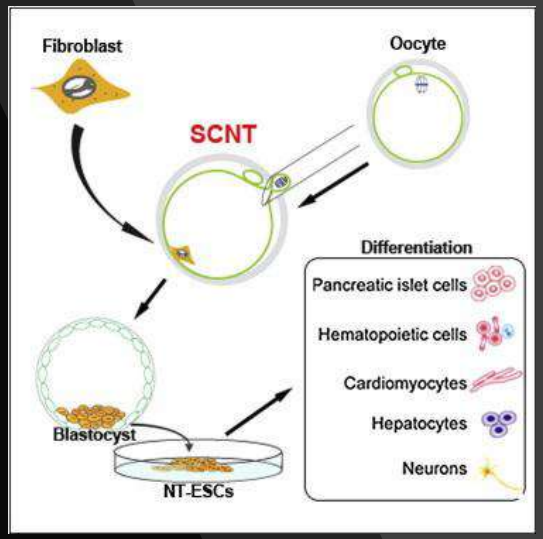


Dezawa M et al. **Muse Cells Provide the Pluripotency of Mesenchymal Stem Cells: Direct Contribution of Muse Cells to Tissue Regeneration.** Cell Transplant. 2016;25(5):849-61.

ABRM – History of Regenerative Medicine

2013: Shoukhrat Mitalipov
(Oregon Health Science University)

- SCNT technique for cloning: NT-ESCs
- Fibroblast nuclear transfer

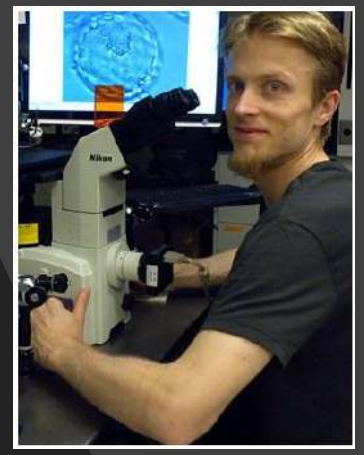


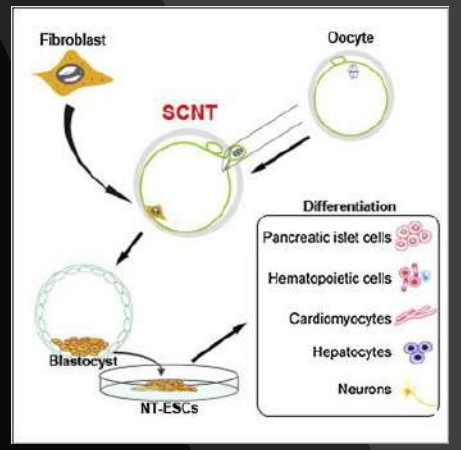
Tachibana M. **Human Embryonic Stem Cells Derived by Somatic Cell Nuclear Transfer. Cell** Volume 153, Issue 6, p1228–1238, 6 June 2013

ABRM – History of Regenerative Medicine

2014: Dieter Egli and Young Gie Chung (NY Stem Cell Foundation, University of Seoul)

- Therapeutic Cloning using SCNT
- HESCs from adult cells
- Egli team uses fibroblasts from diabetic patient and convert to insulin producing beta cells



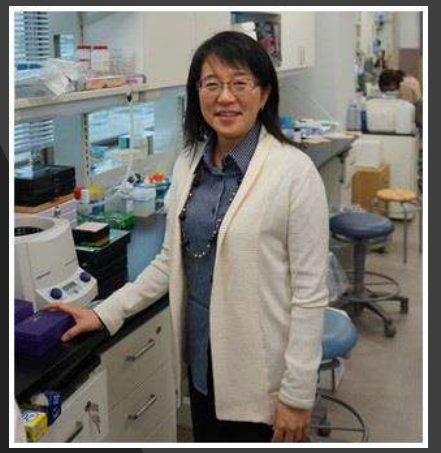


Yamada M. **Human oocytes reprogram adult somatic nuclei of a type 1 diabetic to diploid pluripotent stem cells. Nature 510, 533-536 (26 Jun 2014)**

ABRM – History of Regenerative Medicine

2014: Masayo Takahashi
(Ryken Center for Developmental Biology)

- Retinal Regeneration using retinal pigment iPSCs
- Age related Macular Degeneration
- First patient dosed: September, 2014
- Second patient: genomic mutation in iPSCs
- Trial temporarily on hold, then resumed

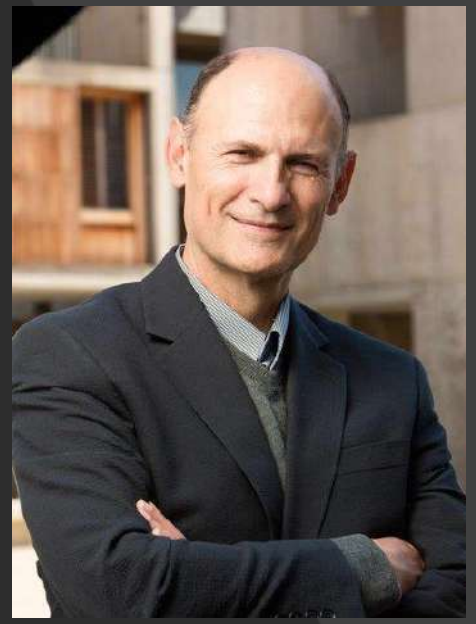


http://www.riken.jp/en/research/labs/cdb/retin_regen/

ABRM – History of Regenerative Medicine

2016: Juan Carlos Izpisua Belmonte (Salk Institute)

- Reversal of cellular and physiologic hallmarks of aging
- Transient expression of cellular reprogramming factors
  - Oct4, Sox2, Klf4, c-Myc
- Intermittent gene activation (cyclic induction)
  - Increase life span (30%)
  - Rejuvenation of mice with progeria
  - No tumorigenesis



Ocampo A, Izpisua Belmonte JC. In Vivo Amelioration of Age-Associated Hallmarks by Partial Reprogramming. Cell. 2016 Dec 15;167(7):1719-1733.e12. doi: 10.1016/j.cell.2016.11.052. PMID: 27984723; PMCID: PMC5679279.

ABRM – History of Regenerative Medicine

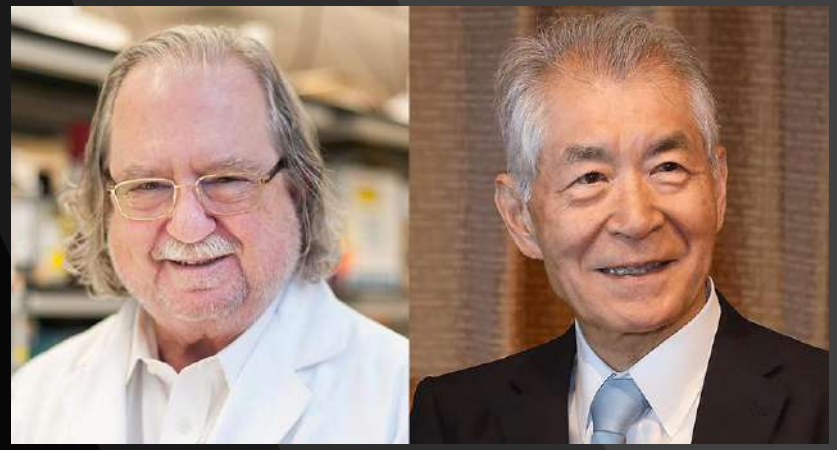
2017: First U.S. FDA approved Gene Therapy product

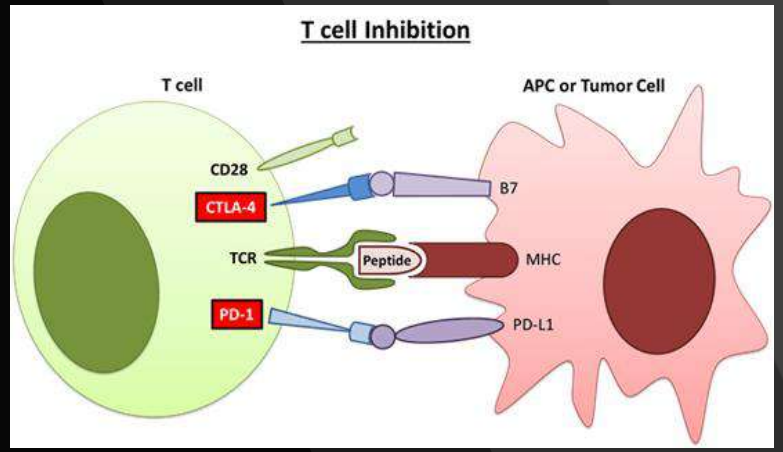
- Kymriah (tisagenlecleucel)
  - Genetically-modified autologous T-cell immunotherapy
- Indication
  - Acute lymphoblastic leukemia (ALL)

ABRM – History of Regenerative Medicine

2018: James P. Allison and Tasuko Honjo
(MD Anderson, Kyoto University)

- Cancer Immunotherapy
- Immune Checkpoint Blockage
  - Ipilimumab (prostate, bladder, NSCCA)
  - Nivolumab (lung)
  - Pembrolizumab (breast, gastric)
  - Atezolizumab (breast, colorectal)
- 2018 Nobel Prize in Physiology



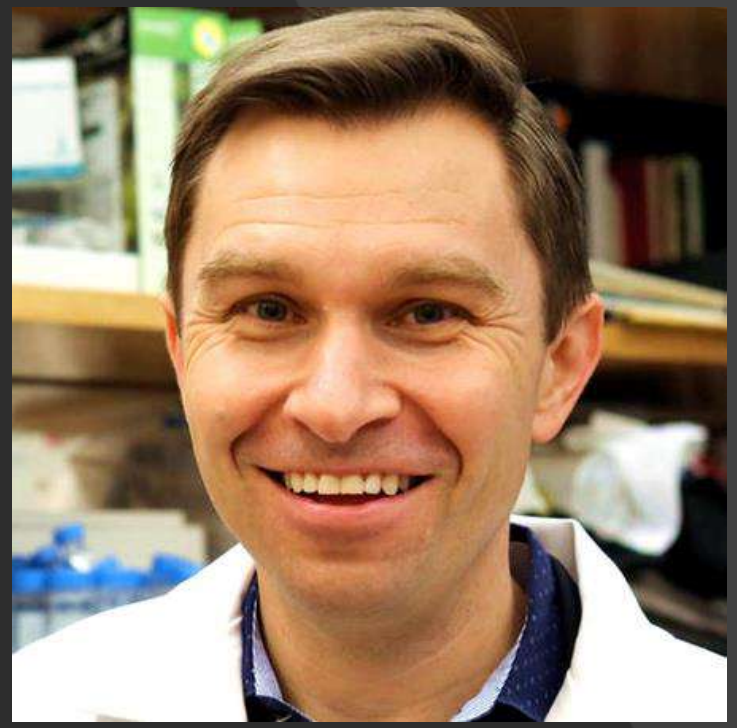


Bernadic M Jr, Duchon R, Aziri R, Mladosievicova B. New principles of cancer therapy give new hope for oncological patients. Bratisl Lek Listy. 2019;120(1):15-18. doi: 10.4149/BLL_2019_002. PMID: 30685987.

ABRM – History of Regenerative Medicine

2019: David Sinclair (Harvard University)

- Partial Cellular Reprogramming
- Combination of three Transcription Factors
  - Oct4, Sox2, Klf4
- Cellular DNA Rejuvenation
- Documented neuronal recovery
  - Murine optic nerve occlusion study



Yang et al., 2023, Cell 186, 1–22 January 19, 2023 ª 2022 Elsevier Inc. https://doi.org/10.1016/j.cell.2022.12.02

ABRM – History of Regenerative Medicine

Stem Cell Clinical Trials (Q3, 2022)

NIH U.S. National Library of Medicine
ClinicalTrials.gov

Phase I

Active: 342

Phase II

Active: 733

Phase III

Active: 147

- Primary Disease Targets:
  - Neurological Disease
  - Cardiovascular Disease
  - Liver Disease
  - Lung Disease
  - Diabetes

ABRM – History of Regenerative Medicine

Gene Therapy Clinical Trials (Q3, 2022)

NIH U.S. National Library of Medicine
ClinicalTrials.gov

Phase I

Active: 264

Phase II

Active: 249

Phase III

Active: 32

- Primary Disease Targets:
  - Myeloma
  - Non-Hodgkins Lymphoma
  - Acute Myelogenous Leukemia
  - B-Cell Lymphoma
  - Ovarian Cancer

ABRM – History of Regenerative Medicine

FDA Approved Stem Cell and Gene Therapy Products (2023)

- Abecma (Idecabtagene vicleucel)
  - Cell-based gene therapy to treat multiple myeloma.
- Adstiladrin (nadofaragene firadenovec-vncg)
  - Gene therapy for the treatment of bladder cancer
- Allocord
  - Hematopoietic Progenitor Cells from Cord Blood
- Breyanzi (lisocabtagene maraleucel)
  - CAR-T cell therapy for B-Cell Lymphoma
- Carvykti (Ciltacabtagene autoleucel)
  - CAR-T cell therapy for Multiple Myeloma
- Clevecord
  - Hematopoietic Progenitor Cells from Cord Blood

ABRM – History of Regenerative Medicine

FDA Approved Stem Cell and Gene Therapy Products (2023)

- Ducord
  - Hematopoietic Progenitor Cells from Cord Blood
- Gintuit
  - Allogeneic Cultured Keratinocytes and Fibroblasts for Mucogingival conditions
- Hemacord
  - Hematopoietic Progenitor Cells from Cord Blood
- Hemegenix (Etranacogene dezaparvovec)
  - Gene therapy used for the treatment of hemophilia B.
- Imlygic (talimogene laherparepvec)
  - Genetically modified oncolytic viral therapy for melanoma
- Kymriah (tisagenlecleucel)
  - CAR T cell treatment for B-cell acute lymphoblastic leukemia

ABRM – History of Regenerative Medicine

FDA Approved Stem Cell and Gene Therapy Products (2023)

- Laviv (azficel)
  - Autologous culture expanded fibroblasts for nasolabial wrinkles
- Luxturna Adenovirus Gene Therapy (Voretigene Neparvovec-rzyl)
  - Gene therapy for Retinal Dystrophy
- MACI
  - Autologous cultured chondrocytes on Porcine Collagen Membrane
- Omisirge (omidubicel-onlv)
  - Nicotinamide-modified allogeneic hematopoietic progenitor cell therapy derived from cord blood
- Provenge (sipuleucel-T)
  - Autologous cell-based cancer immunotherapy for prostate cancer
- Rethymic
  - Allogeneic process thymus tissue for congenital athymia
- Skysona (elivaldogene autotemcel)
  - Autologous gene therapy for cerebral adrenoleukodystrophy

ABRM – History of Regenerative Medicine

FDA Approved Stem Cell and Gene Therapy Products (2023)

- Stratagraft
  - Allogeneic cellularized scaffold product indicated for the treatment of adults with thermal burns
- Tecartus (brexucabtagene autoleucel)
  - Cell-based gene therapy medication for the treatment of mantle cell lymphoma and acute lymphoblastic leukemia
- Vyjuvek (beremagene geperpavec)
  - Gene therapy indicated for the treatment of wounds
- Yescarta (axicabtagene ciloleucel)
  - CAR-T Cell therapy for B-cell lymphoma
- Zynteglo (betibeglogene autotemcel)
  - Gene therapy for beta thalassemia
- Zolgensma (onasemnogene abeparvovec-xioi)
  - Gene therapy to treat spinal muscular atrophy

ABRM – History of Regenerative Medicine

Phases in Regenerative Medicine:

1. Regenerative Medicine 1.0: 1980-2006: Focus on research

2. Regenerative Medicine 2.0: 2006-?: Focus on product development

ABRM Regenerative Medicine Board Certification Review Course

Module I – History of Regenerative Medicine