NASDAQ: FTSV

Forty Seven

Helping Patients Defeat Their Cancer

KOL Breakfast to Discuss Forty Seven´s Expanding Pipeline: Introducing FSI-174 – Anti-cKIT Antibody

22 January 2019

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial condition, results of operations, business strategy and plans, and objectives of management for future operations, as well as statements regarding industry trends, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potentially" "predict," "should," "will" or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: the success, cost and timing of our product development activities and clinical trials; our expectations about the timing of achieving regulatory approval and the cost of our development programs; our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates; the commercialization of our product candidates, if approved; our plans to research, develop and commercialize our product candidates; our ability to attract collaborators with development, regulatory and commercialization expertise; our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates; future agreements with third parties in connection with the commercialization of our product candidates; our ability to maintain, expand, protect and enforce our intellectual property portfolio; our ability to operate our business without infringing, misappropriating or otherwise violating the intellectual property rights of third parties; the size and growth potential of the markets for our product candidates, and our ability to serve those markets; the rate and degree of market acceptance of our product candidates; regulatory developments in the United States and foreign countries; our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately; the success of competing therapies that are or may become available; and our ability to attract and retain key scientific or management personnel. These risks are not exhaustive. New risk factors emerge from time to time and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

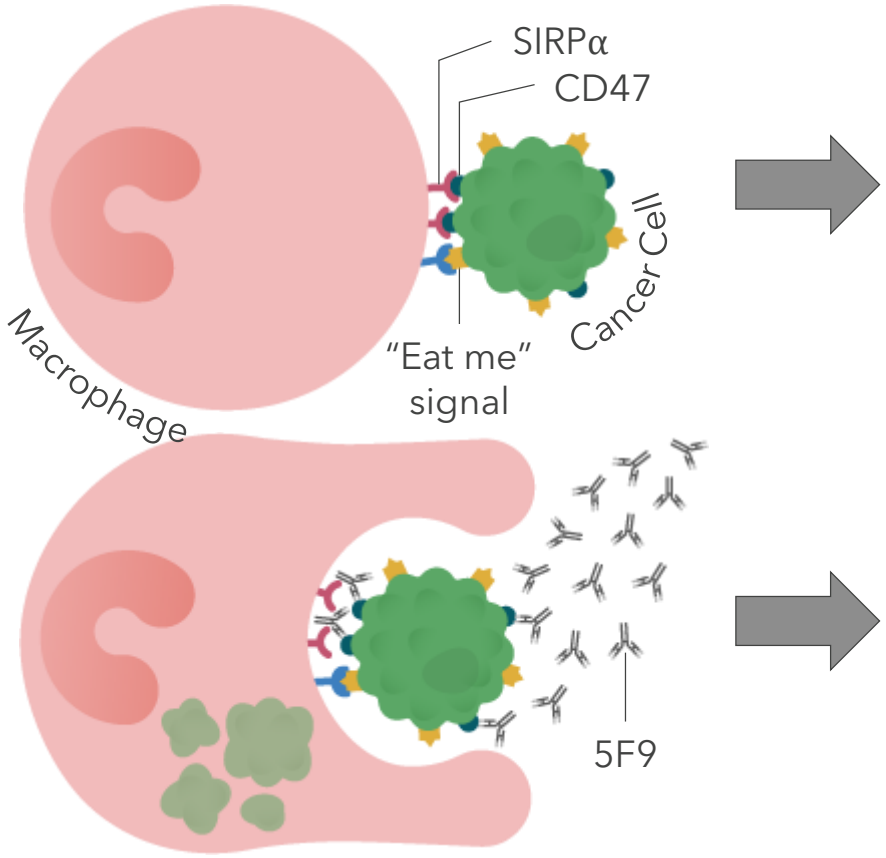
In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

More information about the risks and uncertainties faced by Forty Seven is contained under the caption "Risk Factors" included in the company's periodic filings with the Securities and Exchange Commission at www.sec.gov. Forty Seven disclaims any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

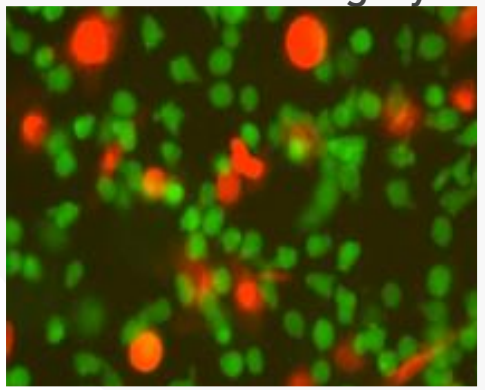
Agenda

○ Welcome and Introduction	Mark McCamish, M.D., Ph.D.
○ History and Broad Vision for the cKIT Program	Irv Weissman, M.D.
○ First Potential Indications for cKIT – Current Landscape and Unmet Medical Need	Maria Grazia Roncarolo, M.D.
○ Forty Seven´s Approach to cKIT	Jens-Peter Volkmer, M.D.
○ Q&A and closing remarks	Mark McCamish, M.D., Ph.D.

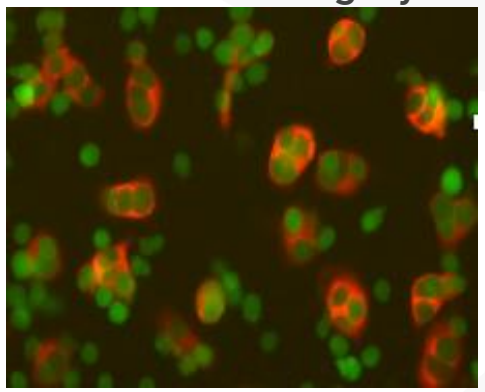
5F9 is a Novel Macrophage Immune Checkpoint Inhibitor Targeting CD47



Control mAb: No Phagocytosis



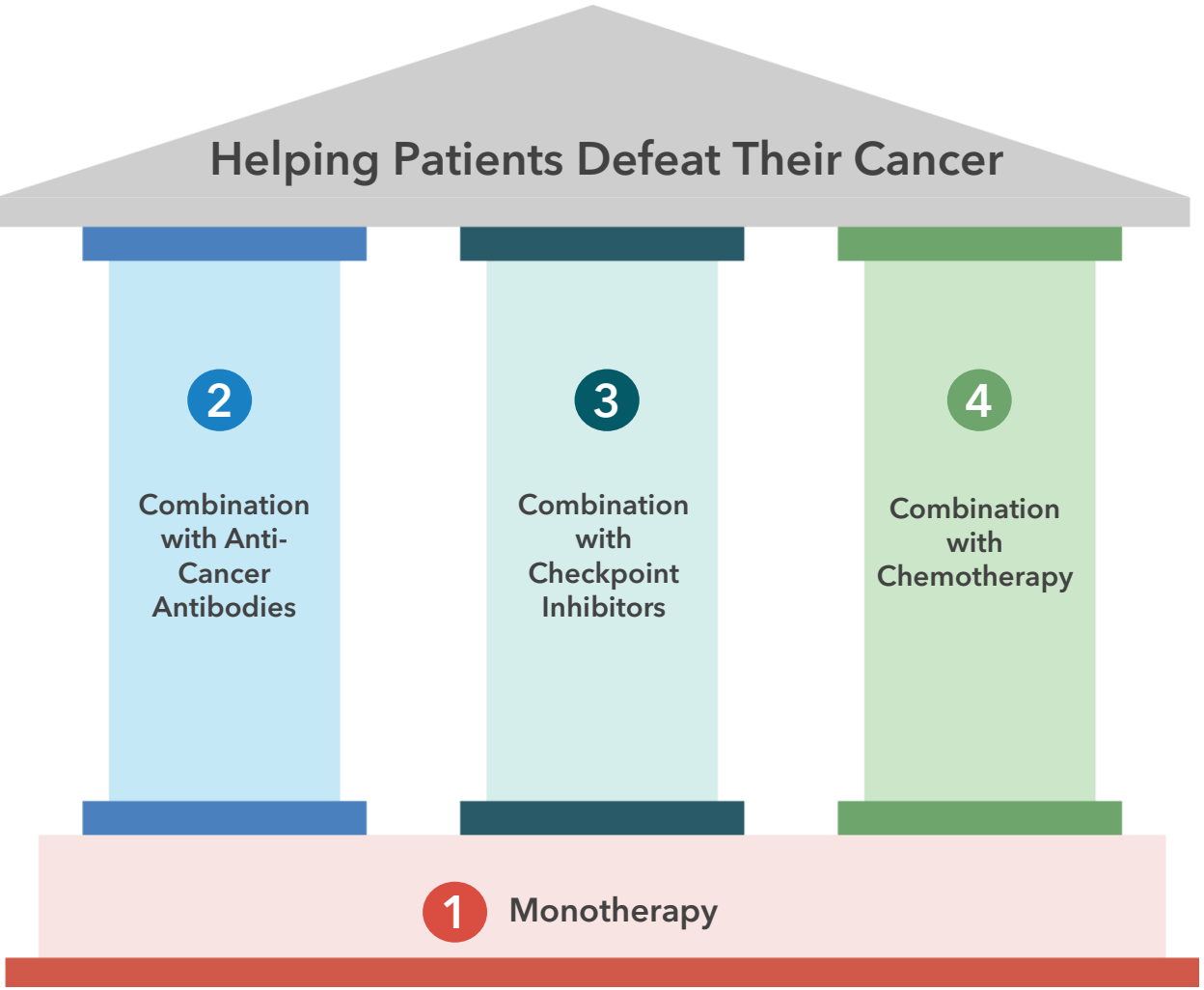
Anti-CD47 mAb: Phagocytosis



Macrophages
Cancer cells

- 5F9 enables macrophages to phagocytose cancer cells by blocking the binding of the "don't eat me" signal CD47 to its receptor SIRPα
- Normal cells are not phagocytosed as they do not express "eat me" signals, except for aged red blood cells
- Additional external "eat me" signals can be provided by cancer-specific antibodies

5F9 Has Applications in Four Treatment Modalities



1 **Monotherapy:**
Proof-of-concept, facilitates phagocytosis and elimination of tumor cells. Provides foundation for combination therapy.

2 **In Combination with Anti-Cancer Antibodies:**
Synergizes with tumor-targeting antibodies in a process called antibody-dependent cellular phagocytosis (ADCP).

3 **In Combination with Checkpoint Inhibitors:**
Enhances T cell activation by cross-presentation of cancer cell antigens and amplifies the efficacy of checkpoint inhibitors.

4 **In Combination with Chemotherapy**
Induction of pro-phagocytic signals on tumor cells by chemotherapy facilitates synergistic phagocytosis.

5F9 Combination With Targeted Antibodies – Rituximab Experience

Phase 1b NHL data published in the New England Journal of Medicine

The NEW ENGLAND JOURNAL of MEDICINE

Original Article

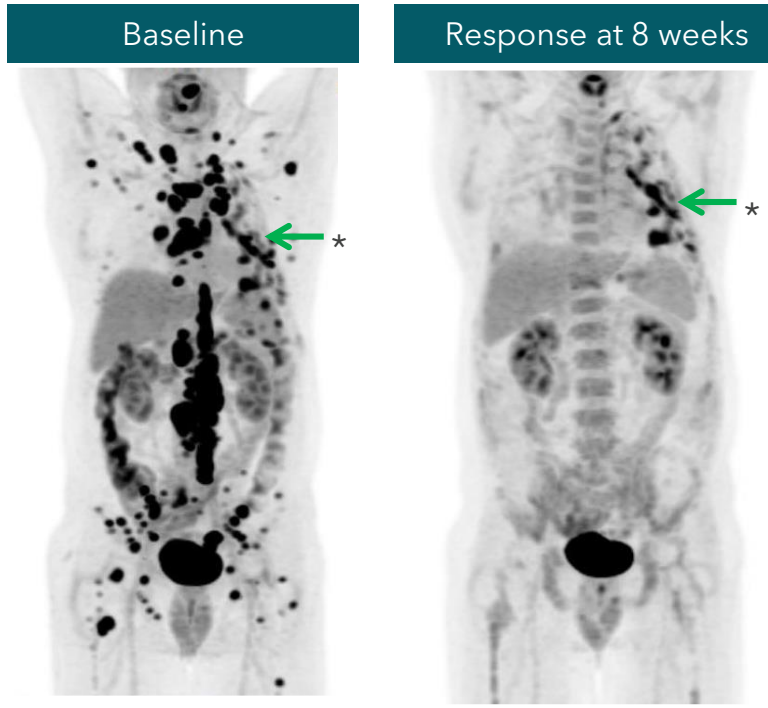
CD47 Blockade by Hu5F9-G4 and Rituximab in Non-Hodgkin's Lymphoma

Ranjana Advani, M.D., Ian Flinn, M.D., Ph.D., Leslie Popplewell, M.D., Andres Forero, M.D., Nancy L. Bartlett, M.D., Nilanjan Ghosh, M.D., Ph.D., Justin Kline, M.D., Mark Roschewski, M.D., Ann LaCasce, M.D., Graham P. Collins, M.D., Thu Tran, B.S., Judith Lynn, M.B.A., B.A., James Y. Chen, M.D., Ph.D., Jens-Peter Volkmer, M.D., Balaji Agoram, Ph.D., Jie Huang, Sc.D., Ravindra Majeti, M.D., Ph.D., Irving L. Weissman, M.D., Chris H. Takimoto, M.D., Ph.D., Mark P. Chao, M.D., Ph.D., and Sonali M. Smith, M.D.

From Stanford University, Stanford (R.A., T.T., R.M., I.L.W.), City of Hope, Duarte (L.P.), and Forty Seven, Menlo Park (J.L., J.Y.C., J.-P.V., B.A., J.H., R.M., I.L.W., C.H.T., M.P.C.) — all in California; Sarah Cannon Research Institute–Tennessee Oncology, Nashville (I.F.); University of Alabama at Birmingham, Birmingham (A.F.); Washington University in St. Louis, St. Louis (N.L.B.); Levine Cancer Institute–Atrium Health, Charlotte, NC (N.G.); University of Chicago, Chicago (J.K., S.M.S.); National Cancer Institute, Rockville, MD (M.R.); Dana–Farber Cancer Institute, Boston (A.L.); and University of Oxford, Oxford, United Kingdom (G.P.C.).

- First clinical publication of a CD47 targeting agent – November 1, 2018

DLBC Patient Treated with 5F9 – Rituximab Antibody Combination



** Hypermetabolic calcified left pleural thickening from prior surgery and not lymphoma*

PET scan

Advani et al., ASCO oral presentation 2018

- 56M with primary refractory DLBCL
- Two prior lines of therapy, bulky disease
- Complete response at 8 weeks

5F9 Monotherapy is Safe and Well-Tolerated

Solid Tumor Summary (n = 73)			
Adverse Event (AE) Term Patients treated at 10 (3 pts), 20 (39 pts), 30 (25 patients), or 45 (6 patients) mg/kg weekly	AE Grade		
	Any	3	4
Anemia	36 (49%)	8 (11%)	0
Hemagglutination	22 (30%)	1 (1%)	0
Hyperbilirubinemia/Blood bilirubin increased	11 (15%)	3 (4%)	0
Thrombocytopenia	9 (12%)	0	0
Neutropenia	2 (3%)	0	0
Lymphopenia/Lymphocyte count decreased	12 (16%)	7 (10%)	3 (4%)
Fatigue	36 (49%)	0	0
Headache	33 (45%)	1 (1%)	0
Chills	28 (38%)	0	0
Pyrexia	26 (36%)	0	0
Infusion-related reaction	16 (22%)	4 (5%)	0
Nausea	13 (18%)	0	0
Photopsia	7 (10%)	0	0
Back pain	7 (10%)	1 (1%)	0
Myalgia	7 (10%)	0	0
AST elevation	4 (5%)	1 (1%)	1 (1%)
ALT elevation	4 (5%)	0	1 (1%)

AEs observed in ≥ 10% or selected for clinical interest; Data cutoff 24 Jul 2018

Key Points:

- Expected red blood cell findings are easy to manage using a priming dose regimen*
- Well tolerated at high and extended exposures
- 5F9 AE profile comparable as monotherapy or in combination
- MTD not reached with dose escalation up to 45 mg/kg and >250 patients treated as monotherapy or in combination

** Dose-regimen proprietary to Forty Seven, Inc.*

Catalyst Events Expected in 2019 – 2020

	Indication (Study Stage)	Therapy	Presented	Projected				
			2018	Q1 2019	Q2 2019	Q3 2019	Q4 2019	2020
Monotherapy	Solid Tumor (Phase 1)	5F9	**ASCO:** Safety + Ovarian Initial Efficacy					
	Acute Myeloid Leukemia (Phase 1)	5F9	**EHA:** Monotherapy Safety					
Combination with Cancer-Specific Antibodies	Non-Hodgkin's Lymphoma (Phase 1b/2)	5F9 + rituximab	**ASCO:** Phase 1b Safety + Efficacy			Phase 2 Efficacy (DLBCL & Indolent Lymphoma)		
	Colorectal Cancer (Phase 1b/2)	5F9 + cetuximab					Phase 1b Safety + Phase 2 Efficacy	
Combination with Checkpoint Inhibitors	Ovarian Cancer (Phase 1b)	5F9 + avelumab					Phase 1b Safety + Efficacy	
	Bladder Cancer (Phase 1b)	5F9+ atezolizumab						Phase 1b Safety + Efficacy
	Acute Myeloid Leukemia (Phase 1b)	5F9+ atezolizumab						Phase 1b Safety + Efficacy
Combination with Chemotherapy	Acute Myeloid Leukemia/ Myelodysplastic Syndrome (Phase 1b)	5F9+ azacitidine				Phase 1b Safety + Efficacy		

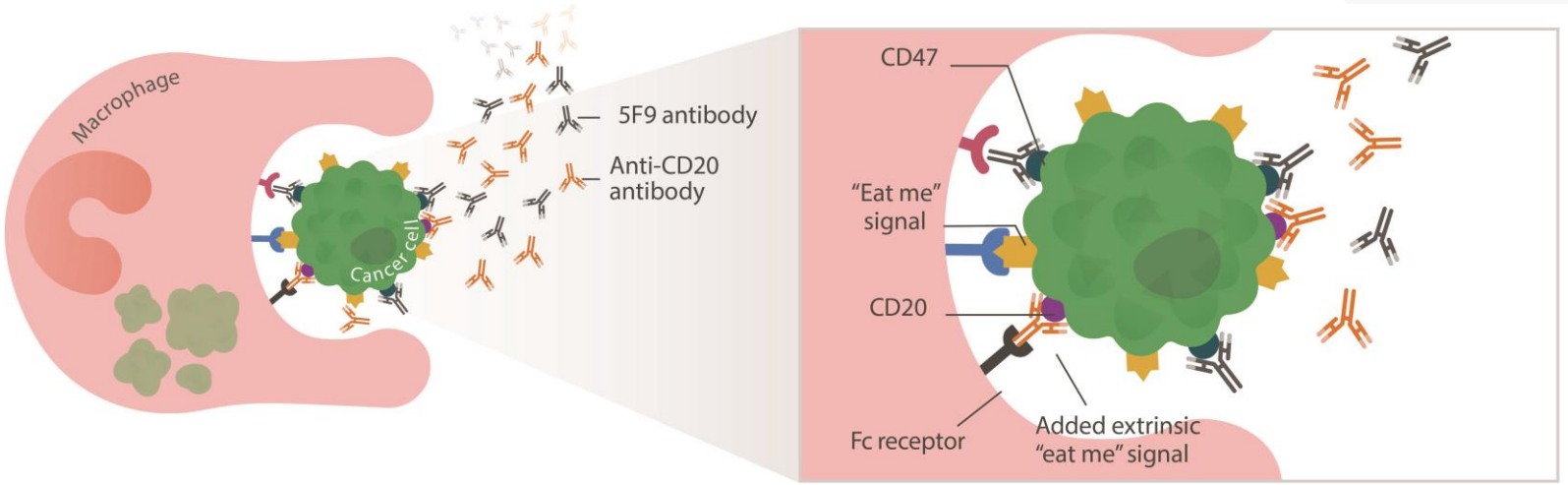
ASCO – American Society of Clinical Oncology; EHA – European Hematology Association

Our Pipeline

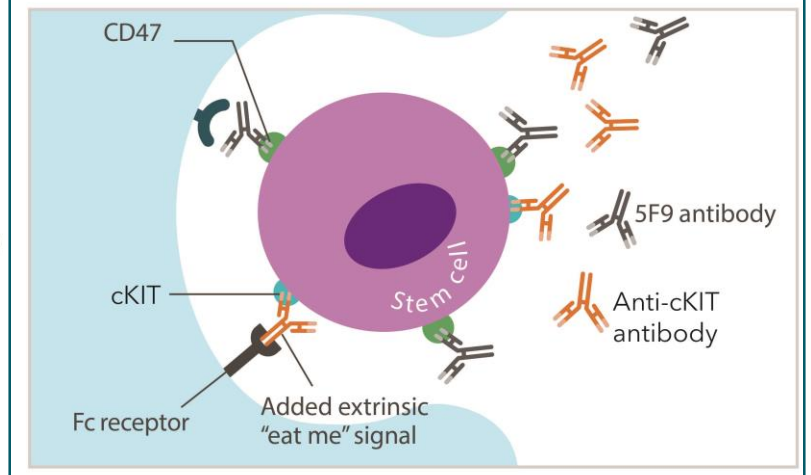
Drug Candidate/Focus		Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Worldwide Rights
5F9 Anti-CD47 Antibody	Monotherapy	Solid Tumor & Ovarian					FortySeven
		AML Mono and Combo: Azacitidine					
	Tumor Targeting Antibody Combinations	NHL Combo: Rituximab					
		CRC Combo: Cetuximab					
	T Cell Checkpoint Inhibitor Combinations	Ovarian: Avelumab					
		Bladder: Atezolizumab					
		AML: Atezolizumab					
FSI-189 Anti-SIRPα Antibody		Solid Tumor					FortySeven
FSI-174 Anti-cKIT Antibody		HSC/Bone Marrow Transplant					FortySeven

5F9 Antibody Combination With Targeted Antibodies – Expanding the Experience with Rituximab to cKIT Antibodies

5F9 + Rituximab



5F9 + cKIT Antibody



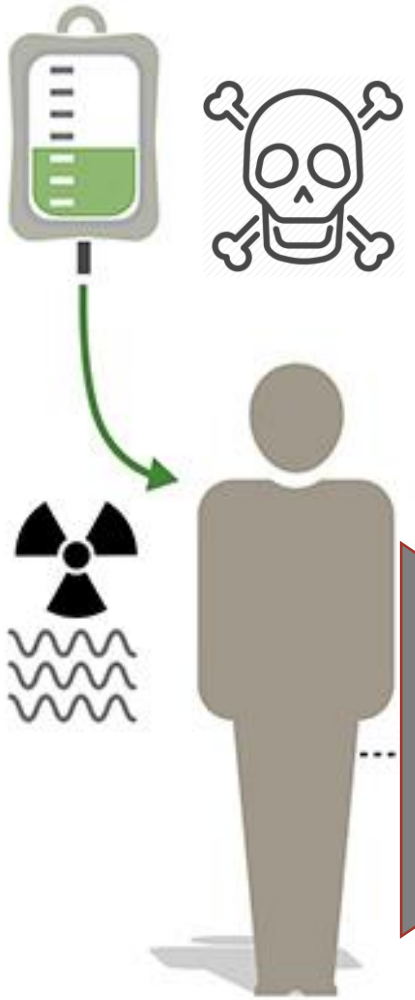
- Combination of 5F9 with targeted Abs, i.e. rituximab (anti-CD20) - enhances phagocytosis of cancer cells
- Hematopoietic stem cells and cancer cells, i.e. AML, MDS, express cKIT and combination of a cKIT Ab with 5F9 can enhance phagocytosis of these cells

Hematopoietic Stem Cell Transplantation - Procedure

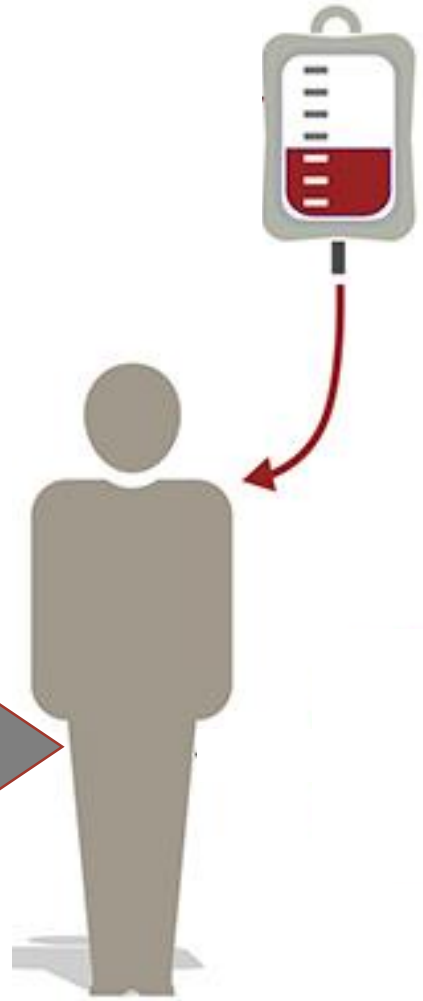
Conditioning

Procedure:
Killing of endogenous hematopoietic stem cells with chemo and/or radiation therapy to make space for transplant cells

Problem/Barrier:
Very toxic procedure that often requires prolonged hospitalization and causes collateral damage to normal tissues resulting in infertility or secondary malignancies



Transplantation



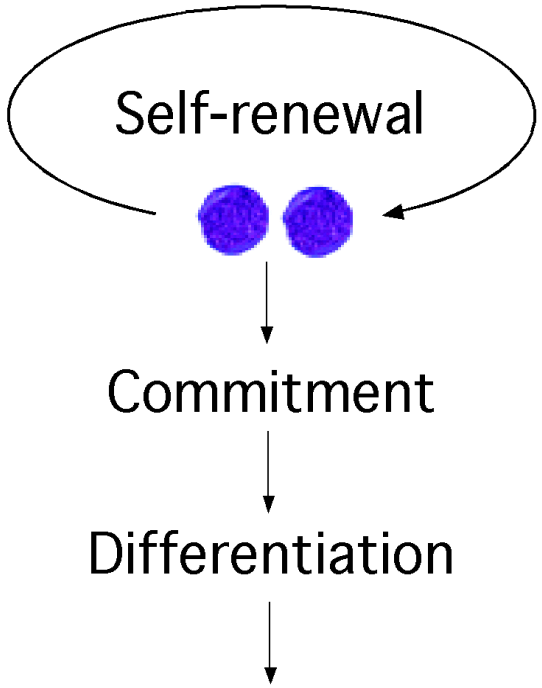
Allogeneic Stem Cells:
Hematopoietic stem cells from healthy donor

Autologous Stem Cells :
Patients' own stem cells with or without gene therapy correction

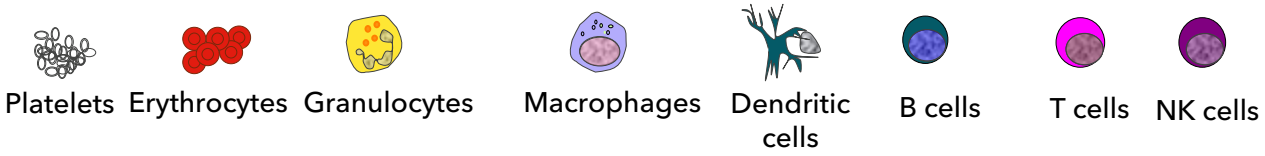
cKIT – CD47/SIRPα Opportunities

Irv Weissman, M.D.
Founder, Forty Seven, Inc.,
Director of the Institute of Stem Cell Biology &
Regenerative Medicine, Stanford University

Hematopoietic Stem Cells - Blood-Forming Stem Cells



1. **Development**
2. **Maintenance**
3. **Malignant transformation and blood diseases**



- Hematopoietic stem cells have unlimited self-renewal capacity and give rise to all blood cells
- Hematopoietic stem cells make only blood cells
- First isolation of hematopoietic stem cells in mice in 1988[1] and in humans in 1992[2]
- Malignant transformations of hematopoietic stem or progenitor cells result in blood malignancies, i.e. leukemia

(1) Spangrude, Weissman, Science 1988
(2) Baum, Weissman, Peault, PNAS 1992

Transplantation of Purified Hematopoietic Stem Cells

Isolation and Transplantation of Purified Hematopoietic Stem Cells

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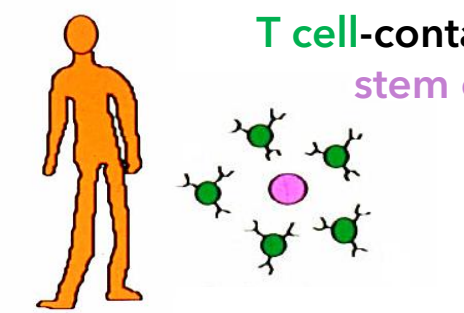
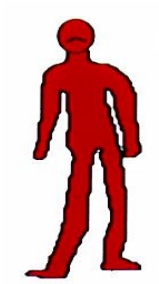
Transplantation of Bone Marrow or Mobilized Peripheral Blood



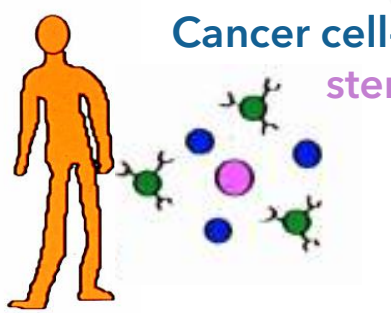
T cell-contaminated stem cells

Graft vs Host Disease



- Dependent on Immunosuppressants
- Risk of Infections

Transplantation of Bone Marrow or Mobilized Peripheral Blood

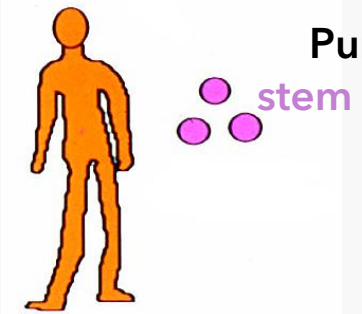


Cancer cell-contaminated stem cells

Cancer Relapse

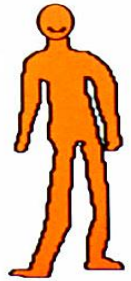
- Re-transplantation of cancer cells
- Cancer relapse

Transplantation of Purified Hematopoietic Stem Cells



Pure stem cells

Healthy



- Donor blood-forming and immune system
- Induction of permanent transplant tolerance
- Cancer-free blood regeneration
- Reverse autoimmune disease

Indications for Hematopoietic Stem Cell Transplantation

Indications for Hematopoietic Stem Cell Transplantation

- **Non-malignant diseases of the blood systems** (***in combination with gene therapy or healthy donor stem cells***)**:** Sickle cell disease, thalassemia (Mediterranean anemia), severe combined immunodeficiency (SCID)

- **Autoimmune diseases:** Juvenile diabetes, systemic lupus erythematosus, multiple sclerosis, juvenile and adult rheumatoid arthritis

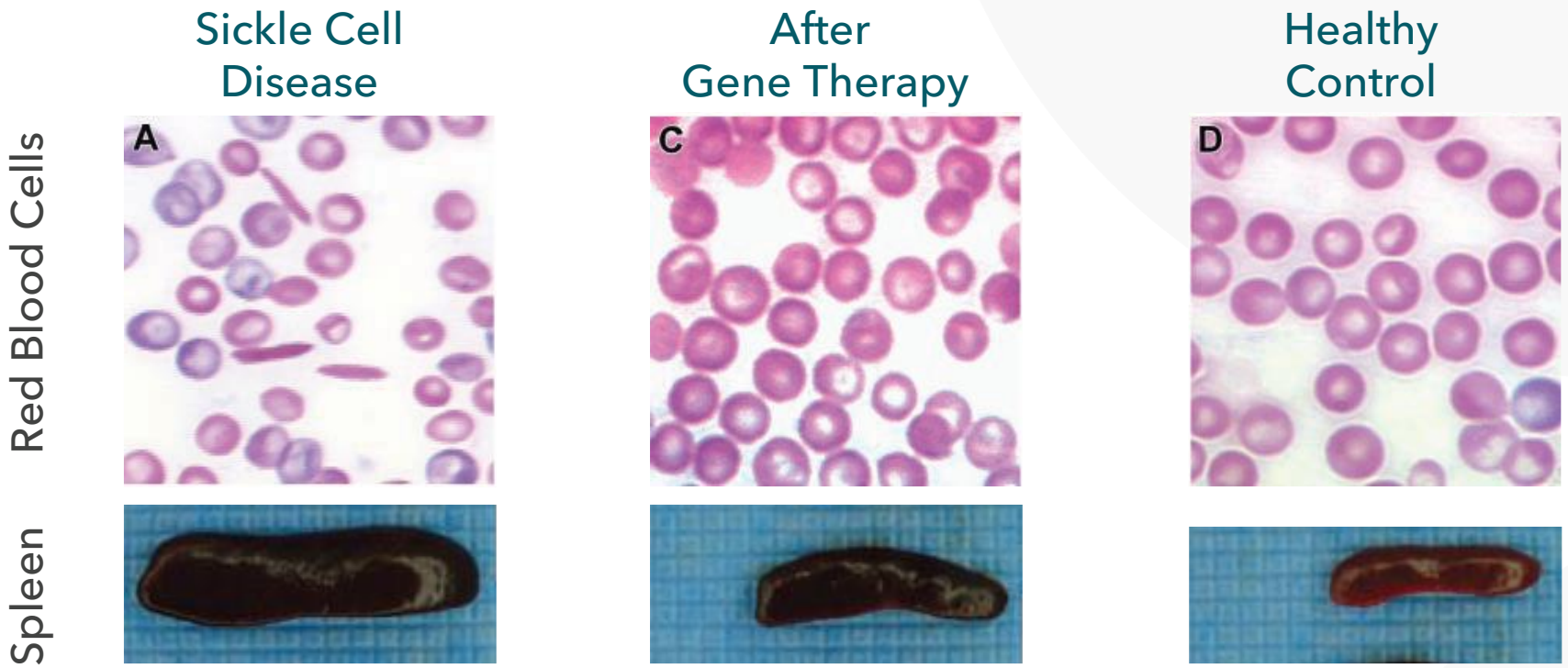
- **Organ transplantation** (by inducing tolerance): liver, kidney, heart, lung, pancreas, intestine in combination with hematopoietic stem cells from the same donor

- **Malignancies**: leukemia, lymphoma, myelodysplastic syndrome (MDS)

- BUT THE CHEMO AND RADIATION CURRENTLY BEING USED FOR CONDITIONING ARE LETHAL AND BRINGS HIGH MORBIDITY AND MORTALITY AND LIMITS ITS USE IN THESE PATIENTS

Hematopoietic Stem Cell Transplantation for Gene Therapy

Transplantation of Hematopoietic Stem Cells After Gene Therapy Correction for Sickle Cell Disease

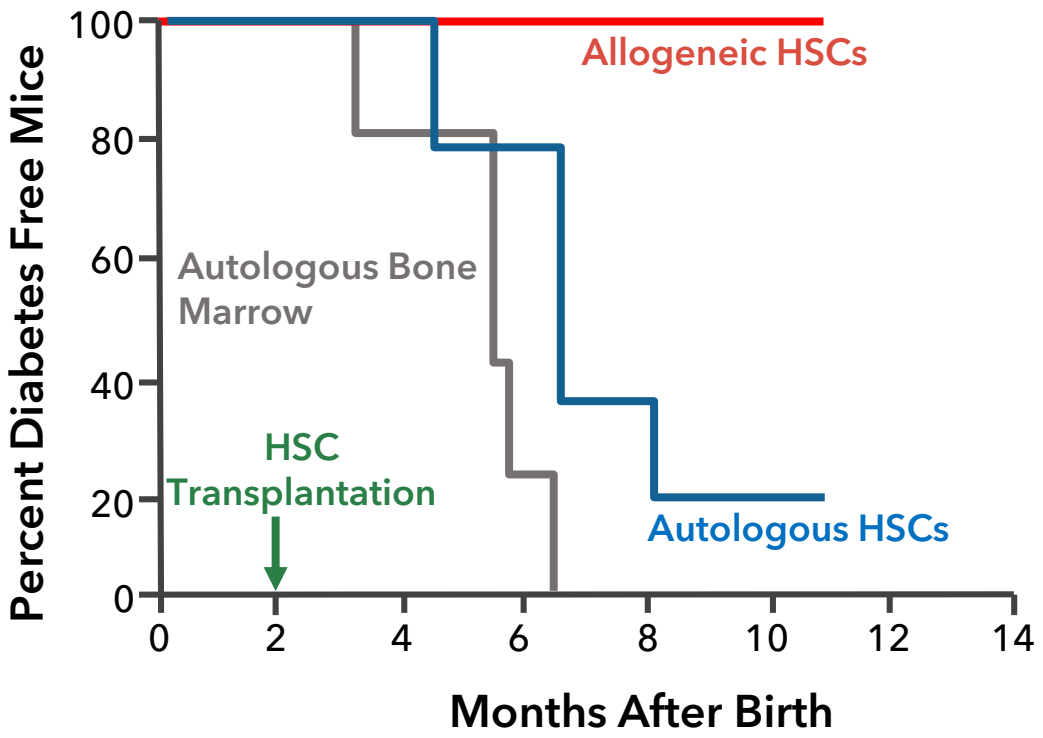


Levasseur, Roncarolo, Townes, 2003

Transplantation of hematopoietic stem cells that have been corrected with gene therapy can overcome genetic blood diseases such as sickle cell disease

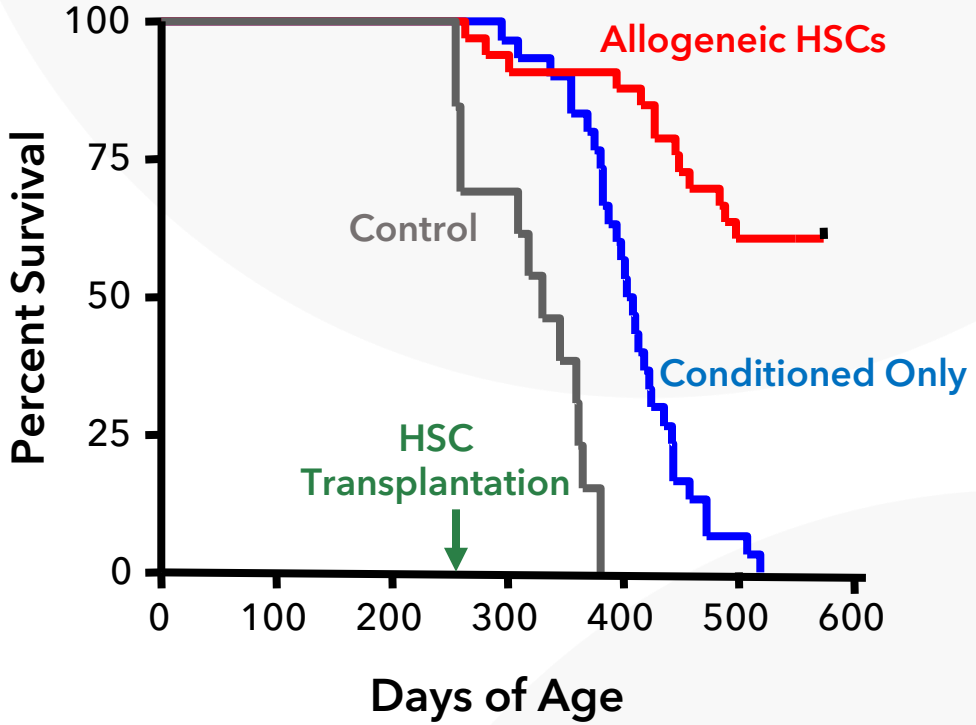
Hematopoietic Stem Cell Transplantation for Autoimmune Diseases

Transplantation of Allogeneic Hematopoietic Stem Cells and Islet Cells in Diabetes Mouse Model



Beilhack, Weissman, Shizuru, Diabetes 2003

Transplantation of Allogeneic Hematopoietic Stem Cells in Lupus Erythematosus Mouse Model



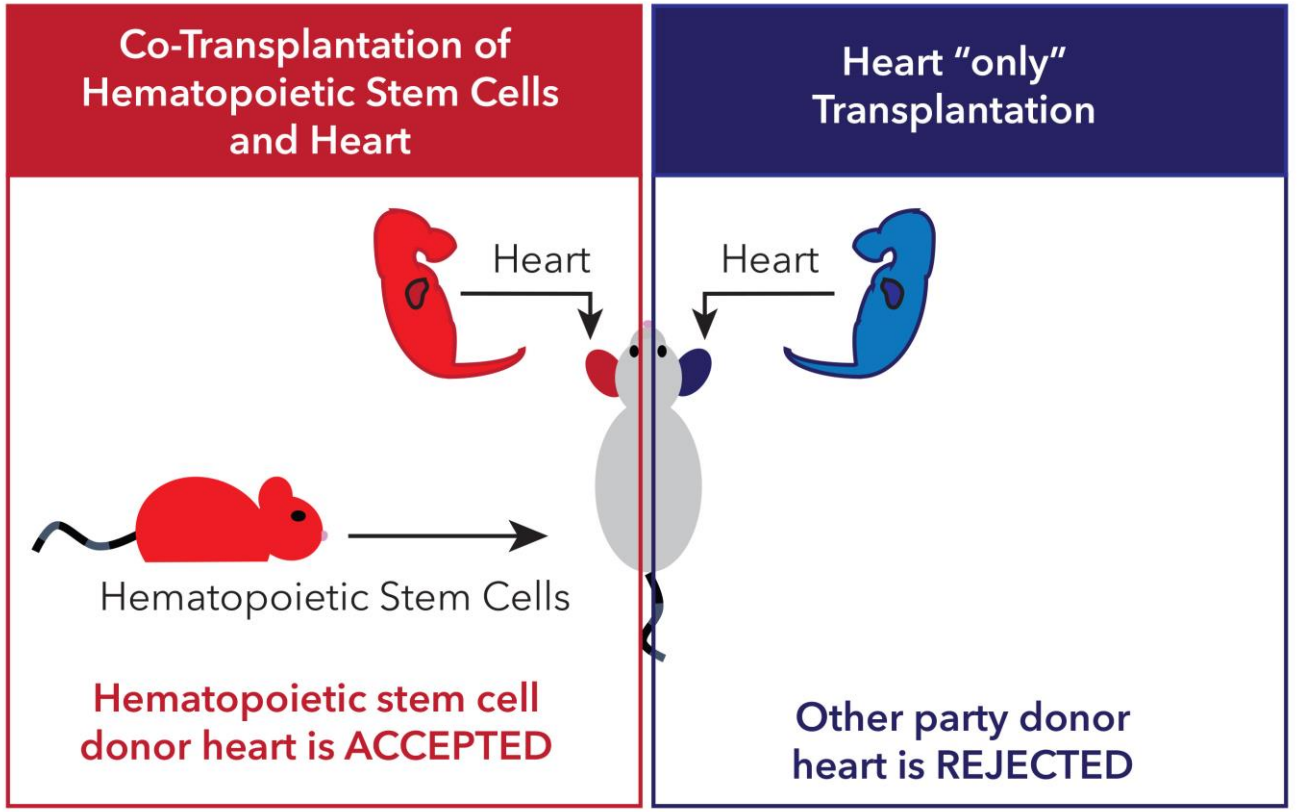
Smith-Berdan, Weissman, Christensen, Blood 2007

Transplantation of hematopoietic stem cells can overcome (cure) autoimmune diseases

- Conditioning regimen depletes autoreactive (disease-triggering) immune cells
- Transplanted hematopoietic stem cells give rise to non-autoreactive (new and healthy) immune cells

Hematopoietic Stem Cell Transplantation for Organ Transplantation

Co-Transplantation of Hematopoietic Stem Cells and Heart From the Same Donor Generates Immune Tolerance to the Transplanted Heart in Mouse Models



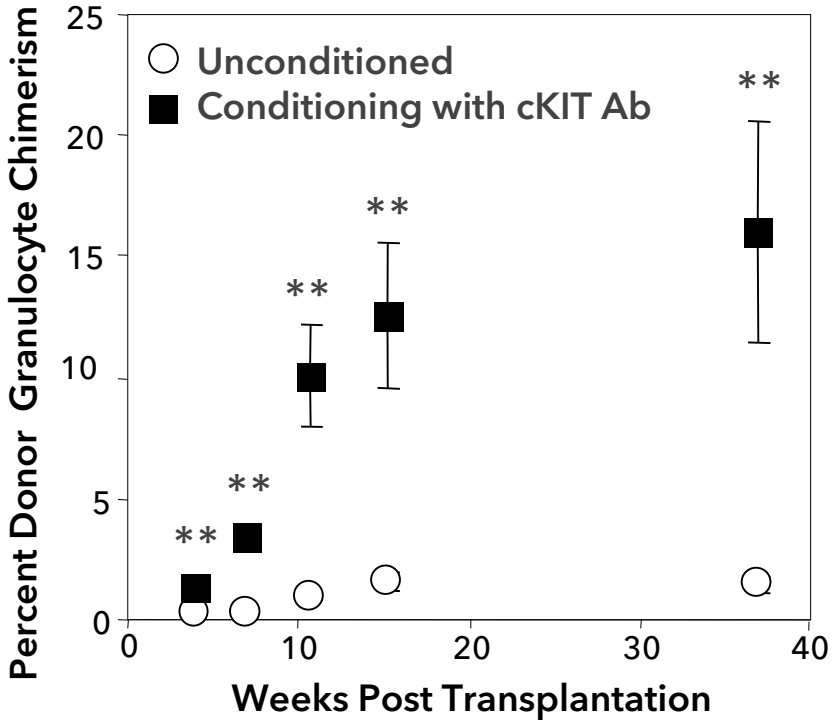
Weissman, Shizuru, Blood 2007

Co-transplantation of donor hematopoietic stem cells generates immune tolerance and allows organ transplantation - heart, kidney, pancreas - without the need for continued immune suppression

cKIT – CD47/SIRPα Antibody-Based Conditioning Regimen for Hematopoietic Stem Cell Transplantation

cKIT Antibody-Mediated Transplantation of Hematopoietic Stem Cells

Blood Cell Chimerism After cKIT Antibody-Mediated Hematopoietic Stem Cell Transplantation

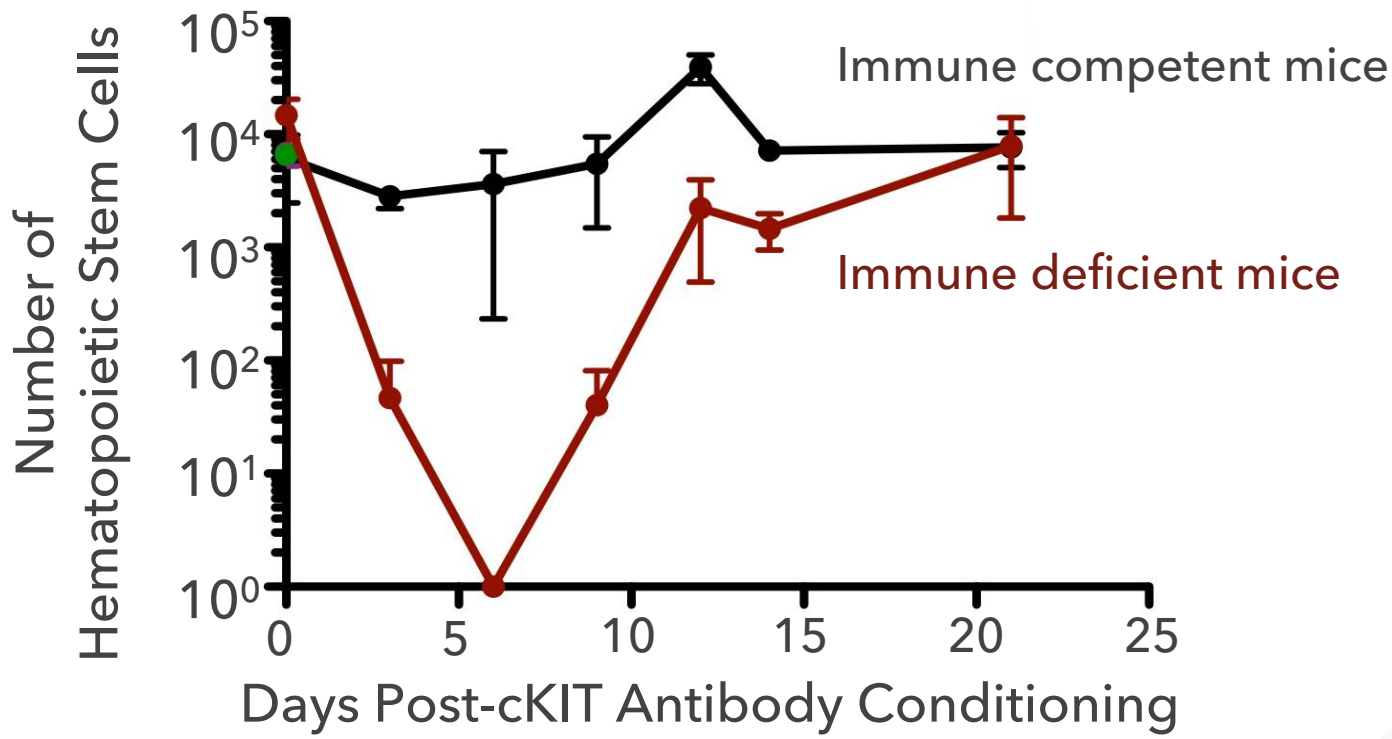


Czechowicz, Bhattacharya, Kraft, IW; Science 2007

- cKIT is expressed on hematopoietic stem cells
- cKIT antibody blocks stem cell factor signaling
- cKIT antibody mediates depletion of endogenous hematopoietic stem cells and enables stem cell transplantation in immune-deficient mice
- *Clinical trial in patients with immune deficiency (SCID- severe combined immune deficiency) ongoing at Stanford University*

cKIT Antibody-Mediated Depletion of Hematopoietic Stem Cells

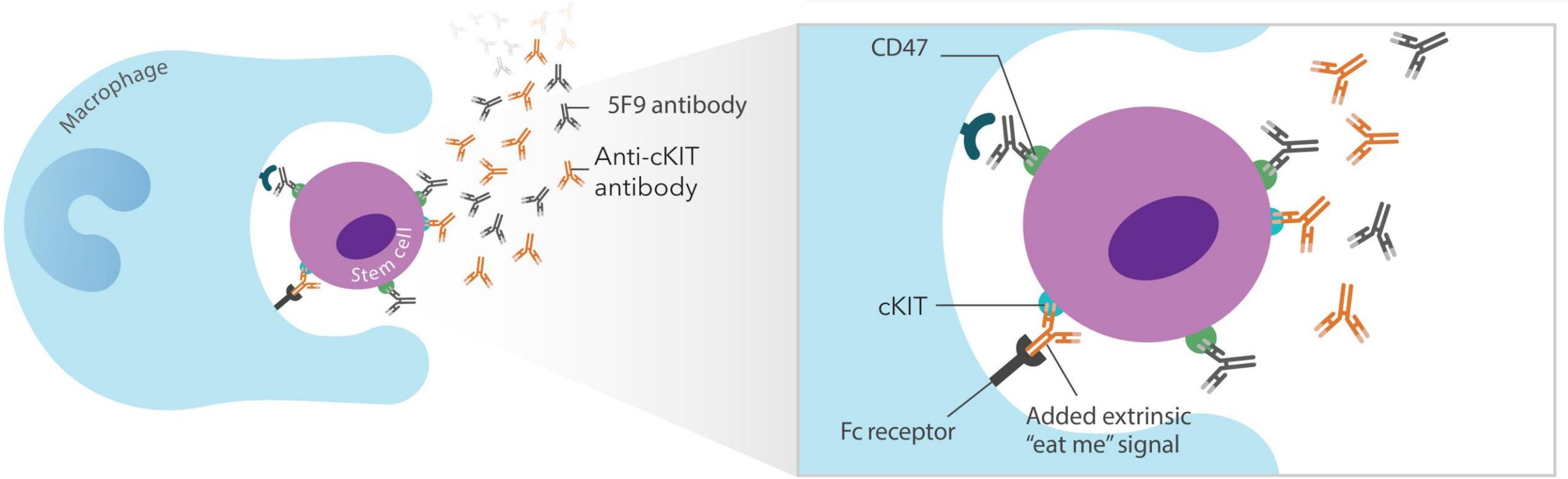
Hematopoietic Stem Cell Depletion With cKIT Antibody



Czechowicz, Bhattacharya, Kraft, IW

cKIT antibody depletes hematopoietic stem cells in immune deficient, but not immune competent, mice

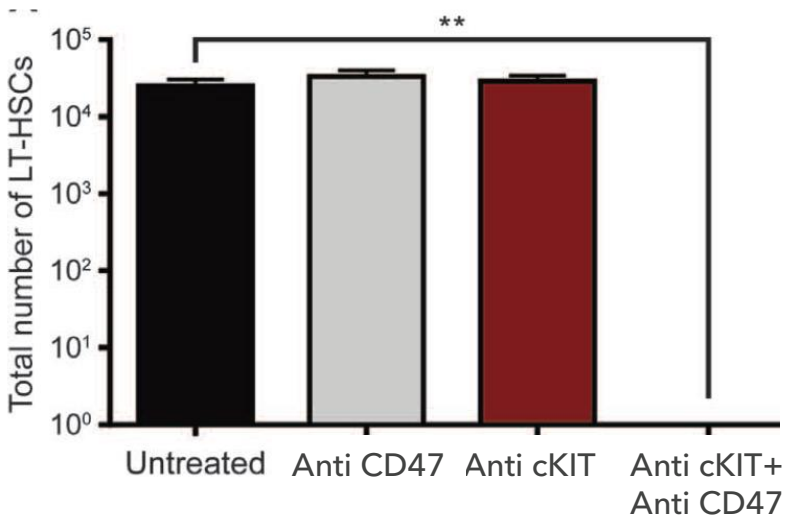
Anti-CD47 Antibody Combination With Anti-cKIT Antibody

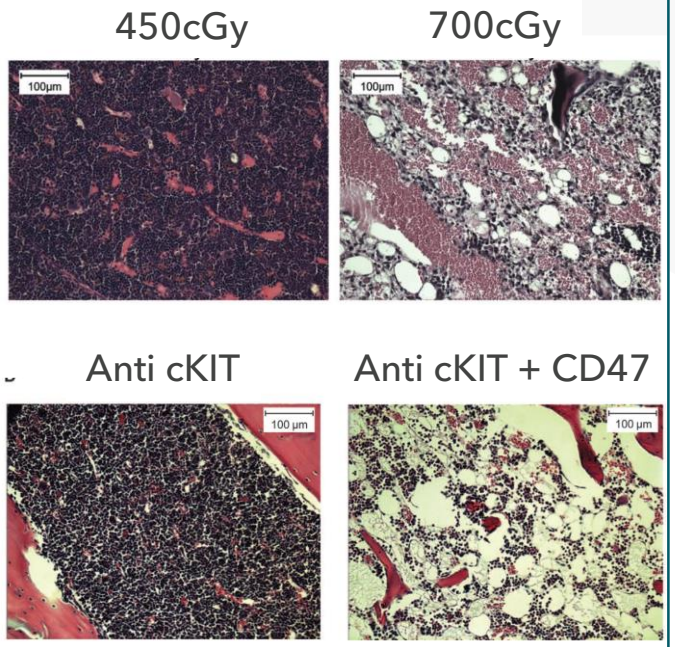


Combination of anti-CD47/SIRPα Ab with targeted Abs - anti-CD20 or cKIT Ab - enhances phagocytosis of target cells – cancer or hematopoietic stem cells - by macrophages

Preclinical Proof of Concept for cKIT-CD47/SIRPα Antibody-Based Conditioning Regimen in Autologous HSC Transplantation

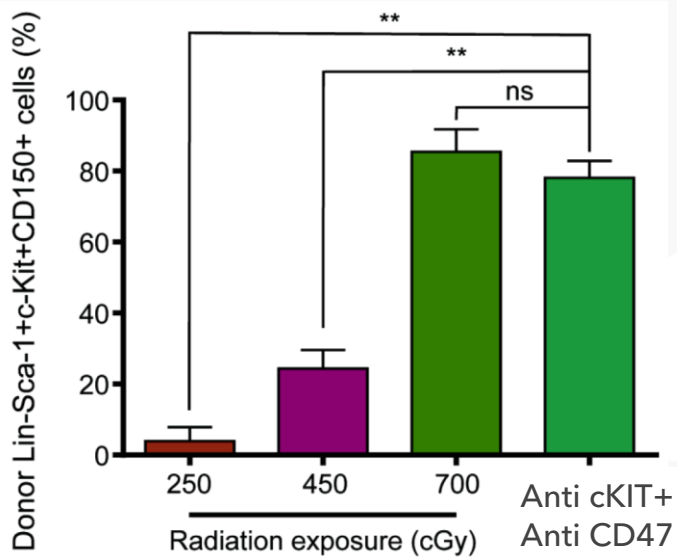
HSC Depletion in Bone Marrow 7 Days After Conditioning





Chhabra, Weissman, Shizuru, STM 2016

HSC Chimerism 24 Weeks After Transplantation

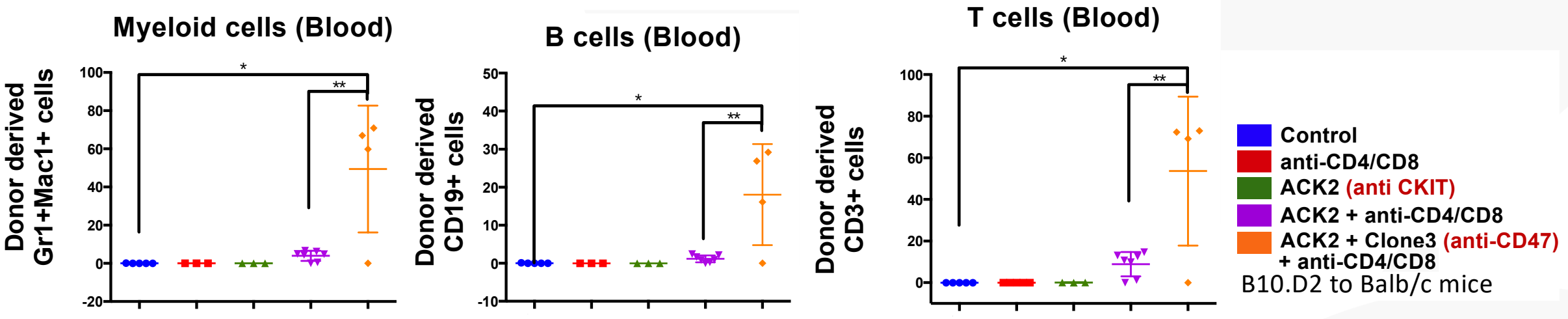


Chhabra, Weissman, Shizuru, STM 2016

- Conditioning with a combination of cKIT + CD47/SIRPα antibodies (but not single cKIT antibody) depletes endogenous hematopoietic stem cells (HSCs) from the bone marrow and enables HSC transplantation comparable to high dose radiation

Preclinical Proof of Concept for cKIT-CD47/SIRPα All Antibody-Based Conditioning Regimen in Allogeneic HSC Transplantation

Multi-Blood Cell Lineage Chimerism After Allogeneic Hematopoietic Stem Cell Transplantation with All Antibody-Based Conditioning Regimen

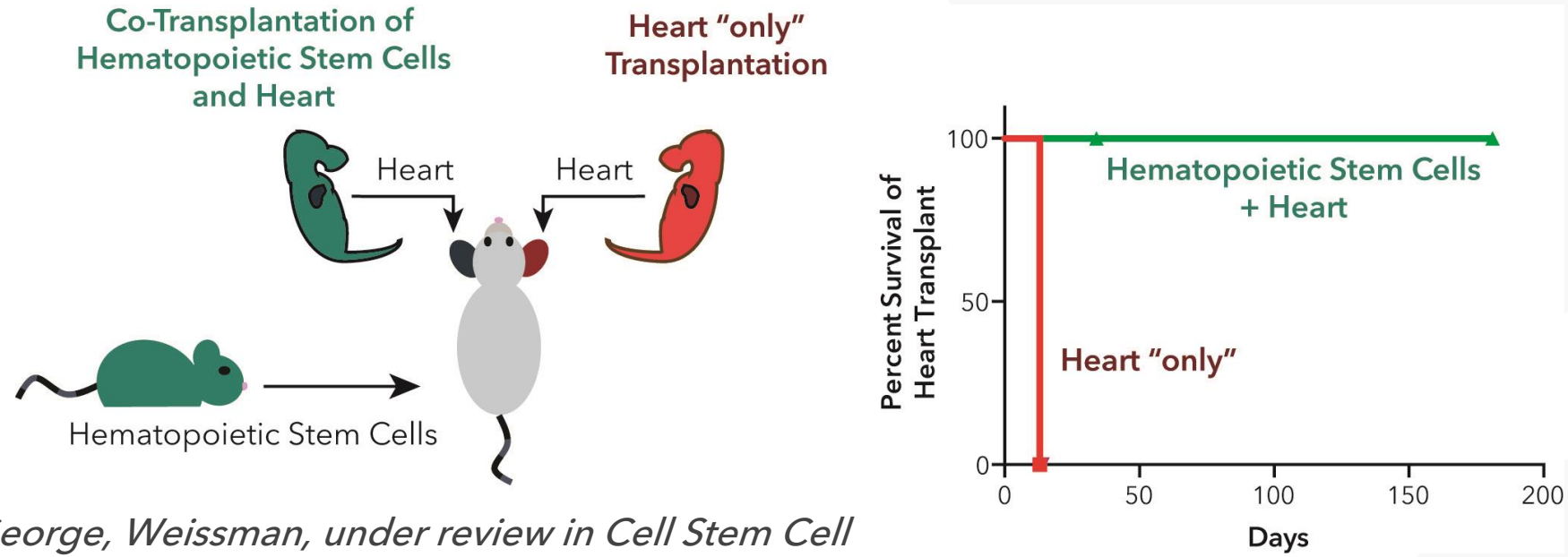


Chhabra, Weissman, Shizuru, STM 2016

Successful allogeneic transplantation of hematopoietic stem cells with cKIT + CD47/SIRPα and T cell all antibody-based conditioning regimen without the need for immune suppression

Preclinical Proof of Concept for cKIT-CD47/SIRPα All Antibody-Based Conditioning Regimen in Allogeneic HSC and Organ Co-Transplantation

Anti-cKIT-CD47/SIRPα and Anti-T Cell All Antibody-Based Conditioning Regimen Enables Hematopoietic and Organ Transplantation with Immune Suppression



George, Weissman, under review in Cell Stem Cell

Successful co-transplantation of hematopoietic stem cells and heart with cKIT + CD47/SIRPα and anti-T cell all antibody-based conditioning regimen without the need for immune suppression

Summary

- Transplantation of hematopoietic stem cells may:
  - Cure genetic blood diseases (in combination with gene therapy), i.e. sickle cell disease
  - Cure autoimmune diseases by generating a new, healthy immune cell pool
  - Enable organ transplantation without need for chronic immune suppression by creating a new immune cell pool that is tolerant to the transplanted organ

- Transplantation of purified hematopoietic stem cells can prevent graft vs host disease and cancer relapse

- **cKIT-CD47/SIRPα all antibody-based conditioning regimens *can replace radiation- and chemo-based toxic regimens* and overcome barriers to transplantation and gene therapies**

Potential cKIT Targets and Market Opportunity

Maria Grazia Roncarolo, M.D.

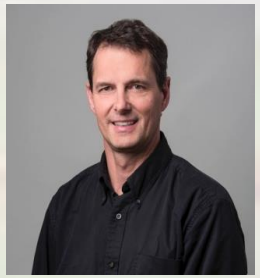
Chief of the Division of Pediatric Stem Cell Transplantation and Regenerative Medicine, Stanford University

Stanford Translational Research Program
In Stem Cell and Gene Therapy

CENTER FOR DEFINITIVE AND CURATIVE MEDICINE (*CDCM*)

"Curing the Incurable"

Maria-Grazia Roncarolo, MD
Professor of Pediatrics and Medicine
Director, Center for Definitive and Curative Medicine



Matthew Porteus, MD/PhD
Professor of Pediatrics
Co-Director, Center for Definitive and Curative Medicine

Anthony Oro, MD/PhD
Eugene and Gloria Bauer Professor of Dermatology
Co-Director, Center for Definitive and Curative Medicine

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The *CDCM* bridges the divide between laboratory discovery and translation to patients in clinical trials

Stem Cell Therapies are powerful new modalities with potential to cure

STEM CELLS AND GENES AS DRUGS
to cure genetic diseases, cancer, metabolic neurodegenerative and autoimmune diseases and other incurable diseases

STEM CELL THERAPY

- **Use of healthy donor stem cells to treat** or prevent a disease or condition

GENE THERAPY

- **Introduction of DNA/genes into patient's stem cells to treat** or prevent a disease or condition

REGENERATIVE MEDICINE

- **Use of IPS/ES derived stem cells to regenerate/replace tissues or organs** to prevent or treat a disease or condition

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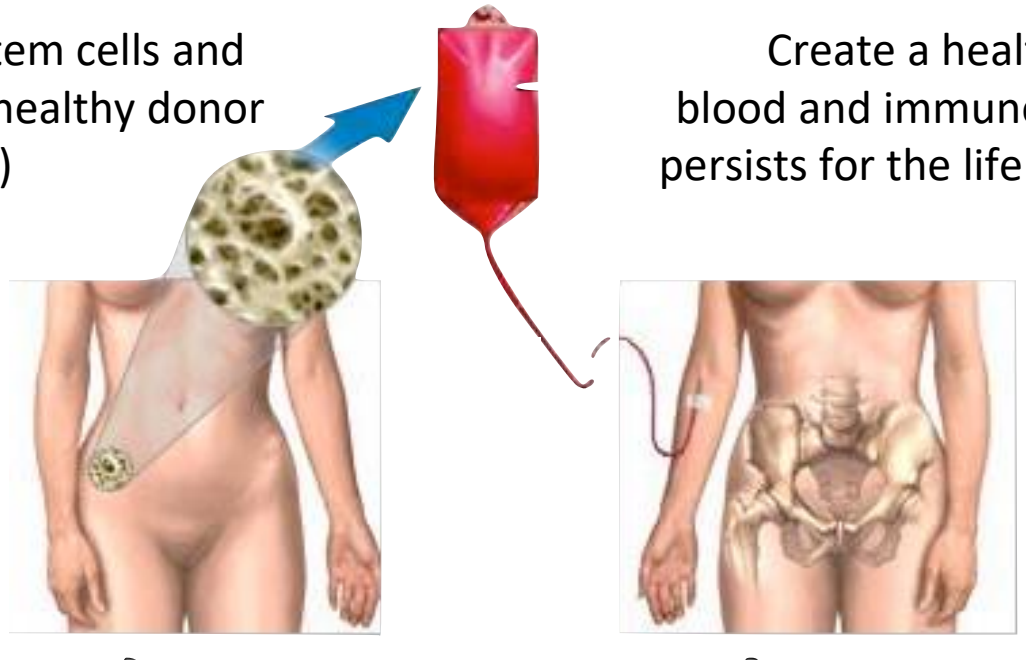
Hematopoietic Stem Cell Transplantation

Unique procedure that allows us to **cure** blood and immune diseases

Utilize healthy blood stem cells and progenitor cells from a healthy donor (allogeneic)



Create a healthy, new blood and immune system that persists for the life of the patient

Has been performed for 60+ years
with over >1,000,000 patients treated to date

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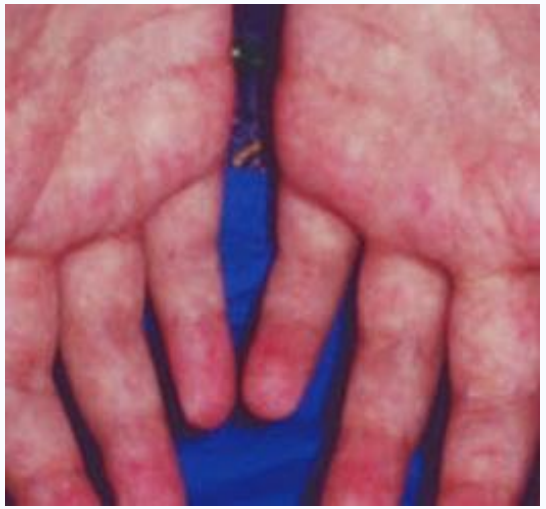
HSCT also carries considerable risk

Main Toxicities:

Serious Infections

Graft vs. Host Disease



Gross Tissue Damage

Clinical use currently limited to states of extreme desperation

Only a fraction of patients who could benefit get transplanted (< 10%)

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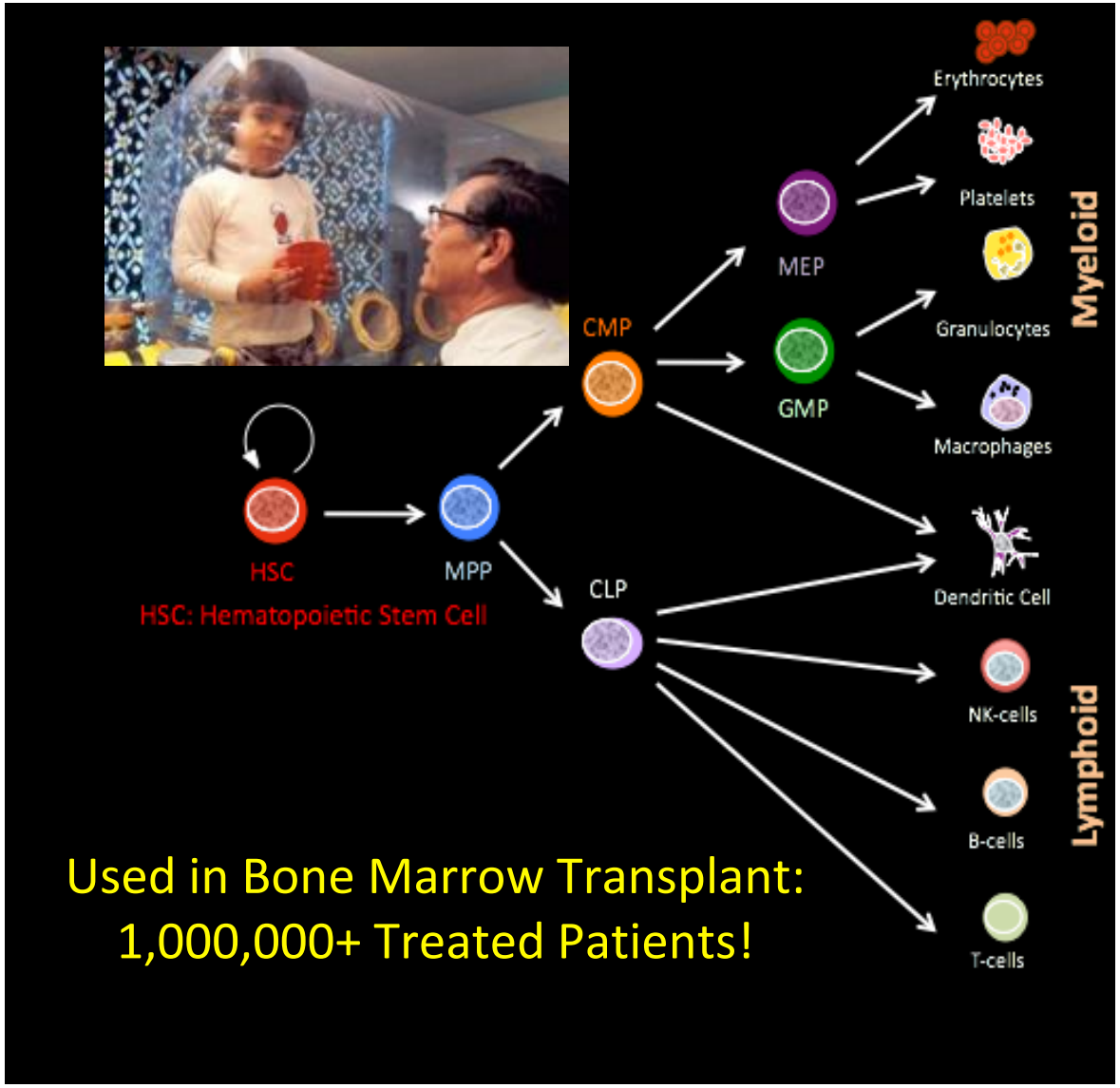
BLOOD STEM CELL THERAPIES NEED TO BE SAFER AND MORE EFFECTIVE



CANCER

Myelofibrosis
Myelodysplastic Syndrome
Acute Myeloid Leukemia
Acute Lymphoid Leukemia
Lymphoma
Multiple Myeloma

GENETIC DISEASES

Severe Combined Immunodeficiency
Fanconi Anemia
Sickle Cell Anemia
Beta Thalassemia
Diamond Blackfan Anemia
Aplastic Anemia
Wiskott-Aldrich Syndrome
Chronic Granulomatous Disease
Adrenoleukodystrophy

Potentially Curable:

Hemophilia A & B
Metachromatic Leukodystrophy
Hurler Syndrome
Osteopetrosis
Common Variable Immune Deficiency
Type I Juvenile Diabetes
Inflammatory Bowel Disease
Scleroderma
Multiple Sclerosis
Solid Organ Tolerance
HIV + Many More….

Gene Therapy is powerful new modalities for curing historically incurable genetic diseases

Traditional modality of supportive therapies

- Small molecules
- Biologicals
- Enzyme replacement
- Allogeneic stem cell transplantation

Technological Advancements

Novel modalities with potential to cure

In vivo gene therapy

Systemic or local delivery of the functional gene copy to treat or prevent a disease

Ex vivo gene therapy

Gene transfer into patient's stem cells which are subsequently reintroduced to the patient's body to treat or prevent a disease

Vast improvements in laboratory science have allowed for the reliable in-vitro production of cells and manipulation of genes

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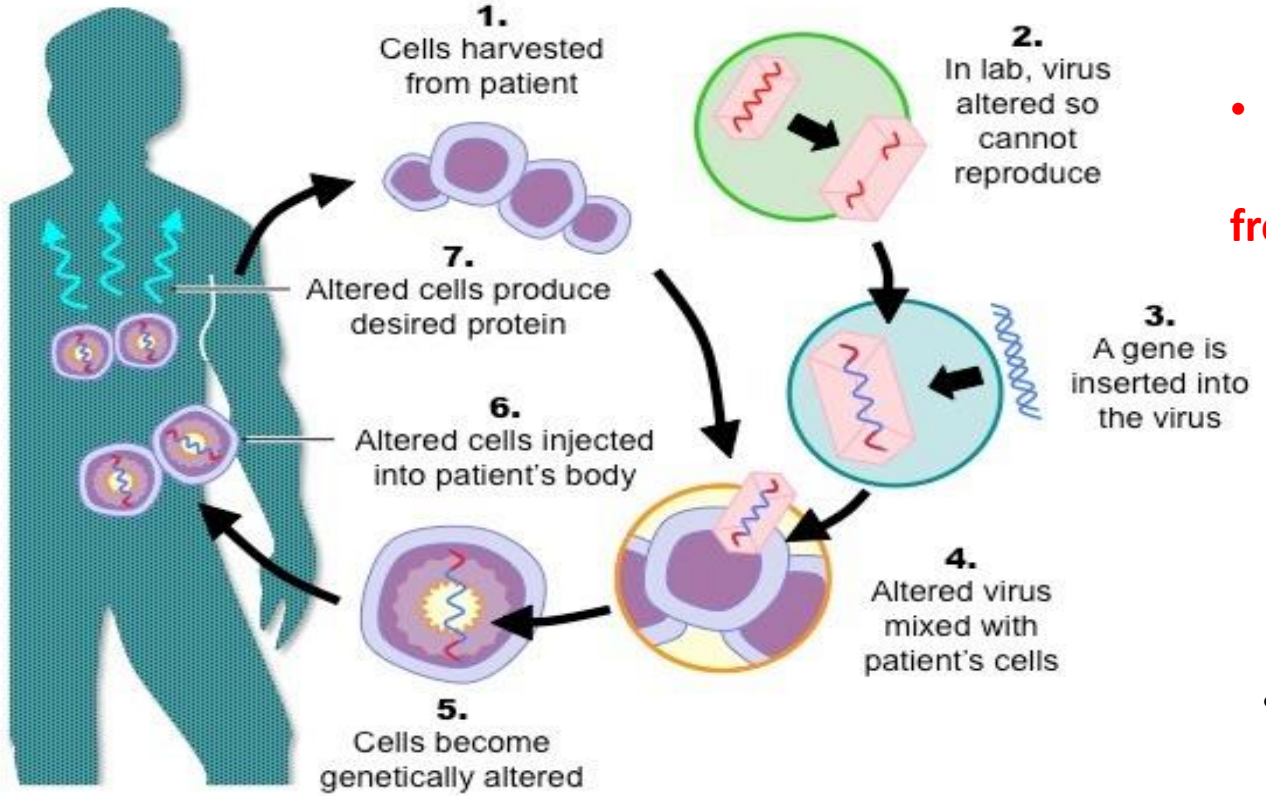
Ex-Vivo Gene Therapy



- **CD34+ hematopoietic stem/progenitor cells from the patient (autologous)**

Retroviral vectors:
Gammaretrovirus
Lentivirus

- **Transduction efficiency:**
  γRV 10-30%
  LV 50-80%
- **VCN: 1-5**

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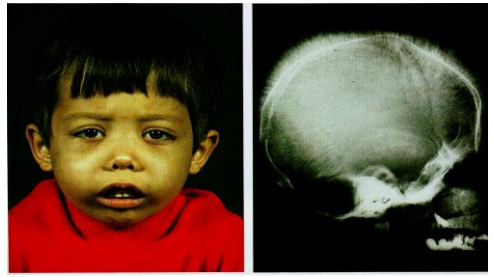
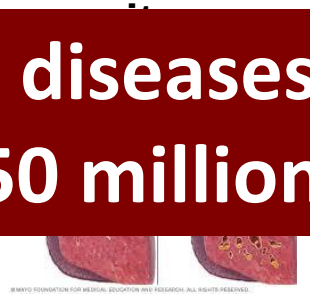
Genetic Diseases Caused by Mutations in Single Genes are potentially curable with GT



Hematology: Sickle Cell Disease, Thalassemia, Hemophilia

Immunology: Primary Immunodeficiencies, Autoimmunity, Chronic inflammatory diseases,

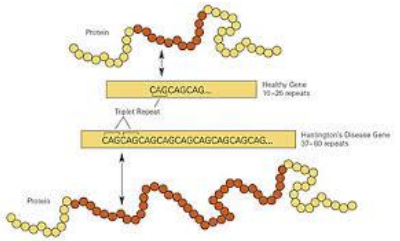
(6,000-10,000 such diseases)
(Patients: 30 million in USA, 350 million worldwide)



Cardiology: Familial Hypercholesterolemia

Neurology: Metabolic neurodegenerative diseases (MLD, ALD, MPS, Gaucher, Tay-Sachs etc.), Huntington's disease, Ngly1

Dermatology: Epidermolysis Bullosa



Clinical spectrum of Severe Combined Immunodeficiency (SCID) due to Adenosin Deaminase Deficiency (ADA)

- **Recurrent and severe infections caused by bacteria, viruses, and opportunistic organisms.**
- **Maternal GVHD.**
- **Failure to thrive.**
- **Autoimmunity and cancer.**
- **Fatal in the first years.**

“bubble boys”

- **Allogeneic HSCT transplant from an HLA identical sibling donor is the first line therapy but donor availability in < 25% of patients and significant morbidity and mortality.**

ADA-SCID WAS THE FIRST GENETIC DISEASE CURED WITH GENE THERAPY

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Autologous genetically modified BM derived CD34+ cells

NO PEG-ADA

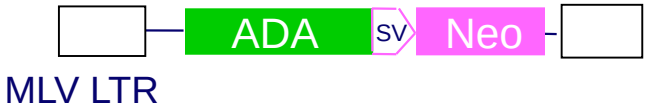
Busulfan

2 mg/Kg/day x 2
(days -3, -2)

Day 0: Infusion

BM Harvest

Day -4: Purification of BM **CD34⁺ cells**



Days -3 to -1:
3 cycles of transduction with RV on retronectin + cytokines

Day -4: Prestimulation
(TPO, FLT3-ligand, SCF, IL-3)

The NEW ENGLAND JOURNAL of MEDICINE

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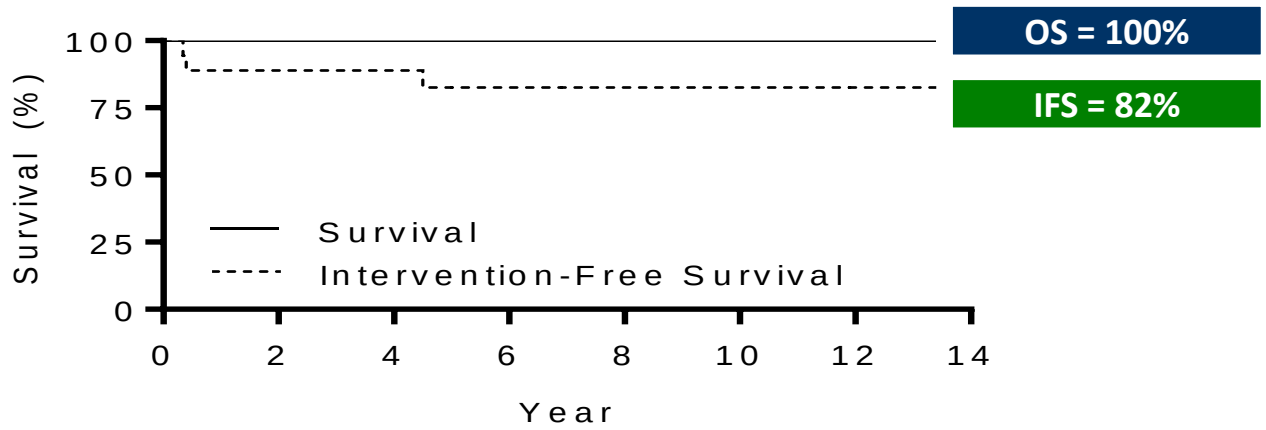
Gene Therapy for Immunodeficiency Due to Adenosine Deaminase Deficiency

Alessandro Aiuti, M.D., Ph.D., Federica Cattaneo, M.D., Stefania Galimberti, Ph.D., Ulrike Benninghoff, M.D., Barbara Cassani, Ph.D., Luciano Callegaro, R.N., Samantha Scaramuzza, Ph.D., Grazia Andolfi, Massimiliano Mirolo, B.Sc., Immacolata Brigida, B.Sc., Antonella Tabucchi, Ph.D., Filippo Carlucci, Ph.D., Martha Eibl, M.D., Memet Aker, M.D., Shimon Slavin, M.D., Hamoud Al-Mousa, M.D., Abdulaziz Al Ghonaium, M.D., Alina Ferster, M.D., Andrea Duppenthaler, M.D., Luigi Notarangelo, M.D., Uwe Wintergerst, M.D., Rebecca H. Buckley, M.D., Marco Bregni, M.D., Sarah Marktel, M.D., Maria Grazia Valsecchi, Ph.D., Paolo Rossi, M.D., Fabio Ciceri, M.D., Roberto Miniero, M.D., Claudio Bordignon, M.D., and Maria-Grazia Roncarolo, M.D.

EDITORIALS

Gene Therapy Fulfilling Its Promise

Donald B. Kohn, M.D., and Fabio Candotti, M.D.



San Raffaele Telethon Institute for Gene Therapy, Milan, Italy

STRIMVELIS

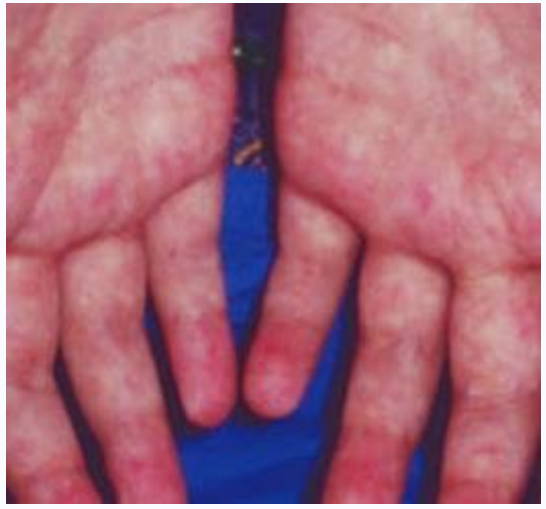
IN MAY 2016 STEM CELL GENE THERAPY FOR ADA-SCID RECEIVED MARKETING APPROVAL FROM THE EMA AS A NEW MEDICINAL PRODUCT

San Raffaele Telethon Institute for Gene Therapy, Milan, Italy

Autologous Stem Cell Gene therapy has several advantages

Serious Infections

Graft vs. Host Disease



- Eliminate need of
  MYELOABLATION
  IMMUNOABLATION
  IMMUNOSUPPRESSION
- Reduce severe complications

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SUCCESSFUL GENE THERAPY IN ADA-SCID

SUCCESSFUL GENE THERAPY IN METACHROMATIC LEUKODYSTROPHY

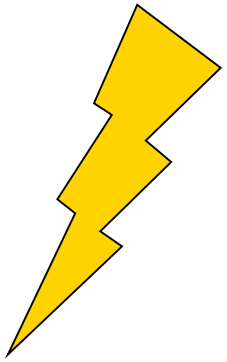
San Raffaele Research Institute

SUCCESSFUL GENE THERAPY IN WISKOTT-ALDRICH SYNDROME

Italian Telethon Foundation

“Conditioning”

Preparation of patients before HSCT to accept new HSCs



Gross Tissue Damage

Serious short-term and long-term consequences from such pre-tx chemotherapy:

- Anemia and thrombocytopenia
- Organ damage (ex. VOD, renal failure, cardiac, lung)
- Sterility and endocrine dysfunction
- Secondary malignancies
- Cognitive decline

Huge Opportunity for HSCT Improvement!

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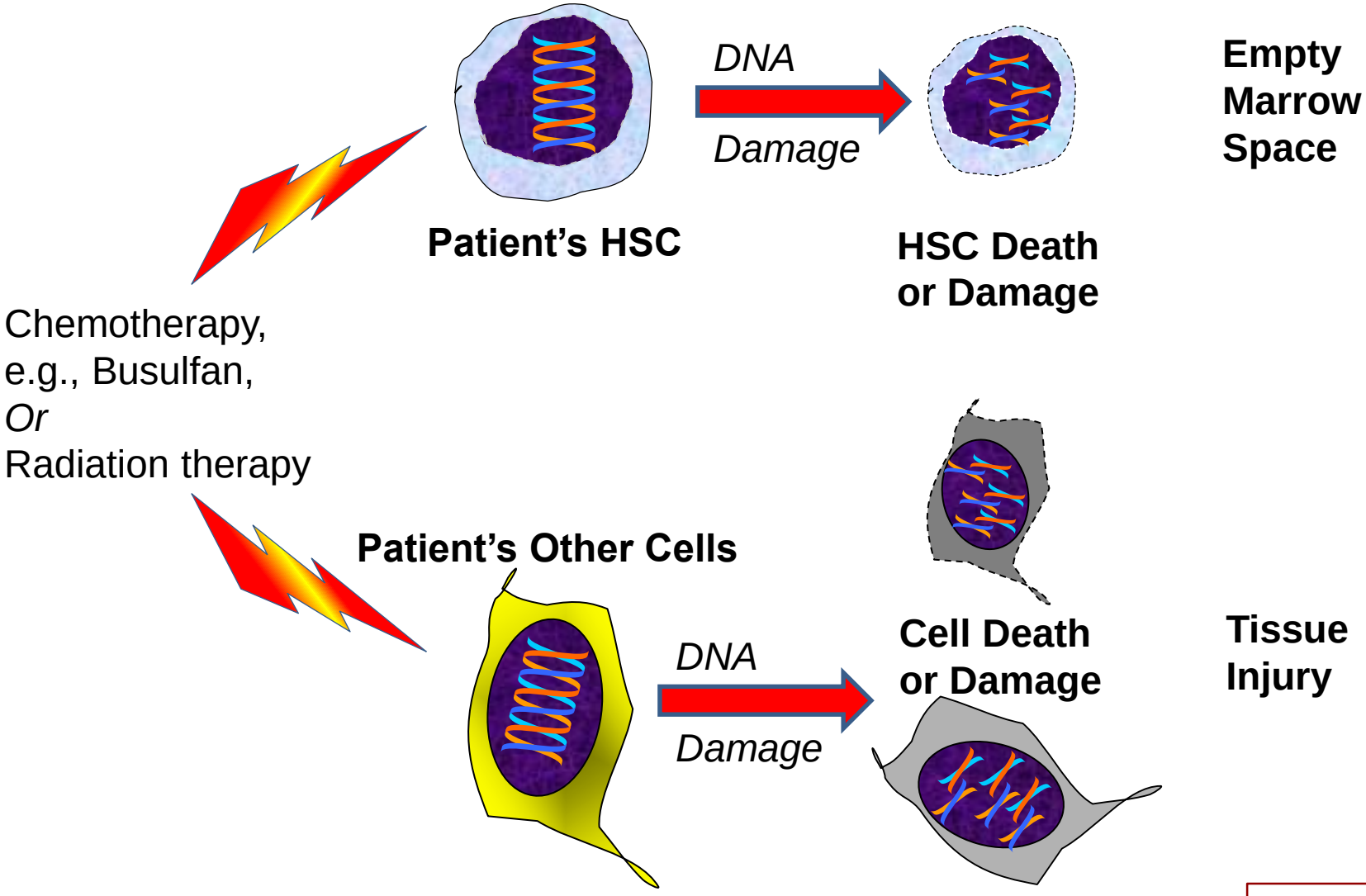
Side Effects of Marrow Ablation by Chemotherapy



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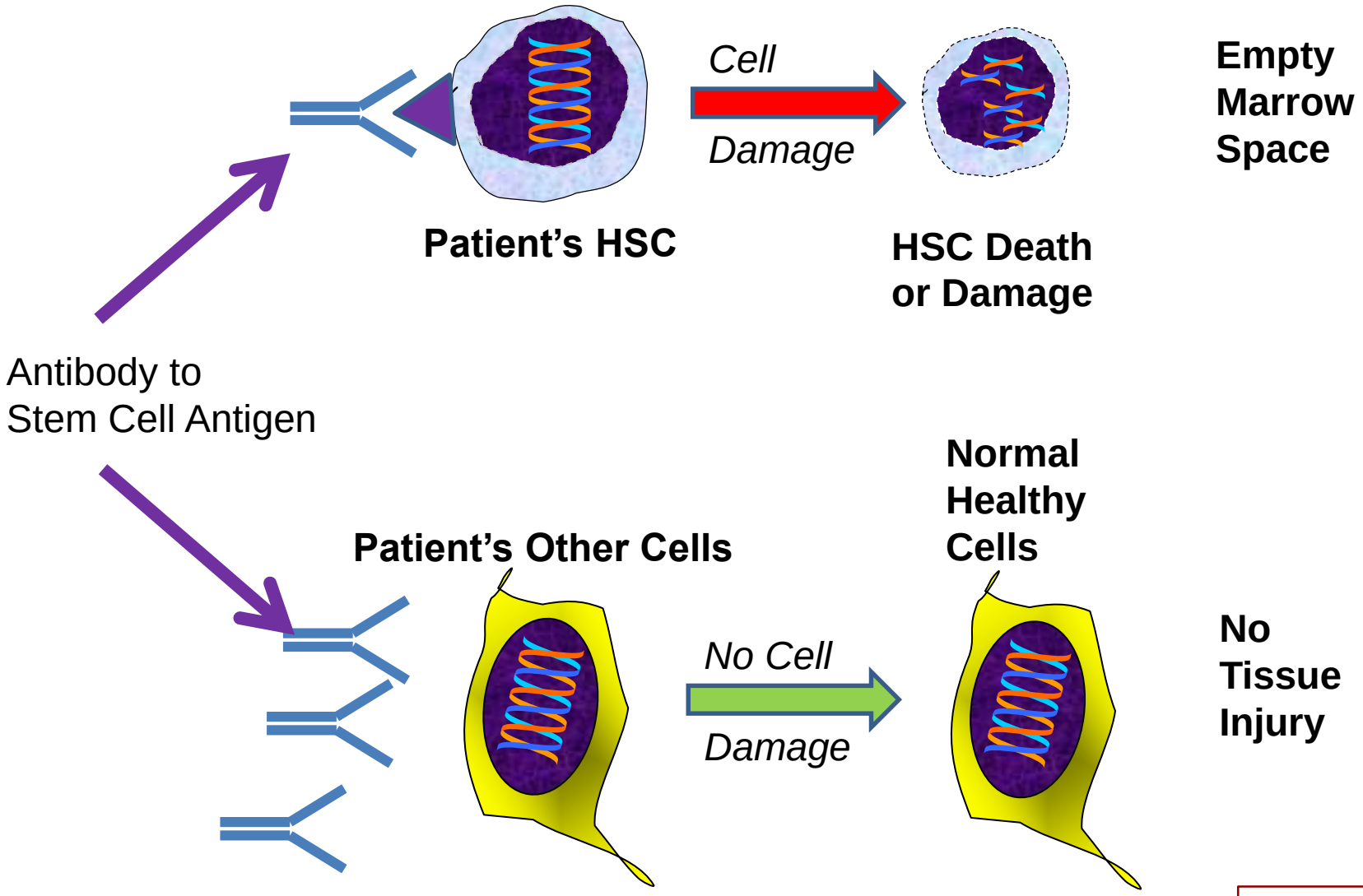
Limited Side Effects of Marrow Ablation by Antibody



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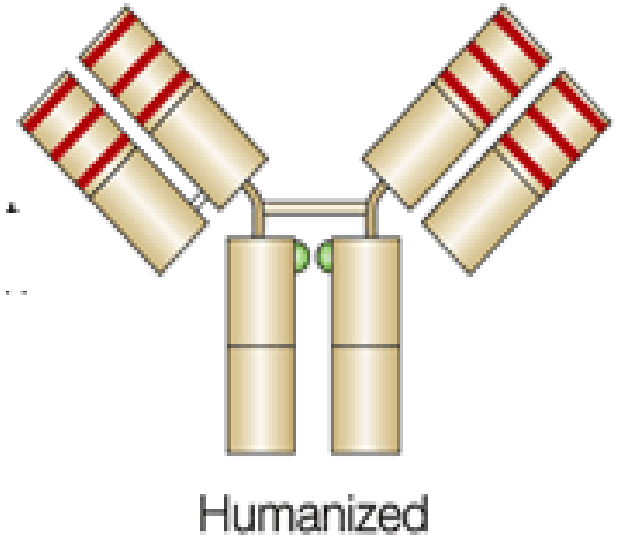
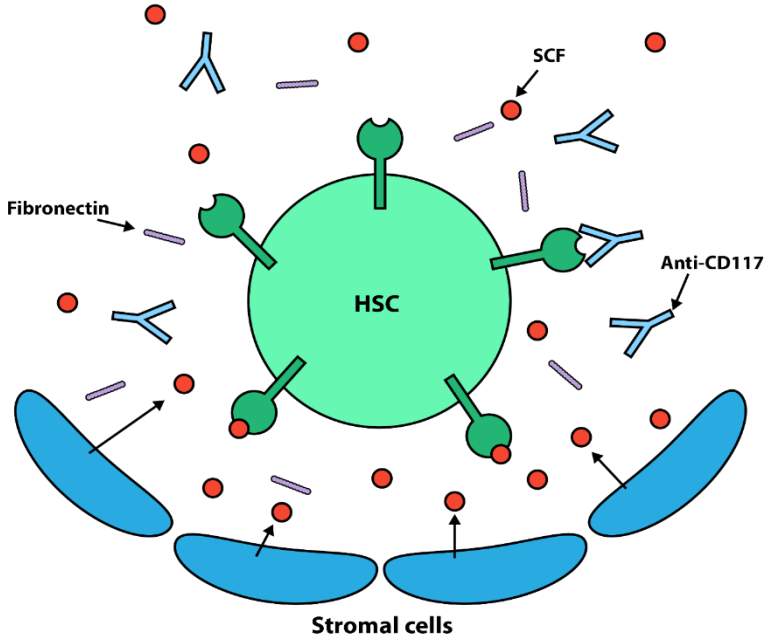
Antibody based conditioning

ADMINISTRATION OF anti-CD117mAb TO:

- **TARGET HSC**
- **CREATE SPACE IN THE BONE MARROW NICHES**
- **REPLACE CHEMOTHERAPY**





CD117 is a receptor tyrosine kinase which binds to SCF

Anti-CD117 antibody as conditioning for SCID

- **Study Objectives**
  - 1º: Safety, tolerability, PK, PD of anti-hCD117
  - 2º: Myeloid engraftment, functional lymphocyte reconstitution

- **Study Design**
  - Phase 1/2: Dose escalation of anti-hCD117 (AMG191) mAb
  - Age de-escalation beginning w/previously transplanted SCID patients w/poor graft function
  - Transplant allogeneic (haploidentical & URD) stem cells purified by CD34+CD90+ cell selection

- **IND approved: 5 patients treated**
  - Safe no SAE. First two patients follow up >1 yr
  - Presence of donor derived HSC in bone marrow and CD15+ cells in peripheral blood
  - Presence of donor-derived CD19+ B cells

Antibody-based conditioning: next applications

- **CANCER**
  - LEUKEMIA
  - SOLID TUMOR
- **BLOOD DISORDERS**
  - FANCONI ANEMIA
  - THALASSEMIA
- **METABOLIC DISEASES**
  - LEUKODYSTROPHIES
  - GAUCHER
- **IMMUNE MEDIATES DISEASE**
  - PRIMARY IMMUNODEFICIENCIES
  - TYPE 1 DIABETES
  - OTHER AUTOIMMUNE DISEASES

BLOOD STEM CELLS FROM HEALTHY DONORS

OR

BLOOD STEM CELLS FROM PATIENTS MODIFIED IN THE LAB WITH GENE THERAPY

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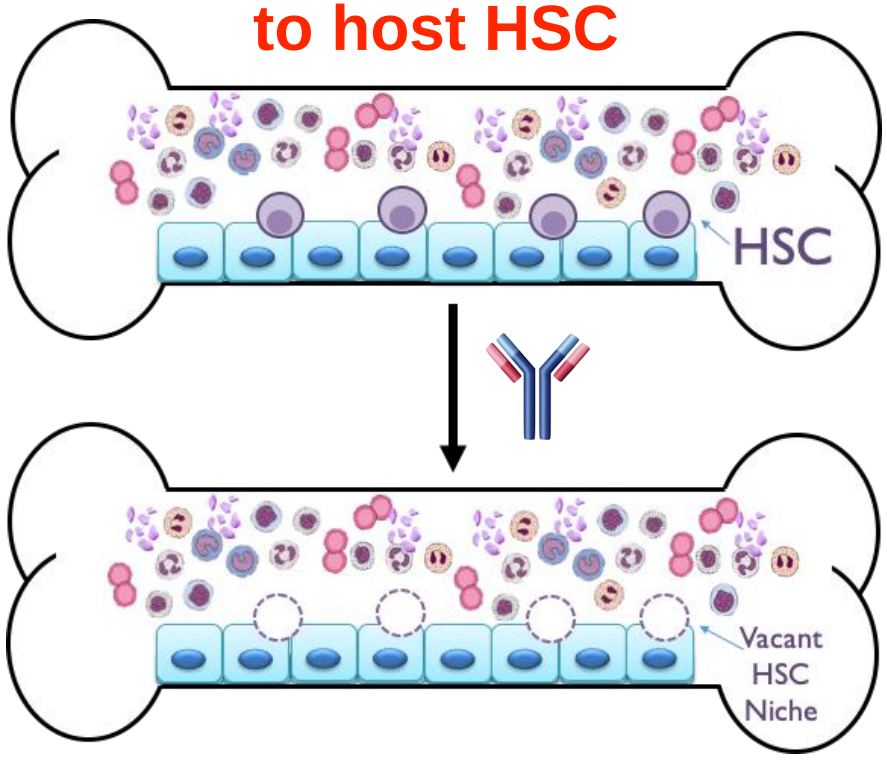
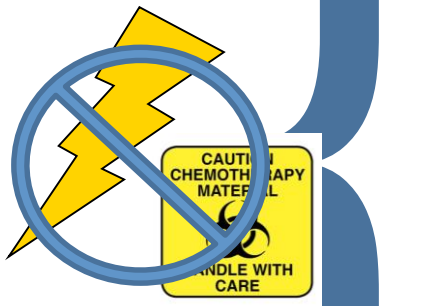
Future of Safe Conditioning for High HSC Engraftment

Targeted Antibodies to host HSC





Create HSC space without causing collateral damage

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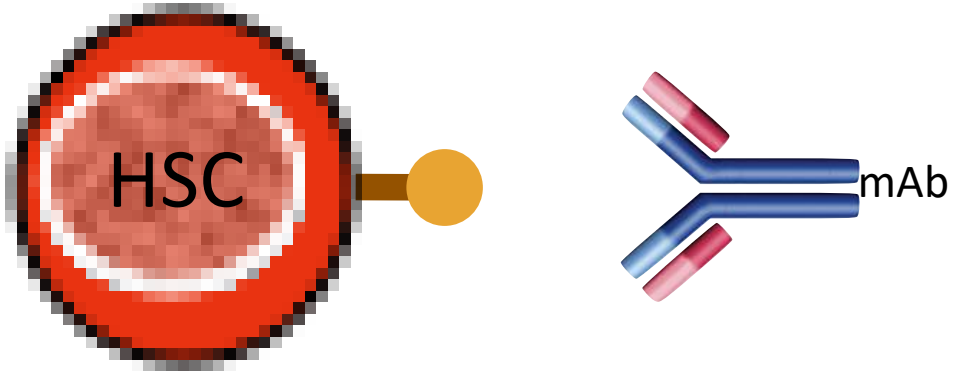
Antibody-Based Conditioning Approaches



Multiple Ways to Use mAb to Eliminate HSC:

- Block Critical Signaling Pathways
- Kill via Immune System (ADCC)
- Poison via Antibody-Drug Conjugates

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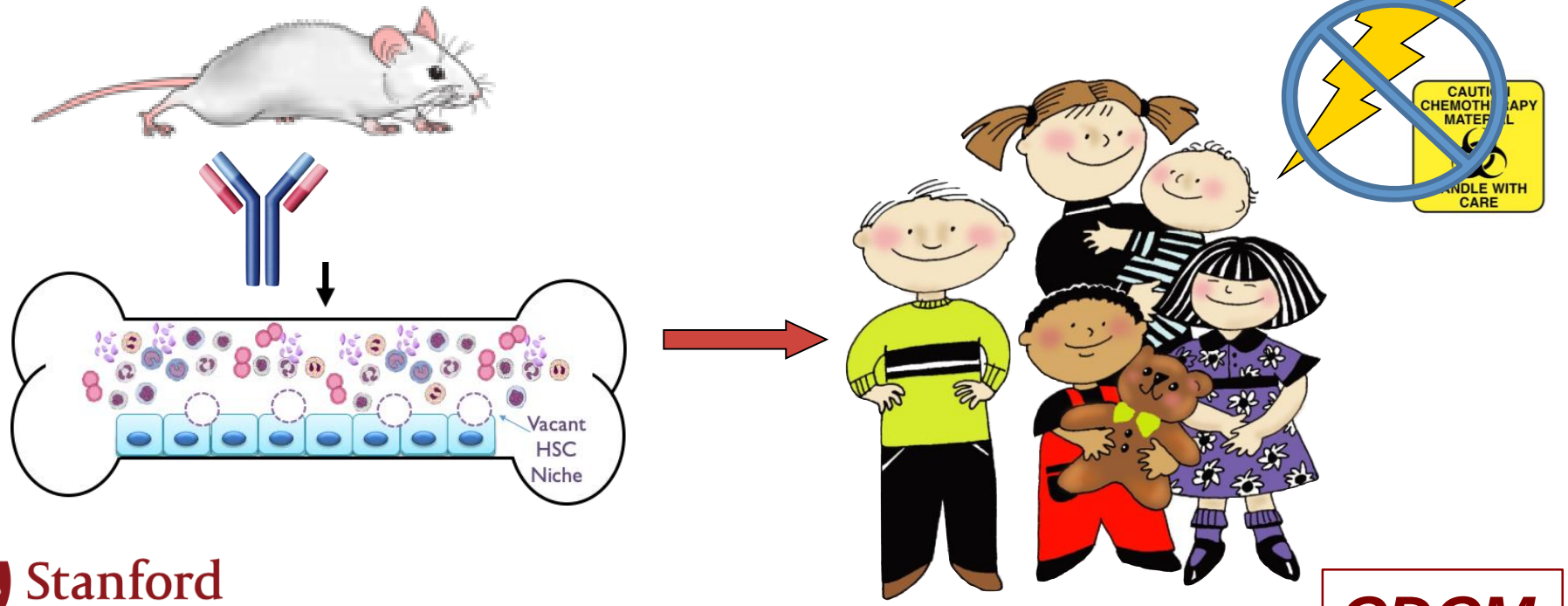
Conclusions

- Promising new opportunities to use stem cells to cure many diseases
- Future of HSCT is targeted depletion of host HSC (no broad damage)
- Various antibody-based targeted conditioning agents are possible



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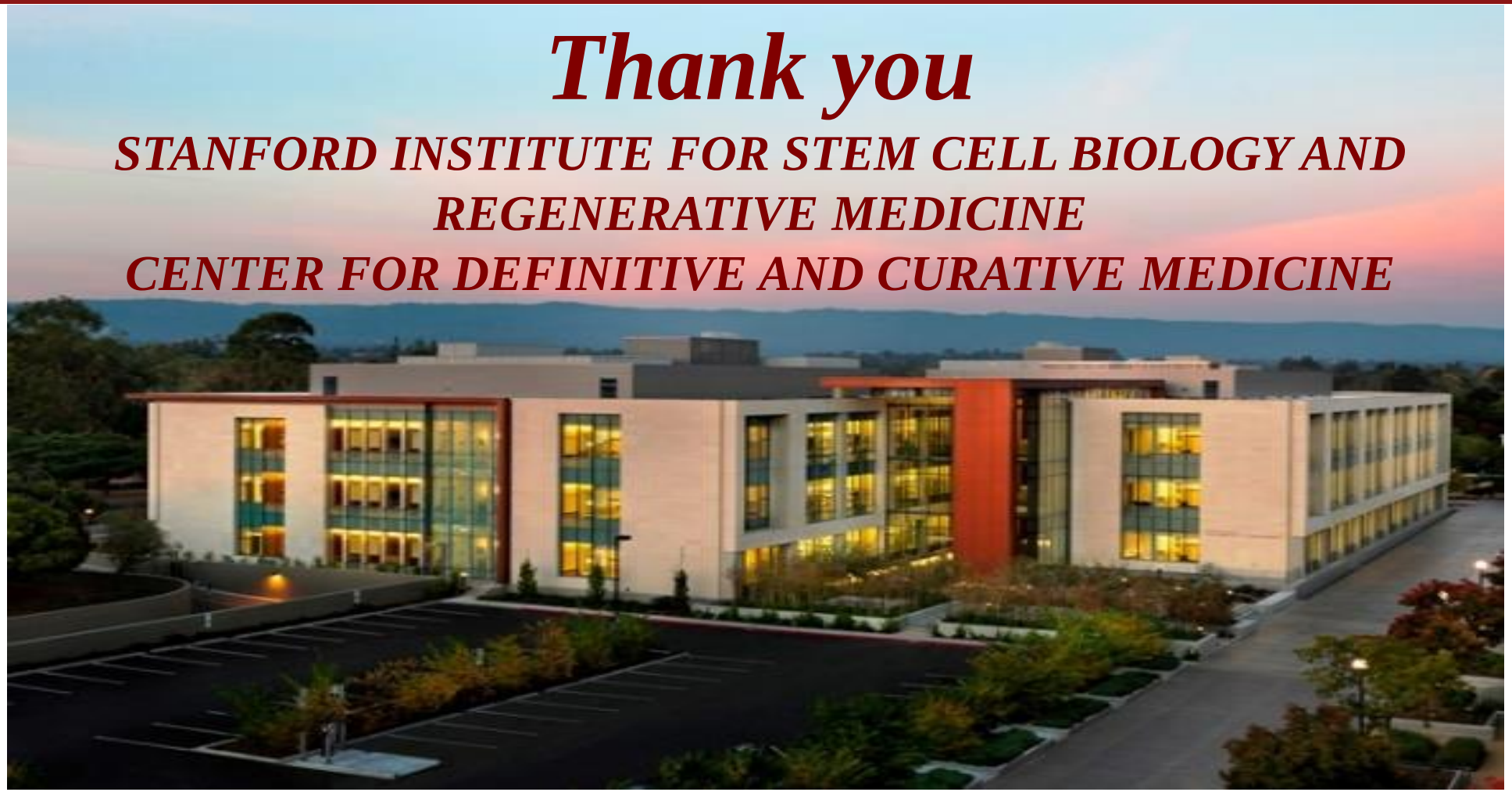
Thank you

STANFORD INSTITUTE FOR STEM CELL BIOLOGY AND REGENERATIVE MEDICINE

CENTER FOR DEFINITIVE AND CURATIVE MEDICINE



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Stanford Children's Health

Lucile Packard Children's Hospital Stanford

Forty Seven´s Approach to cKIT

Jens-Peter Volkmer, M.D.

Founder and VP Research & Early Development,
Forty Seven, Inc.

CURING Life-Threatening and Severe Chronic Diseases by Overcoming Barriers of Transplantation and Gene Therapies

Forty Seven

Barriers of Transplantation

Approaches have not improved in half a century

- Severe damage by toxic radiation and chemo conditioning
  - Impaired brain development in children
  - Infertility
  - Development of secondary malignancies and MDS
  - Too toxic for elderly patients and patients with pre-existing conditions
- Graft vs host disease
- Requirement for (life-long) immune suppression
- Severe life-threatening infections
- Shortage on matched blood/organ donors

Forty Seven's Solution

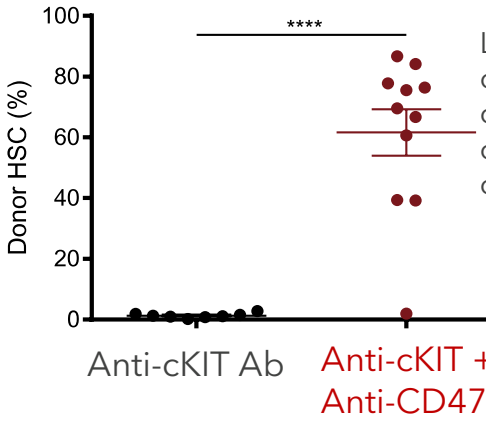
Science-driven approach to overcome risks and limitations of an outdated and toxic regimen

- All antibody-based, non-toxic regimen (radiation- and chemo-free)
- Selective and short-term antibody-mediated immune suppression to facilitate fast immune recovery
- Prevention of graft vs host disease by transplantation of purified hematopoietic stem cells (HSCs)
- Facilitation of immune tolerance for transplanted tissues and organs obviates need for immune suppression
- Co-transplantation approach (HSCs + organ) enables transplantation from non-matched organ donors and extends donor pool

FSI-174 Anti-cKIT Antibody Program

Target	○ cKIT, CD117, stem cell growth factor receptor
MOA	○ Blockade of stem cell factor signaling ○ Depletion of cKIT-expressing cells
Indication	○ Hematopoietic stem cell (HSC) and bone marrow transplantation • Genetic blood disorders • Leukemia & lymphoma • Autoimmune diseases • Organ transplantation ○ Oncology: cKIT-expressing cancers, e.g. leukemia, melanoma, renal cell cancer, gastrointestinal stroma tumor
Addressed Need	○ Improved conditioning regimens • Potential for lower incidence of morbidity and mortality • Expanded patient populations and indications
Development Status	○ Preclinical POC established for both indications ○ Lead candidate selection completed ○ Cell line development initiated June 2018 ○ IND anticipated Q4 2019
IP	○ Method of treatment patents for use of cKIT antibody and cKIT + CD47/SIRPα antibodies filed ○ Composition of matter patents for cKIT and CD47/SIRPα antibodies filed/granted

Combination of cKIT and anti-CD47/SIRPα Antibodies Enables Transplantation of Hematopoietic Stem Cells in Mouse Model

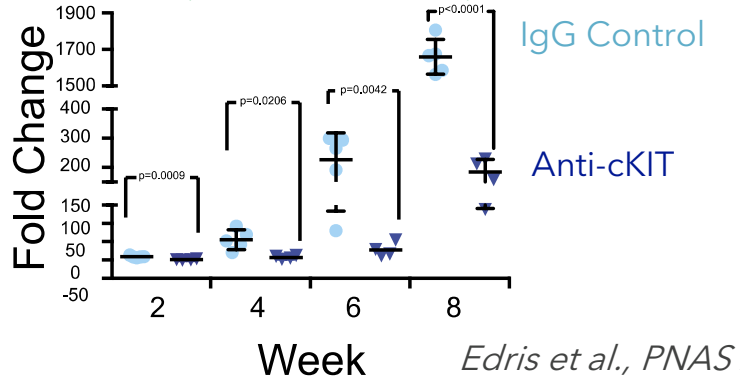


Long-term engraftment of donor hematopoietic stem cells after conditioning with cKIT Ab vs cKIT + CD47 Ab combination

Chhabra et al., STM 2016

cKIT Antibody Inhibits Tumor Growth in Mouse Model

Gastrointestinal Stroma Tumor
(Imatinib resistant)



Edris et al., PNAS 2012

Development Strategy

- First Wave → anti-cKIT Ab + anti-cKIT- CD47/SIRPα Ab conditioning
  - Autologous Transplantation
    - Primary monogenetic non-malignant blood disorders with available gene-therapy (e.g. thalassemia, sickle cell, Fanconi anemia)
  - Allogeneic Transplantation
    - Primary non-malignant blood disorders with matched donor
- Second Wave → anti-cKIT Ab + anti-cKIT- CD47/SIRPα Ab (+ anti-T cell Ab) conditioning (and treatment)
  - Allogeneic Transplantation
    - Autoimmune diseases (e.g. systemic lupus erythematosus, rheumatoid arthritis, multiple sclerosis, diabetes I, Crohn's disease)
    - AML, MDS, and other cKIT-positive blood malignancies (conditioning + anti-cancer cell effect)
- Third Wave → anti-cKIT Ab + anti-cKIT- CD47/SIRPα + anti-T cell Ab conditioning
  - Allogeneic Transplantation
    - Hematopoietic stem cell co-transplantation with organ transplantation

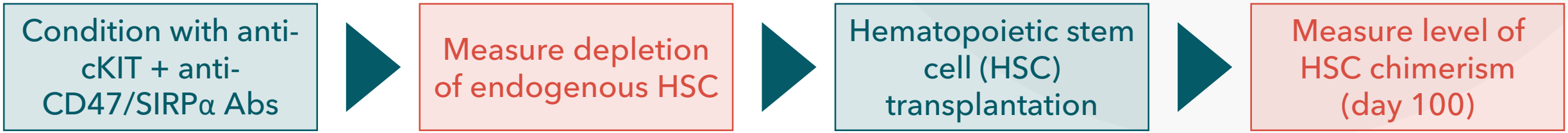
Non-Human Primates Proof of Concept Studies

- Dose range finding study: Anti-cKIT + anti-CD47/SIRPα antibodies
  - Started December 2018

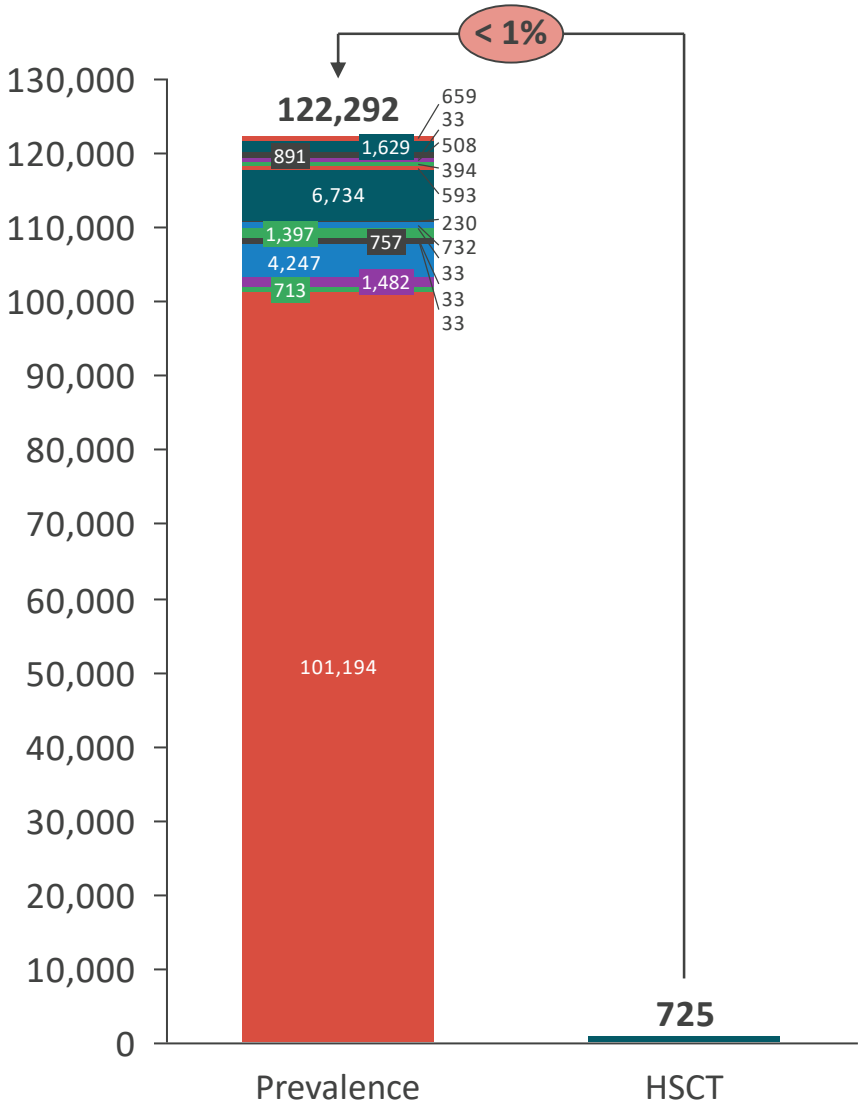
- POC study: Anti-cKIT + anti-CD47/SIRPα antibodies + autologous (gene marked) hematopoietic stem cell transplantation
  - Start Q1 2019

- POC study: Anti-cKIT + anti-CD47/SIRPα + explorative anti-T cell antibodies + purified allogeneic hematopoietic stem cell transplantation
  - Start Q3 2019

First Wave Clinical Trial Approach



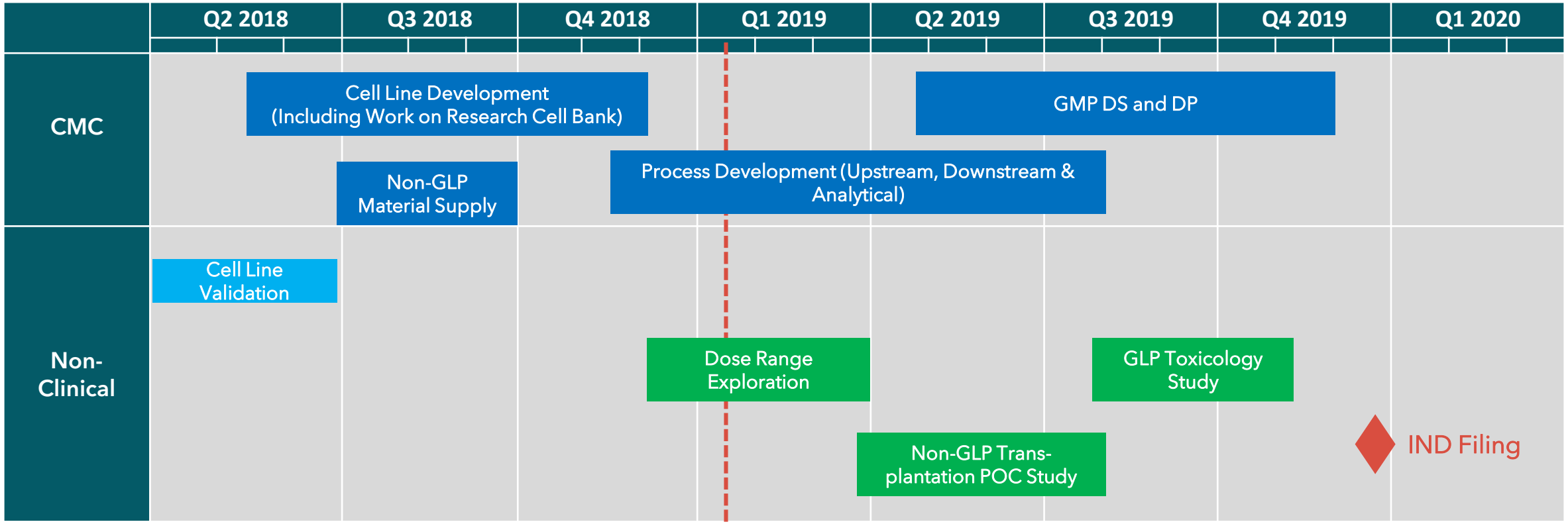
Opportunity Assessment of First Wave Indications – Unmet Need in Genetic Blood Cell Diseases in the US



- Kostmann's syndrome
- Shwachman-Diamond syndrome
- Fanconi Anemia
- Osteopetrosis
- Metachromatic leukodystrophy
- X-linked adrenoleukodystrophy
- Mucopolysaccharidoses
- Gaucher disease
- Wiskott-Aldrich syndrome
- Chronic granulomatous disease
- Leukocyte adhesion deficiency
- Hemophagocytic lymphohistiocytosis
- X-linked hyper igM syndrome
- X-linked lymphoproliferative dis.
- X-linked agammaglobulinemia
- Common variable deficiency
- SCID
- B-Thalassemia
- Sickle cell dis.

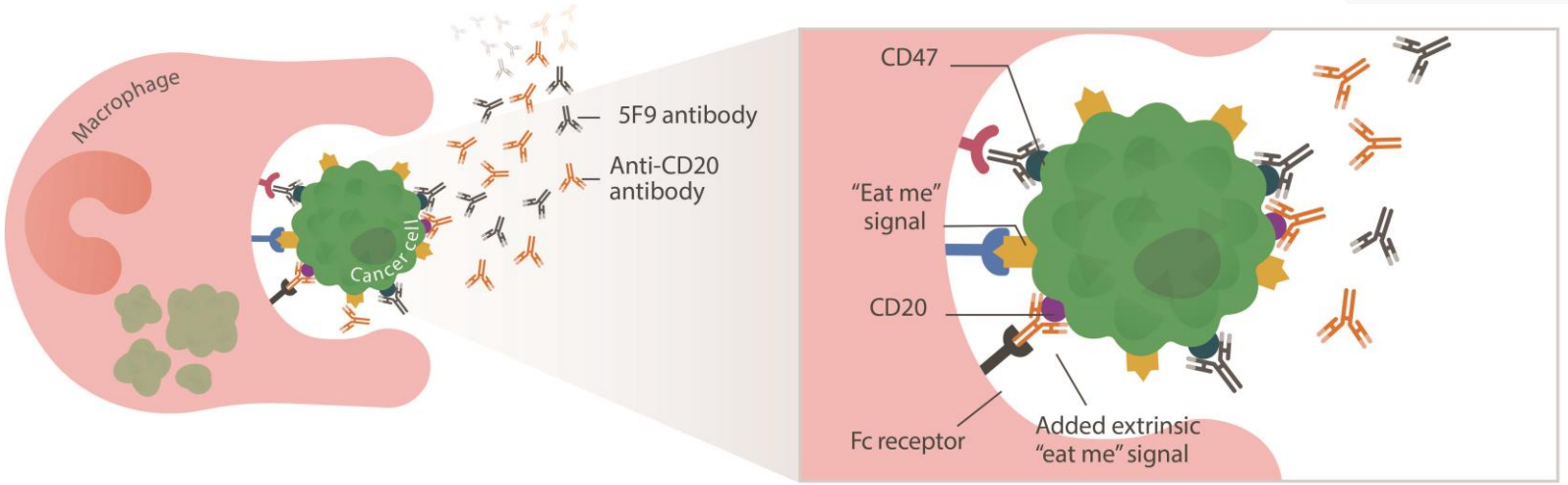
- Current risks and barriers to hematopoietic stem cell transplantations are severely rate-limiting
  - Risk for infertility and secondary malignancies or MDS
  - Lack of matched donors
- Less than 1% of all patients with monogenetic diseases receive a stem cell transplant on an annual basis
- cKIT-CD47/SIRPα program and gene therapy can address these unmet needs

Program Timeline – On Track for IND Filing in Q4 2019

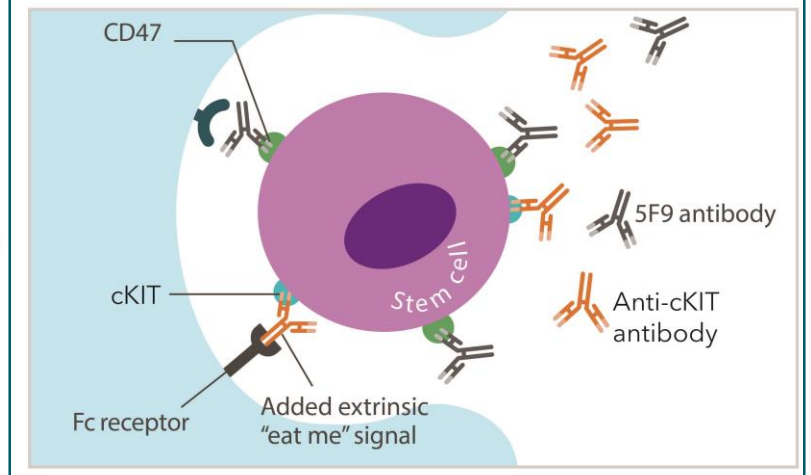


5F9 Antibody Combination With Targeted Antibodies – Expanding the Experience with Rituximab to cKIT Antibodies

5F9 + Rituximab



5F9 + cKIT Antibody



- Combination of 5F9 with targeted Abs, i.e. rituximab (anti-CD20) - enhances phagocytosis of cancer cells
- Hematopoietic stem cells and cancer cells, i.e. AML, MDS, express cKIT and combination of a cKIT Ab with 5F9 can enhance phagocytosis of these cells

Questions and Answers

NASDAQ: FTSV

Forty Seven

Helping Patients Defeat Their Cancer