

STRATEGY FOR CREATING INNOVATION

R&D MEETING 2016



Kenji Yasukawa Ph.D.
Senior Corporate Executive
Senior Vice President & Chief Strategy Officer
Astellas Pharma Inc.
December 8, 2016

Turn innovative science into value for patients by
addressing unmet needs.

OPPORTUNITIES TO PURSUE & NEW STRATEGIES FOR DRUG DISCOVERY RESEARCH

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Opportunities to pursue

- Innovative drug discovery in TAs with high UMNs
- New modalities such as cell therapies, gene therapies, etc.
- Increasing number of technologies with applicability in various fields
⇒ Opportunities to create innovative value for patients still exist

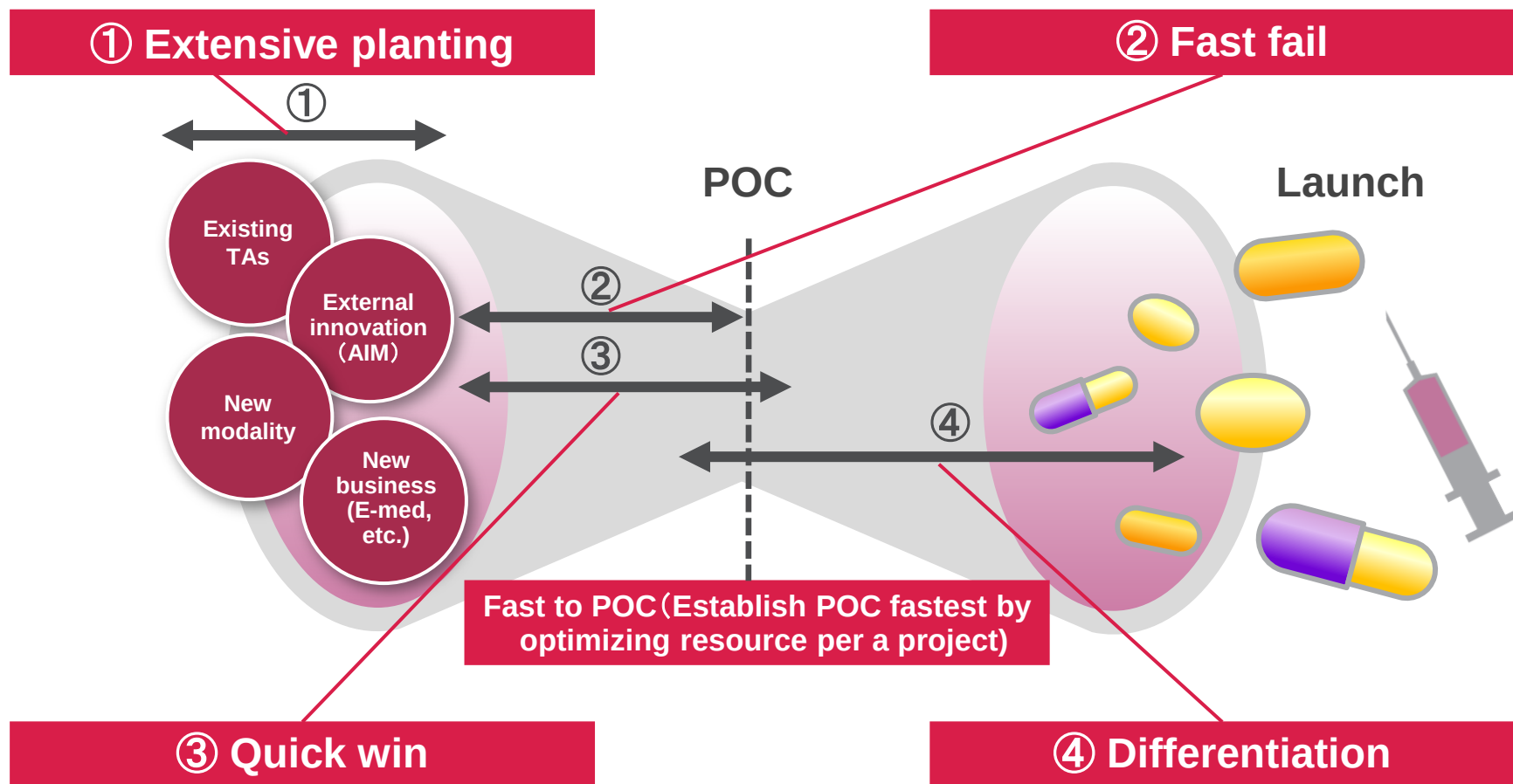


New strategies for drug discovery research

- Research with using strengthens in existing TAs + Advancing into new TAs
- Challenges in Rx business + α (new business): to provide medical solutions
- Utilization of external R&D resources through Network Research System:
Best Science / Best Place / Best Talent
- Extensive input
- FASTEN (Multi-tracking of R&D process)

FOUR PILLARS FOR ENHANCING CAPABILITIES TO DELIVER INNOVATIVE MEDICINES

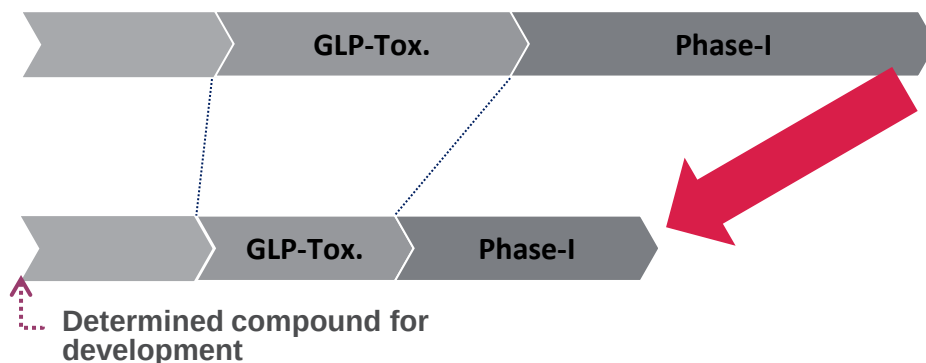
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OUTCOME OF R&D RESHAPING

5

- Sharply increased number of theme inputs
- Shortened timeframe of exploratory R&D stage by 30% after FASTEN implementation



*For illustrative purposes only

- Confirmed a trend of cost reduction during exploratory R&D stage, also

FOCUSED RESEARCH PROGRAMS

6

Core technologies

New technologies, new modalities

Existing TAs

Urology

Oncology

Immunology

Nephrology

Neuroscience

Small molecule Antibody



Dana-Farber
Cancer
institute

Kyoto Univ.
(AK Project)



New TAs

Muscle Diseases

Ophthalmology

Next-generation vaccines



- LAMP-vax
- Institute of Medical Science, Univ. of Tokyo
- Muco-rice



Fusion protein



Gene therapy

- Oncolytic virus immunotherapy

Harvard Medical
School



Cell therapy

AIRM



DRUG DISCOVERY RESEARCH

R&D MEETING 2016



Wataru Uchida Ph.D.
Senior Vice President,
President, Drug Discovery Research
Astellas Pharma Inc.
December 8, 2016

AGENDA

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I Creating innovation

II Therapeutic area: Oncology

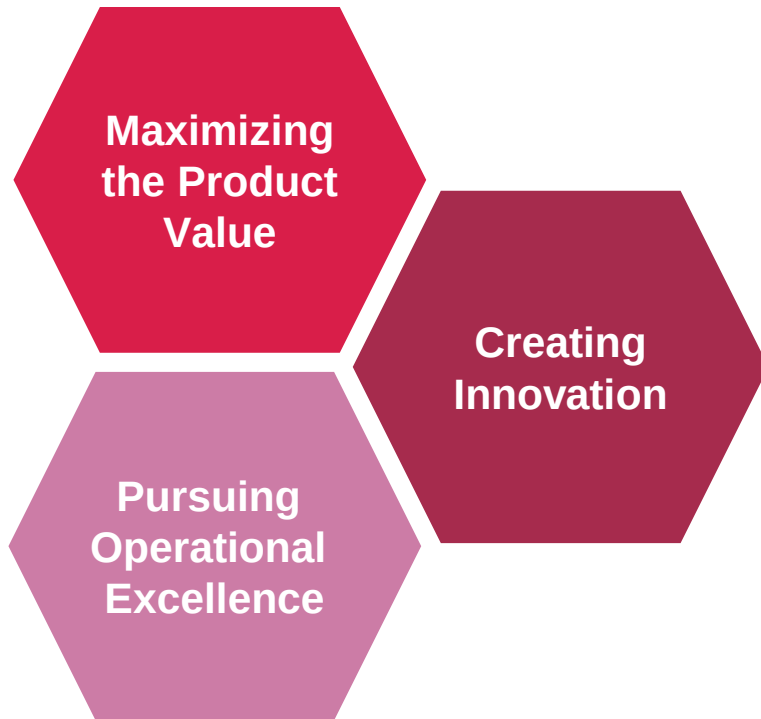
III Therapeutic area: Muscle Disease

IV Therapeutic area: Immunology

CREATING INNOVATION

3

On the forefront of healthcare change to turn innovative science into value for patients



- Enhancing capabilities to deliver innovative medicines
- Advancing into new opportunities

- ✓ Network-type research system
3B (Best Science, Best Talent, Best Place)
- ✓ Multitrack R&D project management
FASTEN
- ✓ Renovate HR system to create innovation
aiPaths, DISC

CREATING INNOVATION

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Renovate HR system to create innovation

New HR program to encourage the creation of innovation from a personnel perspective
aiPaths (Astellas Research Multi-Career Paths)

Career paths for researchers

Principal Investigator (PI)

The goal is to encourage researchers to ambitiously develop innovative ideas that were difficult to take on under existing systems and produce concrete R&D results in a timely manner. PIs will be given a certain degree of discretionary authority for personnel and budgets to initiate drug development for incorporating cutting-edge science.

Research Professional

The goal is strengthening research base by acquiring cutting-edge science and technologies through a range of specialties based on abundant knowledge and experience.



Recruitment for diverse researcher to create innovation

DISC (Drug Discovery Innovator Selection Camp)

Astellas has incorporated a unique program called DISC into the process of recruiting drug discovery researchers who are able to constantly create new forms of value with sharing of multifaceted values and solve issues by drawing upon all resources including specialized expertise, experience, knowledge, information and human networks.



AGENDA

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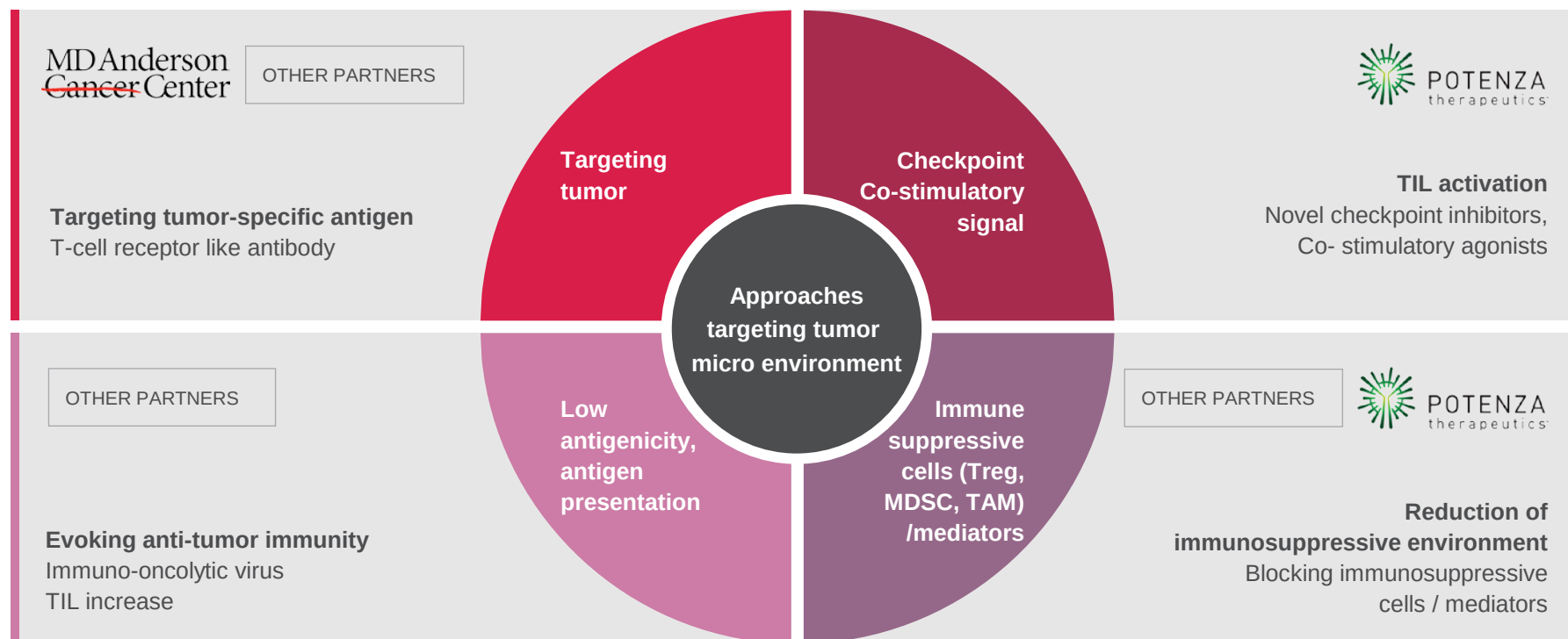
I Creating innovation

II **Therapeutic area: Oncology**

III Therapeutic area: Muscle Disease

IV Therapeutic area: Immunology

Building a portfolio of novel immuno-oncology therapeutics targeting tumor microenvironments to address tumor types unresponsive to anti-PD-1/PD-L1



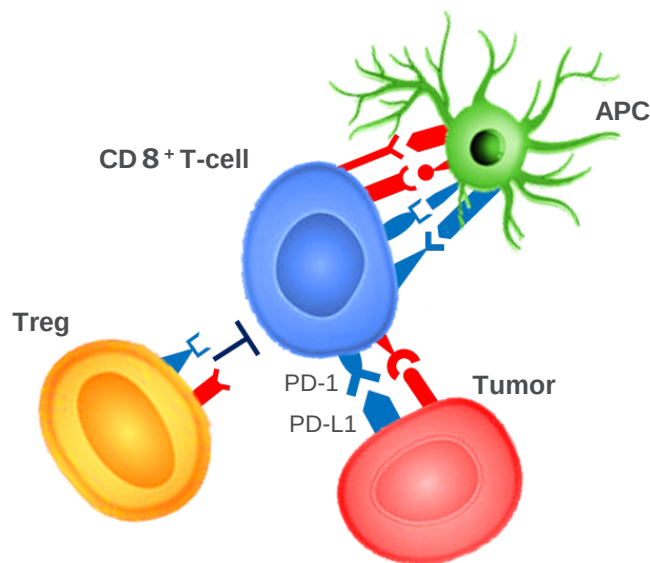
ONCOLOGY: Potenza Therapeutics COLLABORATION



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A pipeline of novel checkpoint inhibitor, co-stimulatory agonist and modulator of immunosuppressive cells etc. for patients and tumor types unresponsive to PD-1/L1 blockers

Immunomodulatory mechanisms



Potenza program portfolio

Program	Development Progress	
	Pre-clinical	Clinical
Checkpoint inhibitor		2017 IND scheduled
Treg modulator		2017 IND scheduled
Co-stimulatory agonist		



POTENZA
therapeutics



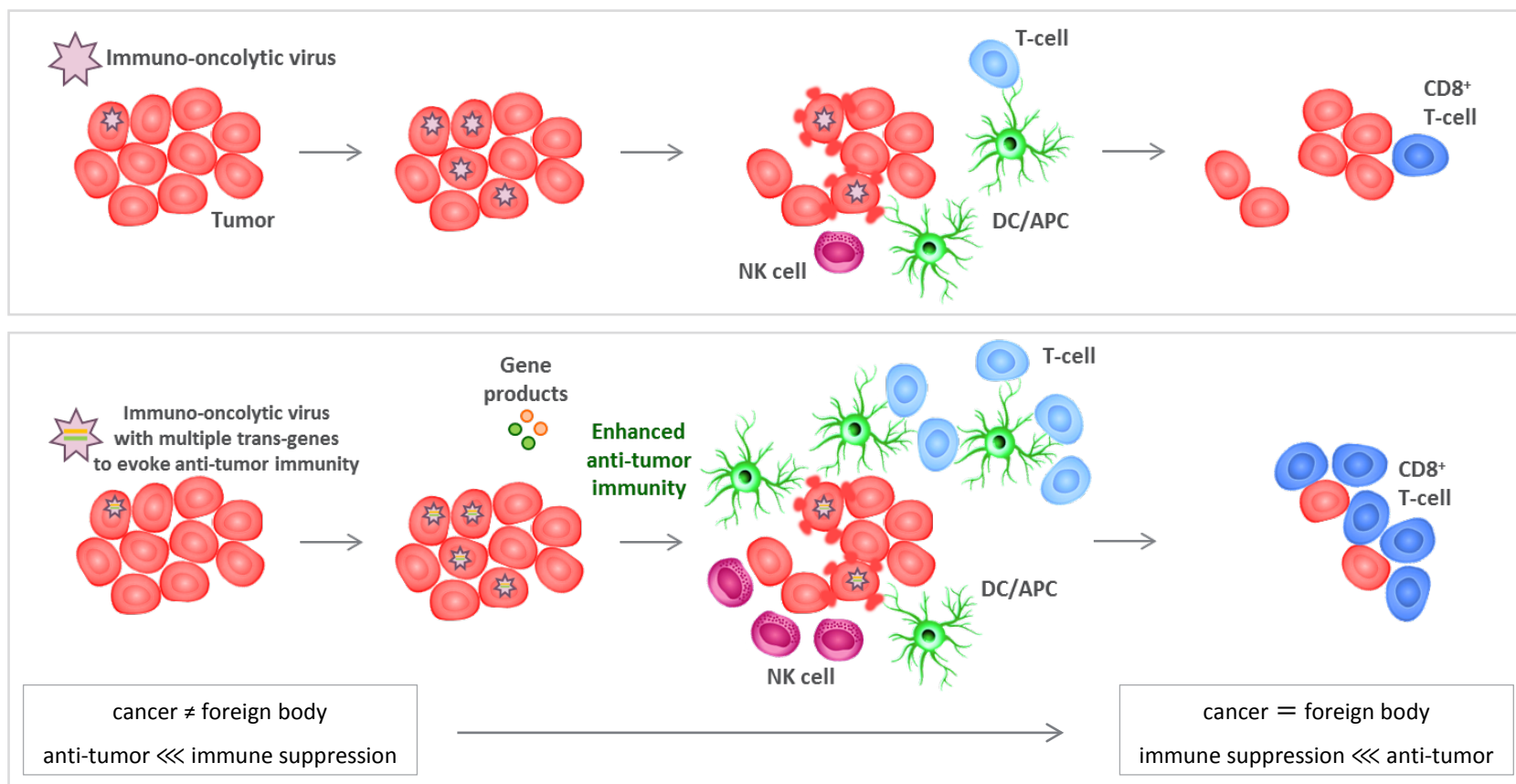
PD-1: Programmed cell Death-1, PD-L1: Programmed cell-Death Ligand 1,
Treg: regulatory T cell, APC: Antigen Presenting Cell

ONCOLOGY: IMMUNO-ONCOLYTIC VIRUS APPROACH



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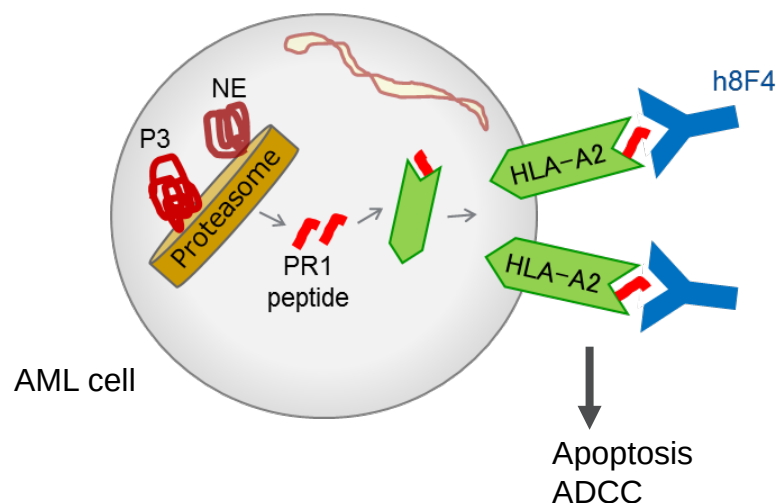
Immuno-oncolytic virus with multiple trans-genes to evoke anti-tumor immunity (Collaboration)





T-cell receptor like antibody, h8F4 against PR1/HLA-A2 which eliminates the target positive human AML cells

Anti-tumor mechanism of h8F4



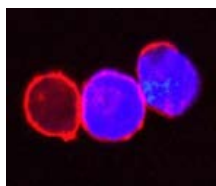
Development progress

Program	Development Progress	
	Pre-clinical	Clinical
h8F4		2017 IND scheduled

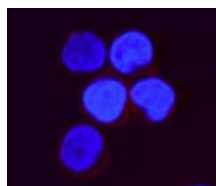
Expression of PR1/HLA-A2

8F4
(anti-PR1/HLA-A2)

AML



Normal leukocytes



AGENDA

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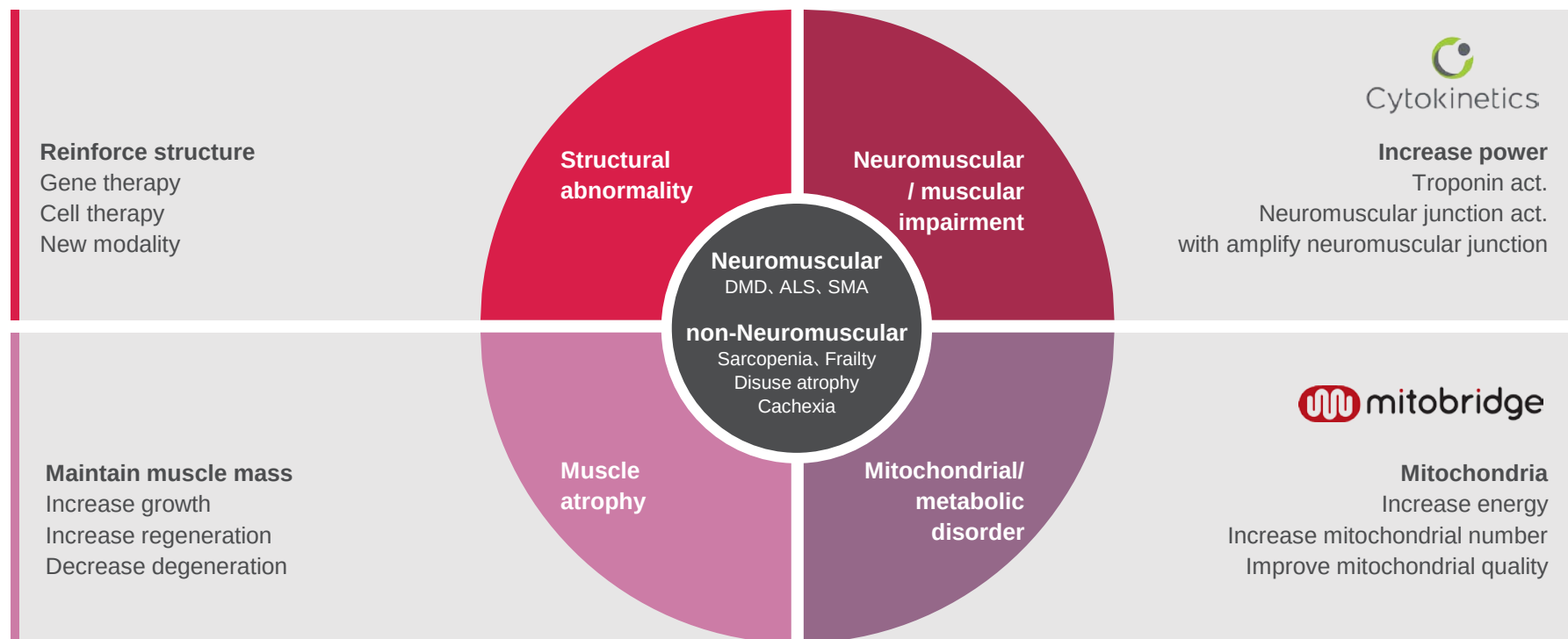
I Creating innovation

II Therapeutic area: Oncology

III **Therapeutic area: Muscle Disease**

IV Therapeutic area: Immunology

Create novel NMEs by innovation from research collaborations and in-house R&D capability based on the approach to improve muscle functions



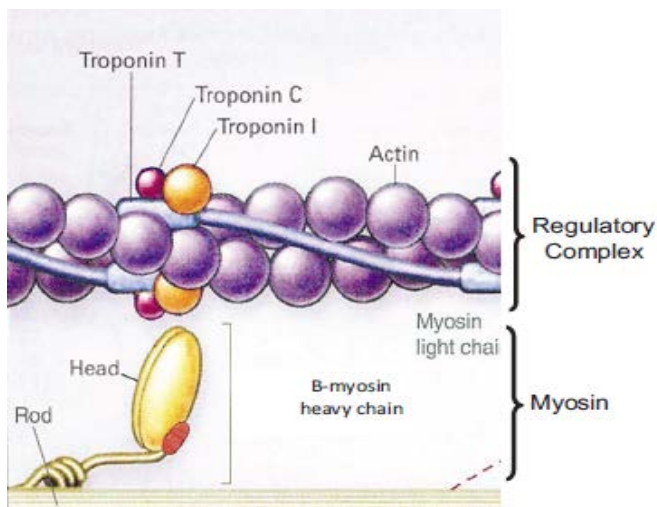


Combat against muscle impairment/weakness with innovative approaches

Skeletal muscle biology-driven treatments for diseases

Advantages of Cytokinetics, Inc.

- Great expertise in muscle biology
- Broad technical platform to assess muscle functions in non-clinical/clinical studies
- Extensive human network in the muscle research field
- Experience in clinical development including ALS



Progress in the fast skeletal muscle activators

CK-2127107

- Fast skeletal troponin activator

CK-3672889

- Next-generation activator

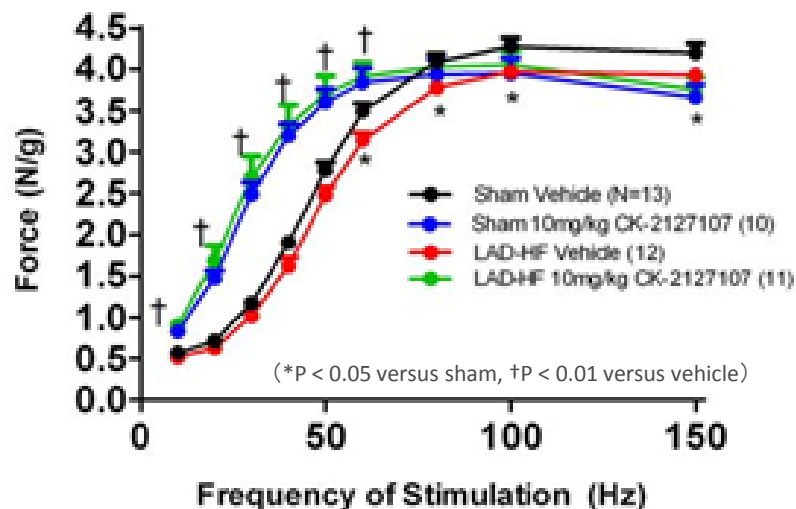
Program ▪ Disease	Development Progress	
	Pre-clinical	Clinical
CK-2127107 ▪ SMA, ▪ COPD		Ph2
CK-2127107 ▪ ALS		Ph2 ready
CK-3672889		





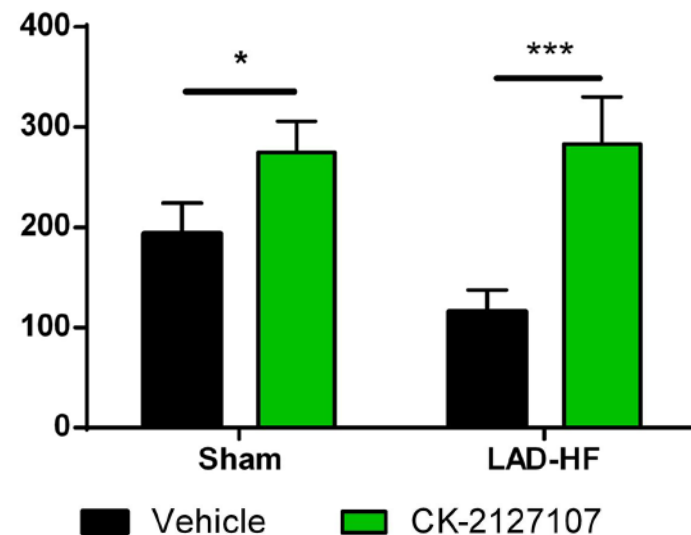
CK-2127107 improves muscle contractility and exercise tolerance in a rat model of heart failure

Isometric force-frequency



CK-2127107 significantly increased isometric tension in LAD-HF plantarflexor.

Time on rotarod (sec)



CK-2127107 significantly increases running performance in LAD-HF rats with exercise intolerance.

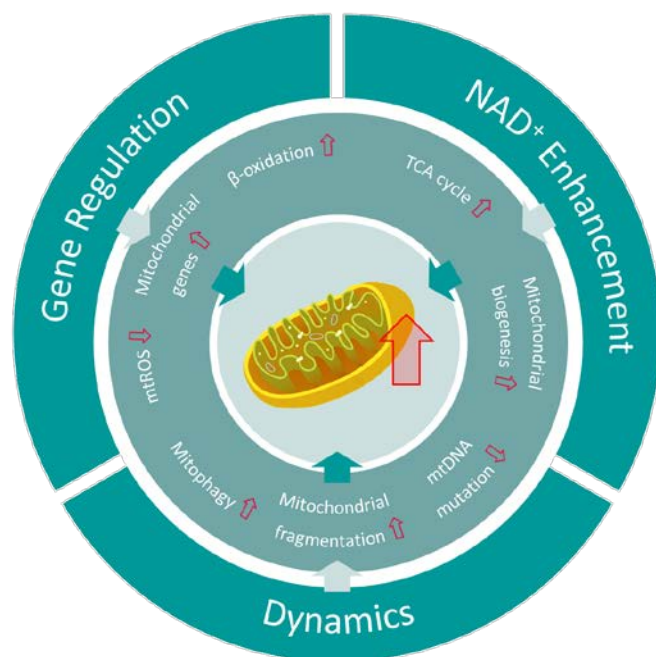
MUSCLE: Mitobridge COLLABORATION



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Create novel NMEs for broad indications by Mitobridge's proprietary strength of mitochondrial biology and biotech-style research

Activation of mito. function by multiple biological approach



Strength of Mitobridge

Biology-based approach

- Research platform based on mitochondrial biology
- Plural research pipeline by multiple approach

Biotech-style research

- Agile research using enriched network
- Hybrid R&D with Astellas' developmental capability

Scientific Advisory Board and talented researchers

- Research expertise based on mitochondrial biology
- Intake of newest science by prompt cooperation among researchers

Identify gene regulator "MTB-1" for clinical trial

MUSCLE: Mitobridge COLLABORATION



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Candidate (MTB-1) for clinical development is now on preparation toward IND for Duchenne muscular dystrophy therapy

Consultation with TREAT-NMD

Mitobridge had a meeting with TREAT-NMD advisory committee to discuss potential of MTB-1 for the treatment of DMD.

<http://www.treat-nmd.eu/resources/tact/reviews/past/mtb-1/>

Action of MTB-1 to activate mitochondrial function could be reasonable for the possible use in DMD treatment because mitochondrial dysfunction in muscle has been reported in DMD patients.

Additional experimental data to increase clinical benefits of MTB-1 and proactive investigation of regulatory guidance from the FDA and EMEA could accelerate early entry to clinical trials.

Development progress

Program • Disease	Development Progress	
	Pre-clinical	Clinical
MTB-1 • DMD		2017 IND scheduled
Other programs		

AGENDA

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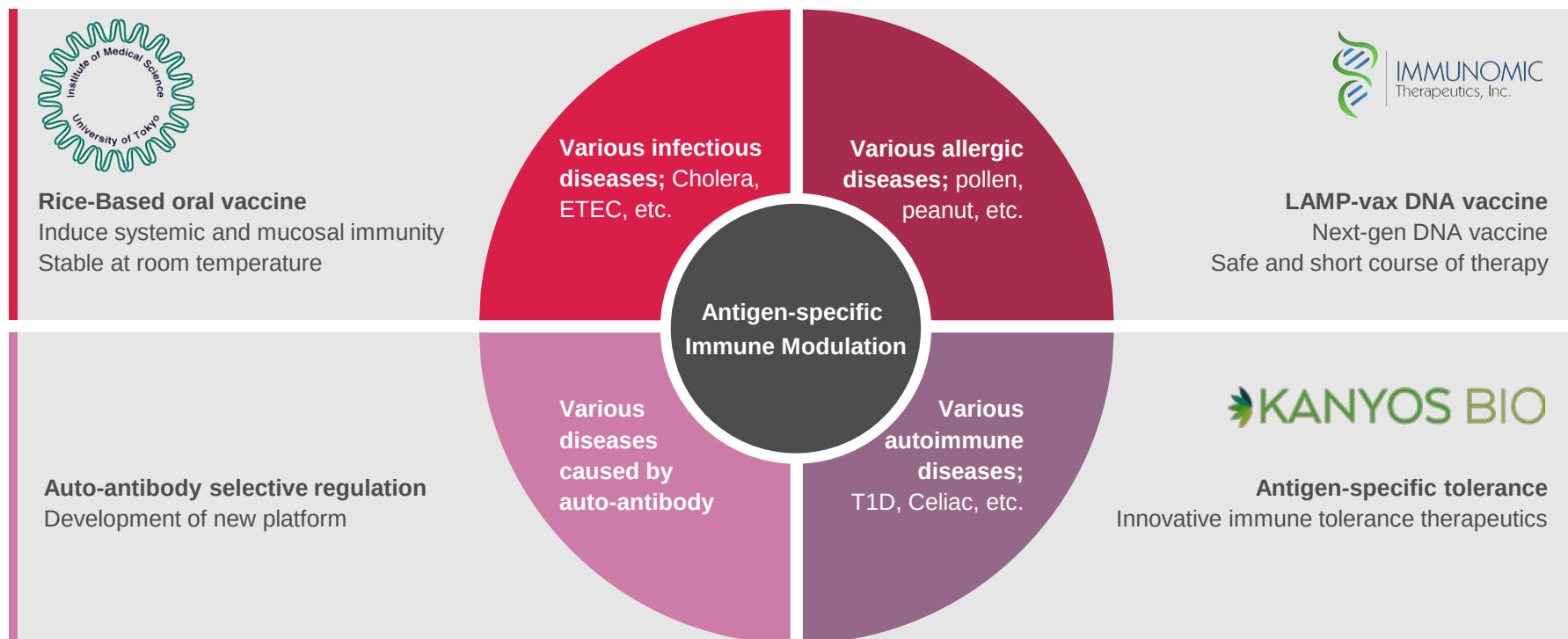
I Creating innovation

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IV **Therapeutic area: Immunology**

Develop an innovative platform which can achieve antigen-specific immune modulation, and create curative and safe therapeutics against allergy, autoimmune diseases and infectious diseases



IMMUNOLOGY: Immunomic Therapeutics COLLABORATION



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LAMP-vax DNA vaccine platform

Revolutionary Technology

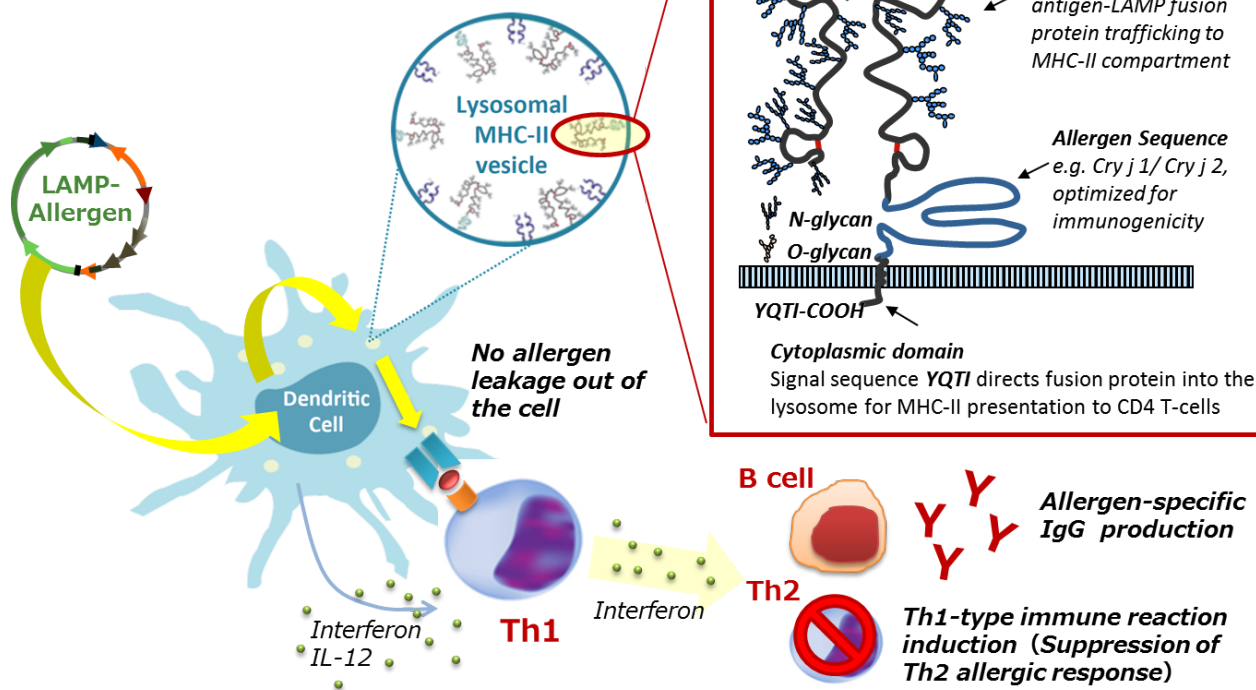
- LAMP-vax induce a robust Th1 immune response

High Safety and Convenience

- Short course curative therapy without systemic allergen exposure

Versatile platform

- Applicable to a wide variety of allergic diseases



IMMUNOMIC
Therapeutics, Inc.



IMMUNOLOGY: Immunomic Therapeutics COLLABORATION



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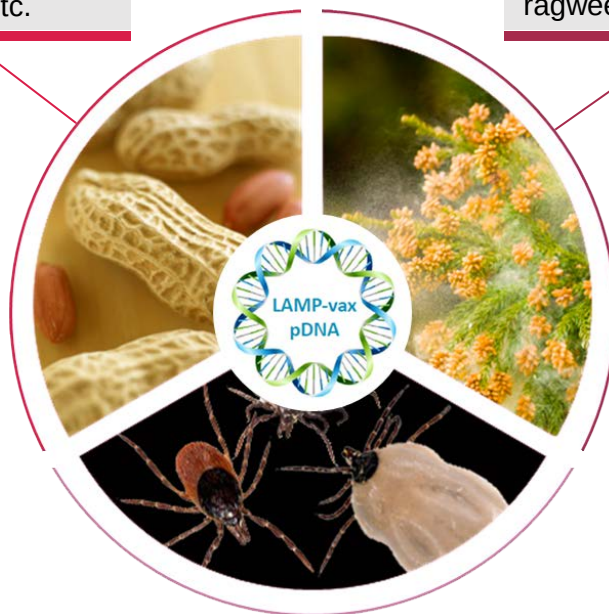
Versatile platform which can be applied to a wide variety of allergic diseases by changing inserted allergen DNA sequence

Food allergy

e.g. peanut, milk, wheat, egg, etc.

Seasonal pollen allergy

e.g. cedar, cypress, ragweed, grass, etc.



Perennial allergy

e.g. house dust mite, pet, mold, etc.

Program	Development Progress	
	Pre-clinical	Clinical
ASP0892 [peanut]		Ph1
Other food allergies		
ASP4070 [Japanese red cedar]		Ph1
Other seasonal allergies		
Perennial allergies		



IMMUNOMIC
Therapeutics, Inc.

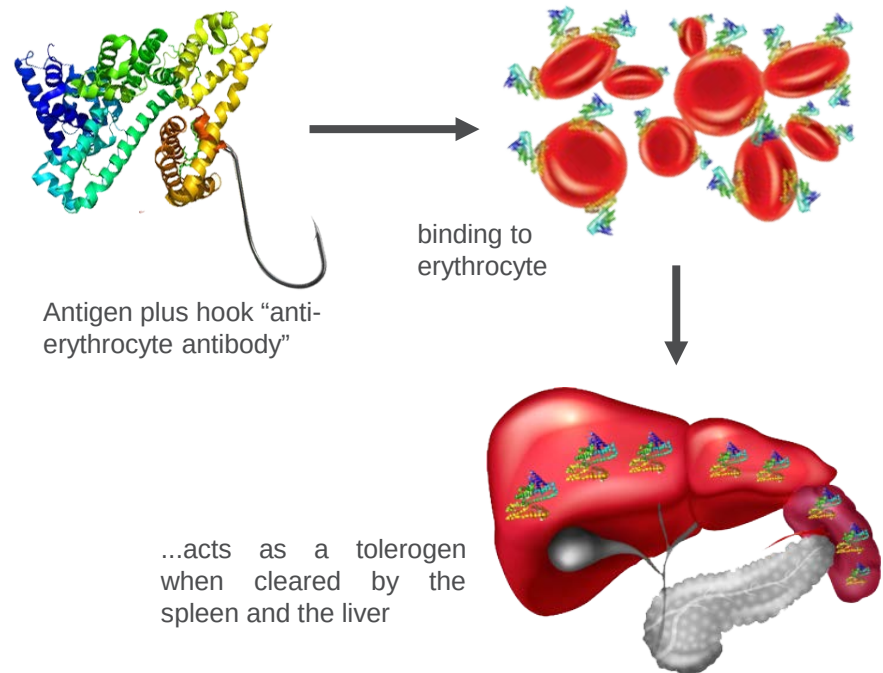




New platform for the induction of antigen-specific immune tolerance

- “Endogenous tolerogenic pathway” in liver and spleen is exploited to prevent autoimmunity
- The technology targets antigens to the surfaces of red blood cells in vivo; the associated antigens are processed to induce antigen-specific T cell deletion and Treg
- Applicable to a wide variety of autoimmune diseases whose pathogenic antigens are identified, including Type 1 Diabetes and Celiac Disease
- Additional tolerance induction platforms are being explored with Kanyos Bio
- Pre-clinical stage

Mechanism of action



Turn innovative science into value for patients by
**embodying outcome
of Network Research System.**

REGENERATIVE MEDICINE

R&D MEETING 2016



Robert Lanza, M.D.

Head of Astellas Global Regenerative Medicine

and Chief Scientific Officer Astellas Institute for Regenerative Medicine (AIRM)

December 8, 2016

AGENDA

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I Introduction

II Ophthalmology program
(Retinal pigment epithelium, Photoreceptor progenitors, Retinal ganglion progenitors and Corneal endothelium)

III Application in other fields
(Hemangioblast-derived MSCs and Vascular progenitors)

IV Joint research with academia in Japan

ADVANTAGE OF CELL THERAPY

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Cell Therapy has a huge potential in clinical usage

Information : Cell >>> Biotherapeutics > chemical compound

- **Safe** : Cell is an ultimate “natural product” of human origin
- **Efficacious** : Efficacy is not limited to depressing progression, but complete recovery of function is expected theoretically
- **Responsive** : Only cells recognize its environment and respond
ex. sugar sensor → insulin secretion by β -cells

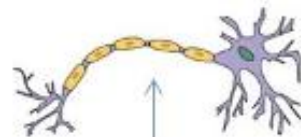
Advantages of PSC-derived Tissues in Regenerative Medicine

- Virtually unlimited supply of cells
- Can be derived under GMP conditions pathogen-free
- Can be produced with minimal batch-to-batch variation
- Can be thoroughly characterized to ensure optimal performance

PLURIPOTENT STEM CELLS (PSCs) – THE BODY’S MASTER CELLS

Neurons for neurodegenerative disorders

Skin and/or hair follicles for wounds, ulcers & hair loss



Retinal cell types for ocular diseases

Cardiac cells for heart disease



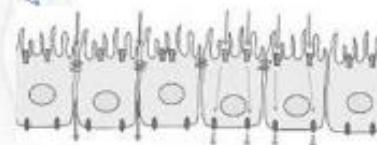
Alveolar cells for lung diseases

Hepatocytes for liver disease



Insulin-producing cells for diabetes

Blood cell types for hematologic disorders



Intestinal cells for Crohn's/irritable bowel syndrome



ADVANTAGE OF ASTELLAS INSTITUTE FOR REGENERATIVE MEDICINE (AIRM)

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Advanced technology that can establish fully-differentiated cells from pluripotent stem cells (PSCs) and strengths in clinical studies and manufacturing for cell therapy

Research

- Technology to establish differentiated target cells from PSCs that could provide functional replacement or trophic support to worn-out or dysfunctional cells and tissues
- Strong IP positions
- Cutting-edge science accepted by top journals

Development

- Expertise in cell-based therapy for high and unmet needs in ophthalmology
- 38 patients treated safely to date
- Active programs currently for macular degeneration (dry AMD and SMD)

Manufacturing

- Capabilities and track records to manufacture clinical grade cell product that was supplied to US and UK
- Strong process and analytical development capabilities (e.g. hyper sensitive impurity cell detection method, novel cell formulation)

CURRENT R&D PROGRAMS

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AIRM (US)

	Program	Potential Disease	Development Progress	
			Pre-clinical	Clinical
Renewable Pluripotent Stem Cells ES cell iPS cell next gen	Retinal pigment epithelium (RPE)	• Dry AMD • SMD		
	Photo-receptor progenitors (PhRPs)	• Retinitis pigmentosa • Macular degeneration		
	Retinal ganglion progenitors (RGPs)	• Glaucoma • Optic neuropathies		
	Hemangioblast-derived MSCs (HMCs)	• Autoimmune diseases • CNS/vascular indications		
	Vascular progenitors	• Critical limb ischemia • Pulmonary hypertension		
	Corneal endothelium	• Corneal diseases • Corneal injuries		

DDR RML (JP)

Other cell sources				
	Program	Potential Disease	Pre-clinical	Clinical
	Joint research with Kyoto Univ. CiRA	• Kidney diseases		
	Joint research with Osaka Univ.	(non-disclosure)		
	Other programs	(non-disclosure)		

AGENDA

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I

Introduction

II

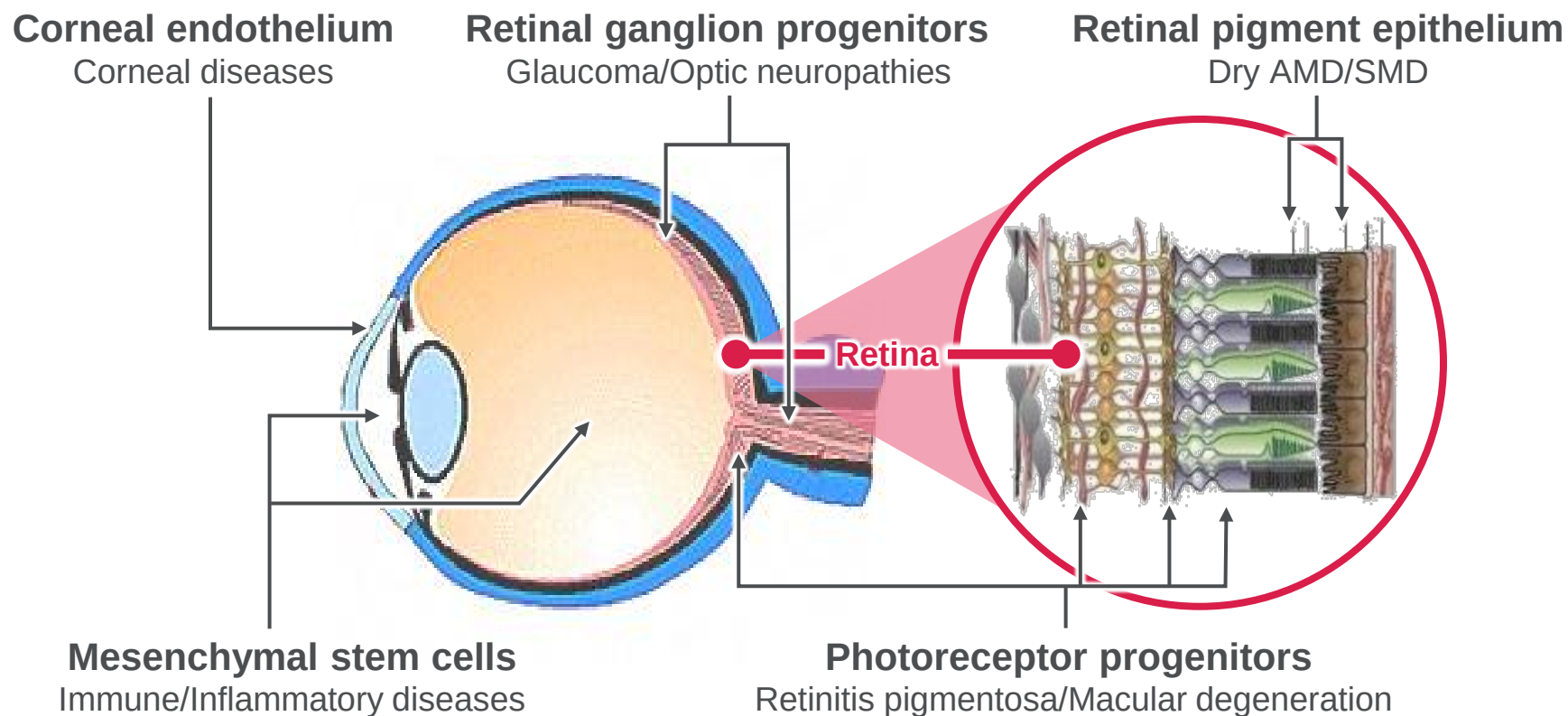
Ophthalmology program
(Retinal pigment epithelium, Photoreceptor progenitors,
Retinal ganglion progenitors and Corneal endothelium)

III

Application in other fields
(Hemangioblast-derived MSCs and Vascular progenitors)

IV

Joint research with academia in Japan



Vision loss costs \$3 Trillion worldwide



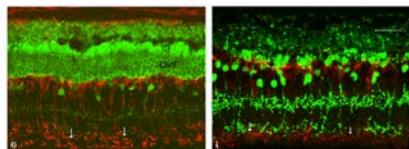
RPE

RPE PROGRAM - TRACK RECORD

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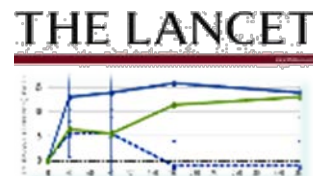
Start of human RPE program



Published first-ever paper showing hESC-RPE can prevent visual loss in animals



UK approval for Stargardts trial
NCT01469832



Paper on long-term safety and possible efficacy signal of hESC-RPE



Acquired Ocata Therapeutics
Changed the name to AIRM

2003

2004

2006

2010

2011

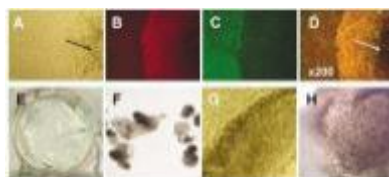
2012

2014

2015

2016

Published first-ever paper describing the derivation and characterization of RPE from human pluripotent stem cells



FDA approval for Stargardts trial
NCT01345006

FDA approval for dry-AMD trial
NCT01344993

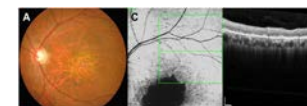


KFDA approval for Stargardts & dry AMD trials in South Korea

Published first-ever report of the safety of pluripotent stem cells (hESC-RPE) in humans with any disease

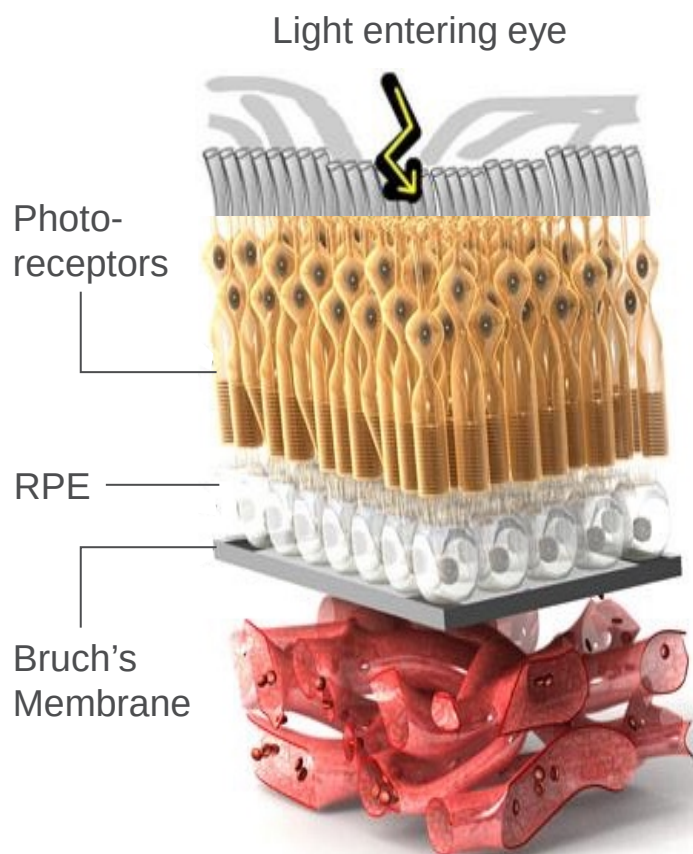


Study published showing hESC-RPE safe in Asian patients



RPE – LIFE SUPPORT TO PHOTORECEPTORS

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Function of RPE Layer

- Provides critical nutrients, growth factors, ions and water
- Recycles photopigments & vitamin A
- Phagocytosis of photoreceptor fragments
- Detoxifies photoreceptor layer
- Prevents abnormal blood vessel growth
- Maintains Bruch's Membrane
- Absorbs stray light and protects from UV

RETINAL DEGENERATIVE DISEASES

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AMD & SMD are the leading causes of adult & juvenile blindness in the developed world

- Number of people with AMD is projected to increase to 288 million worldwide by 2040
- SMD & dry AMD (which accounts for 80-90% of all AMD cases) are currently untreatable
- In US alone, the economic burden of vision loss/blindness is expected to reach \$717B by 2050



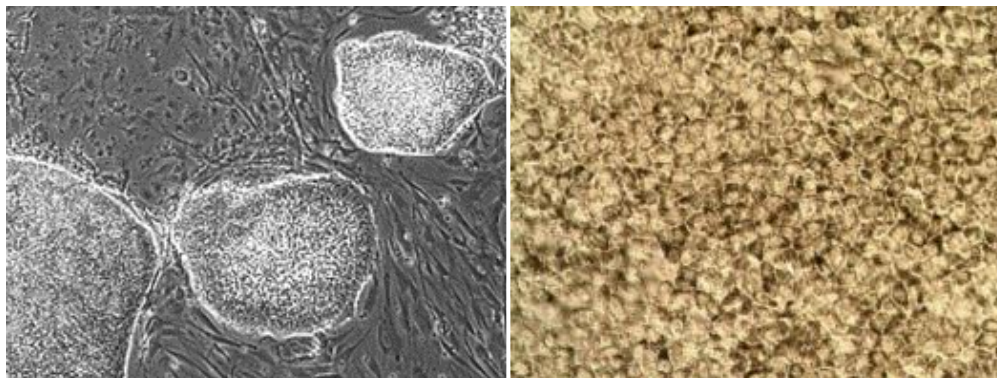
AIRM successfully completed two Phase I/II clinical trials in the U.S. using RPE derived from hESCs to treat macular degeneration:

- Dry AMD
- SMD

Completed the only clinical trial in Europe using pluripotent stem cells hESC-RPE to treat SMD

RPE can be reliably generated from embryonic stem cells

- We have studied dozens of hESC lines – all reproducibly generate RPE lines that can be passaged, characterized, and expanded
- We have secured an extensive patent protection



hESC

RPE

NEXT STEPS FOR AIRM RPE PROGRAM

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***Take a new step toward product launch:
Phase-Ib/II dose-ranging and proof-of-concept trial for dry AMD is
planned to start with a new ES cell line and formulation in 1H/2017***

Advantages of new cell line and formulation

- Comparable preclinical data to RPE cells derived from the previous ES cell line
- Fully comport with the FDA tissue donor compliance regulations revised in 2005
- Non-xenogeneic product which allows to eliminate patient blood sampling
- Larger cell bank which ensures a stable supply
- Longer shelf-life which enables centralized DP preparation
- Protective effect on cells which reduces cell loss during extrusion and debris at injection site
- More clinical trial feasibility

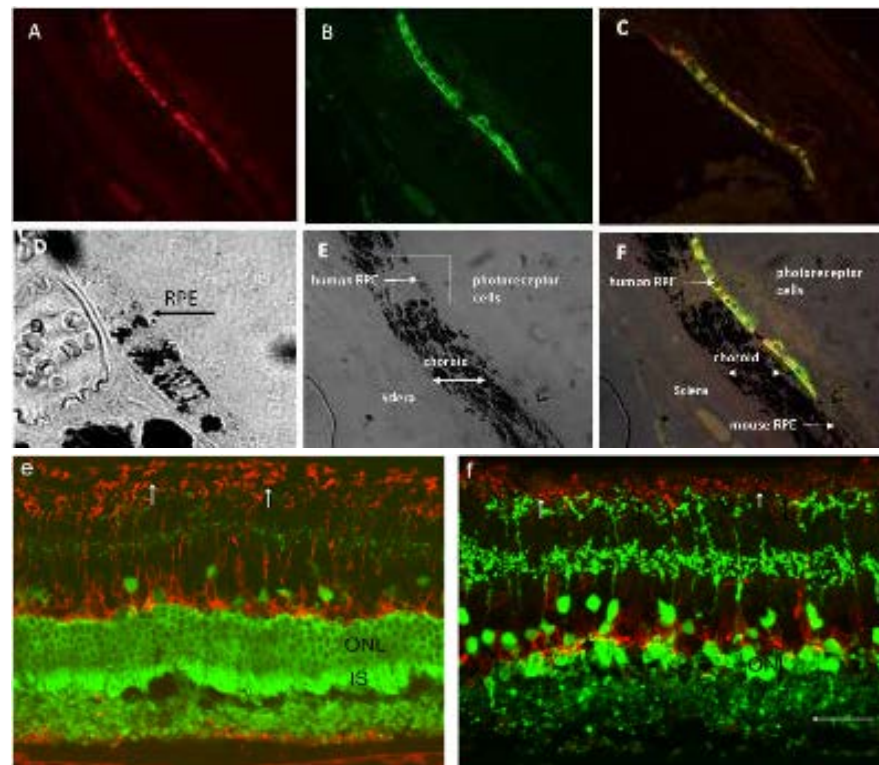
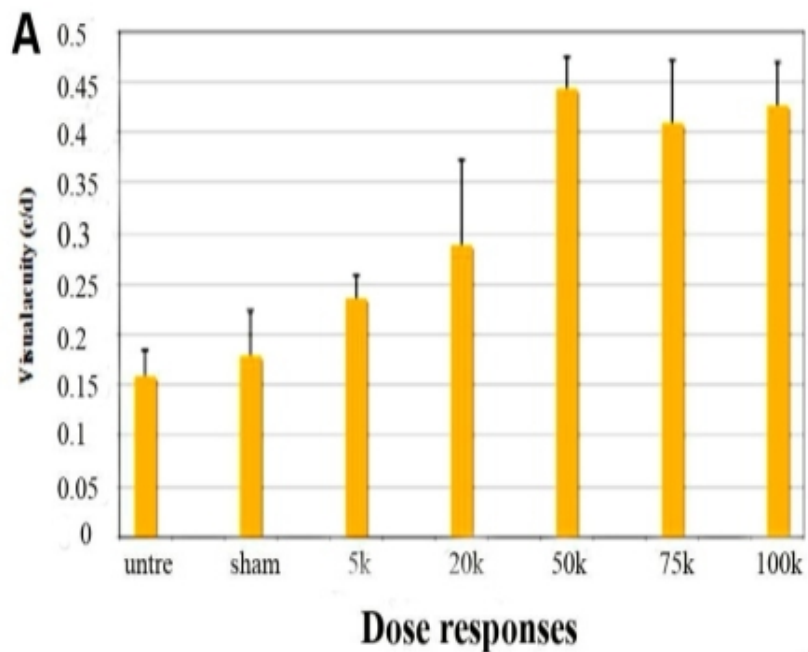
Phase-II PORTRAY study for dry AMD with the conventional cell line has been suspended due to cell line change



RPE IMPROVE VISUAL ACUITY & RESCUE PHOTORECEPTORS IN ANIMALS

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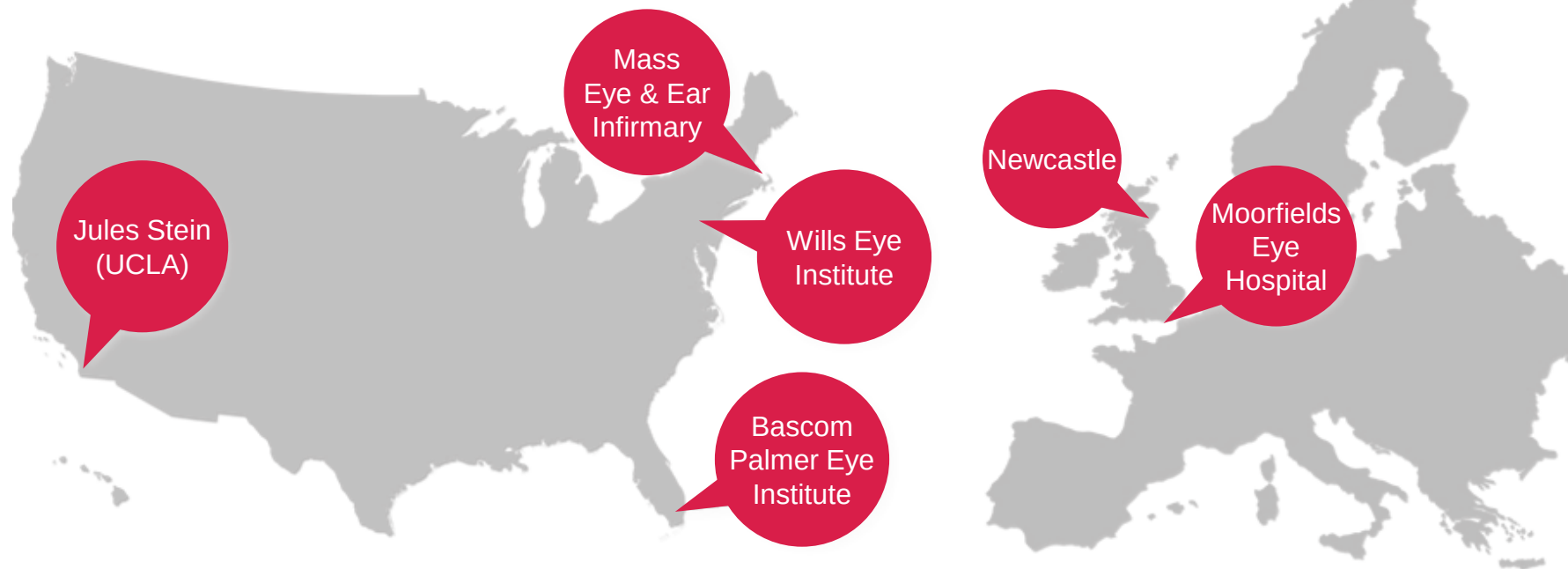
RCS Rats (d90)



hESC-RPE CLINICAL TRIALS

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Treated 38 patients and confirmed safety



US Clinical Trial

Dry AMD

Thirteen patients treated
(50K – 200K cells)

SMD

Thirteen patients treated
(50K – 200K cells)

European Clinical Trial

SMD

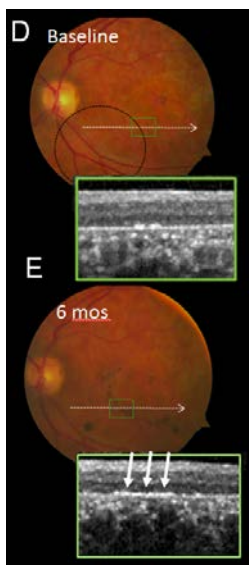
Twelve patients treated
(50K – 200K cells)



THE LANCET

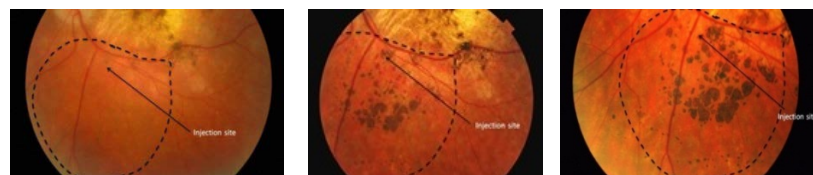
Human embryonic stem cell-derived retinal pigment epithelium in patients with age-related macular degeneration and Stargardt's macular dystrophy: follow-up of two open-label phase 1/2 studies

Steven D Schwartz, Carl D Regillo, Byron L Lam, Dean Elliott, Philip J Rosenfeld, Nind Z Gregori, Jean-Pierre Hubschman, Janet L Davis, Gad Heilwell, Marc Sporn, Joseph Maguire, Roger Gay, Jane Bateman, Rosaleen M Ostrick, Debra Morris, Matthew Vincent, Eddy Anglade, Lucian V Del Priore, Robert Lanza



Overall Results

- No safety issues related to the transplanted cells
- Clear signs of long-term engraftment & survival



DAY 1

2 MONTHS

6 MONTHS

During the 1-year follow-up period, patients in both the SMD and dry AMD clinical trials have shown significant improvement in visual acuity in the RPE-treated eyes

- 8/18 (44%) patients improved >3 lines
- 3/18 (17%) patients improved 1-3 lines
- 6/18 (33%) patients remained stable
- 1/18 (6%) patients decreased >1 line

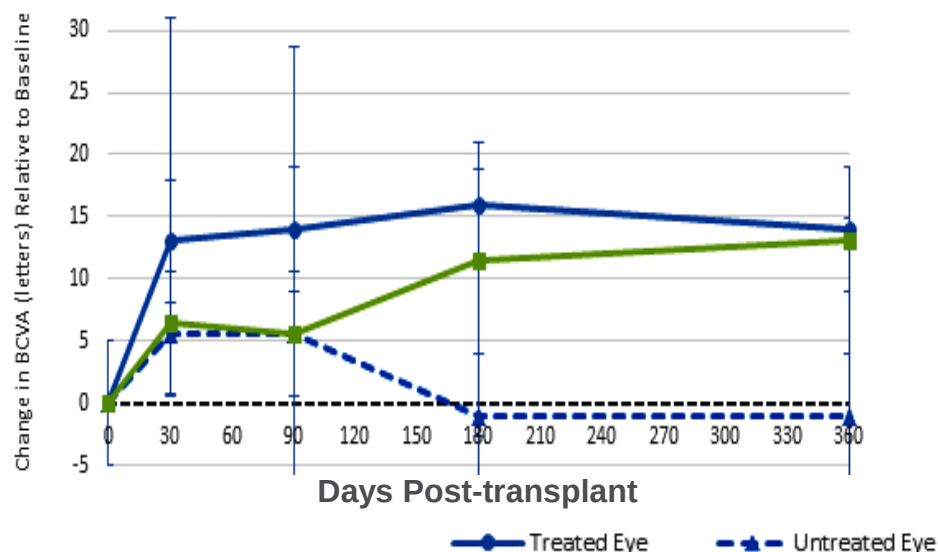
Untreated eyes did not show similar improvements in visual acuity during the same time period

PHASE I/II STUDY RESULTS

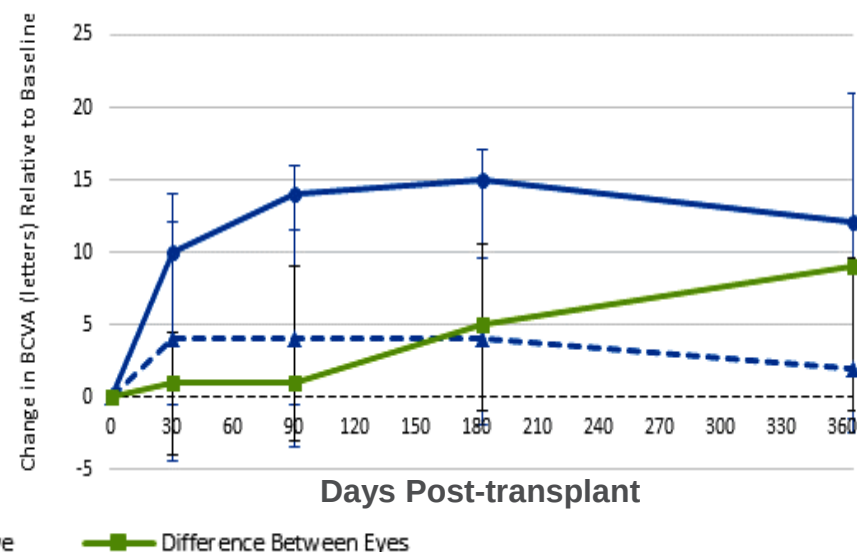
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Confirmed positive change in BCVA in AMD & SMD patients relative to baseline

AMD Patients

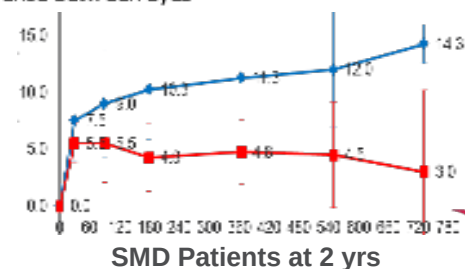


SMD Patients



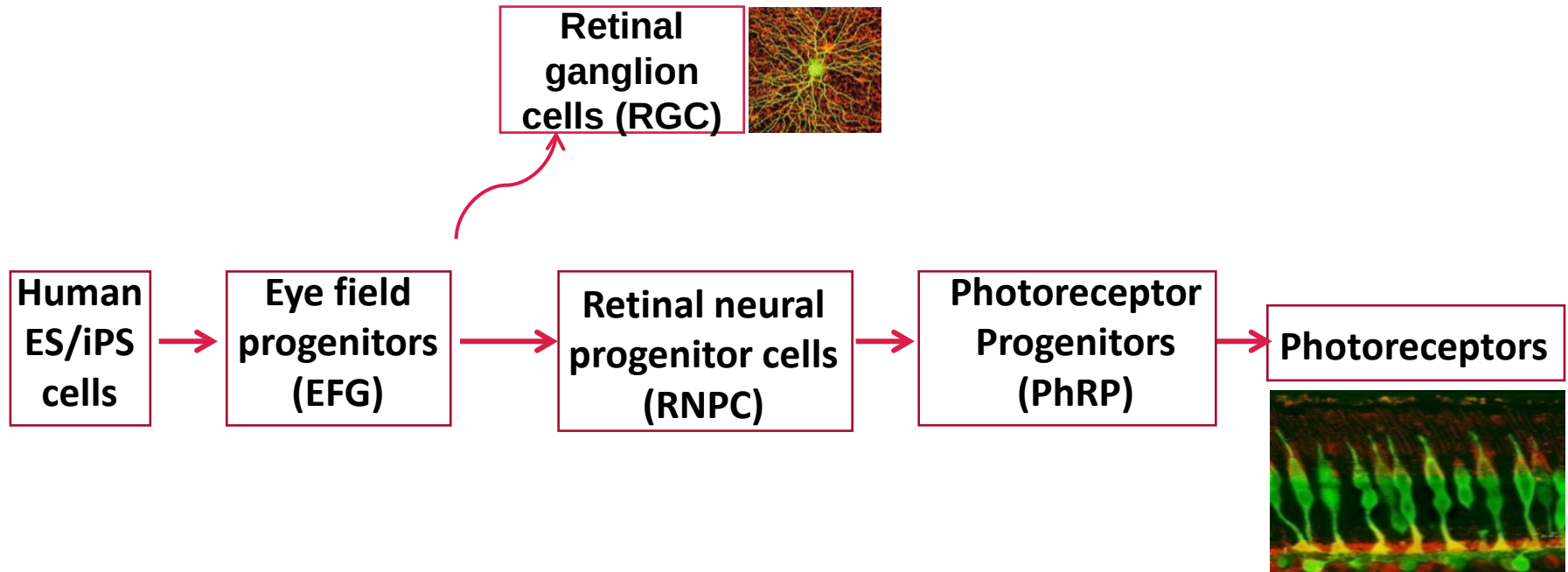
UPDATE:

BCVA improvement continues to be sustained 2–3 years after transplantation in both AMD & SMD patients



GENERATION OF NON-RPE RETINAL CELL TYPES FROM PSCs

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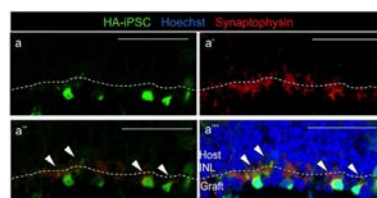
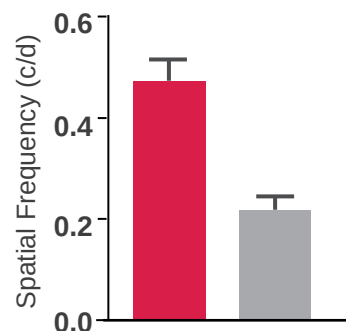
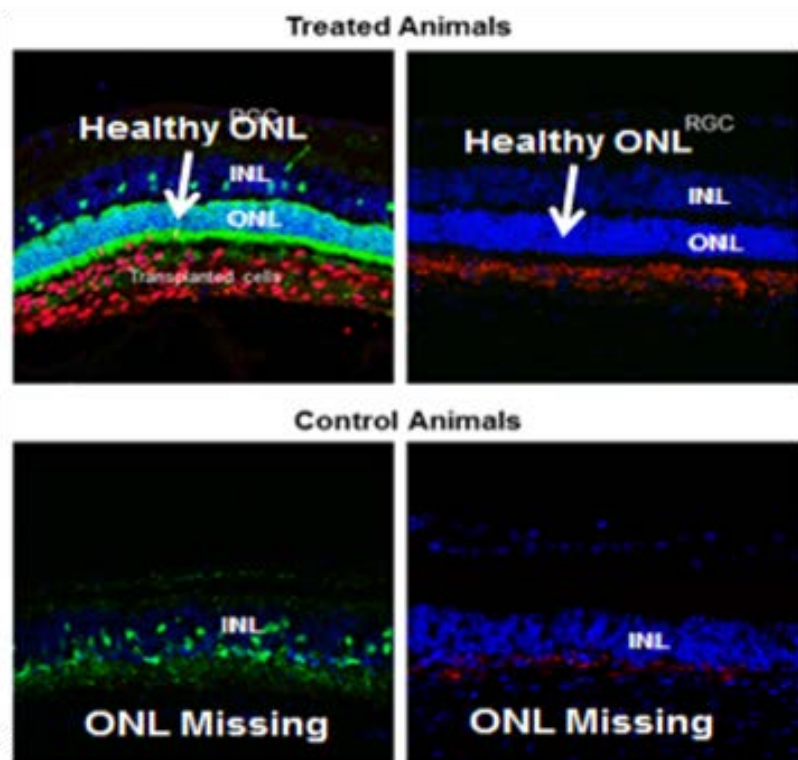
- 3-4 month differentiation process from PSCs resulting in high purity (~95%) PhRPs
- 2 month differentiation process from PSCs resulting in high purity (~99%) RGP

PHOTORECEPTOR PROGENITORS

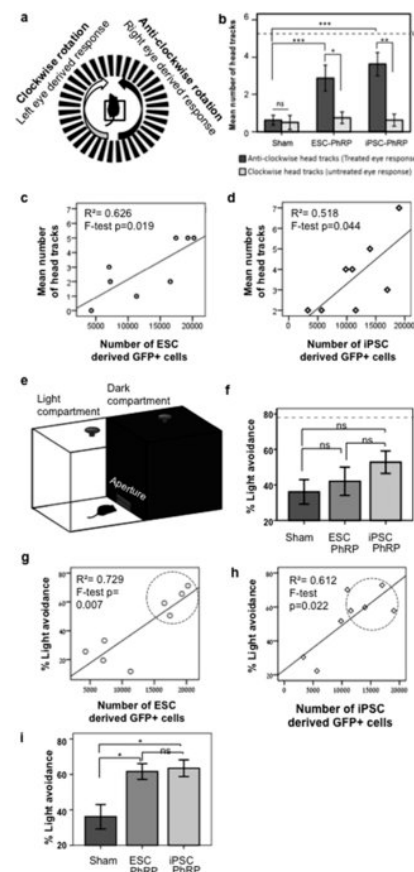
PHOTORECEPTOR PROGENITORS IN RCS RATS & Rd1 MICE

21

Photoreceptor progenitors restore vision in completely blind animals



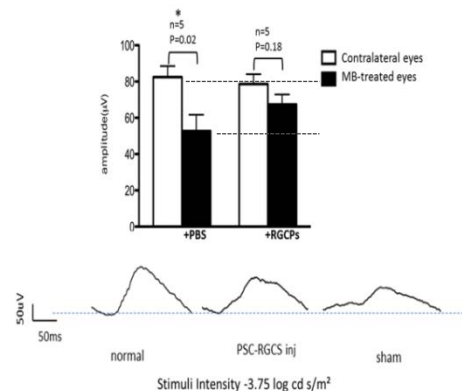
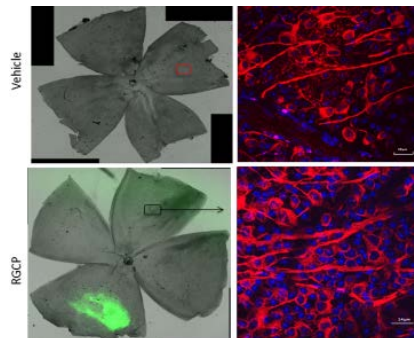
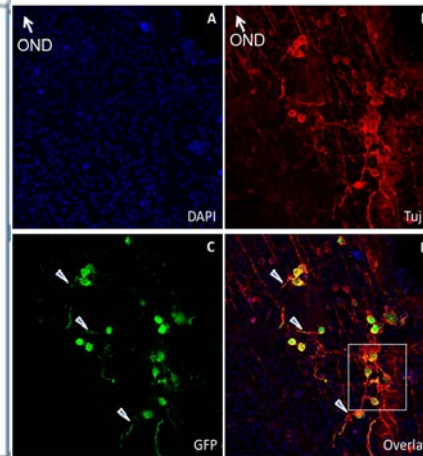
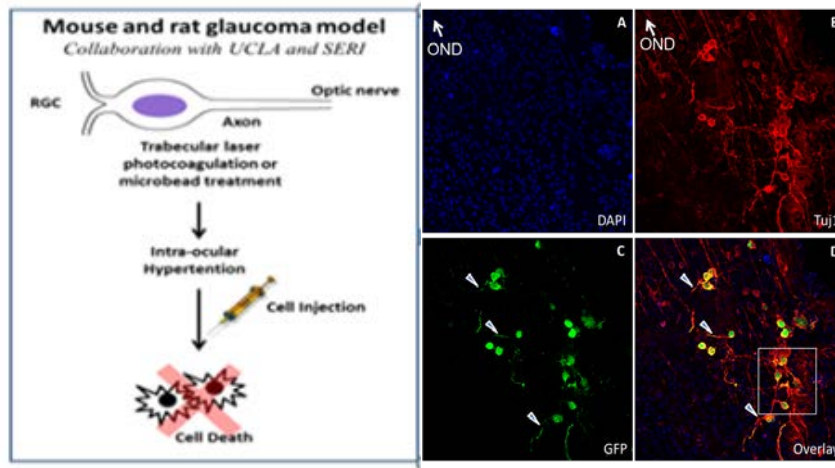
Graft-Host Connectivity
Synaptophysin is localized between the host and graft indicating synaptic transmission between the grafted cells & host retina (dashed line delineates the boundary between them).



RETINAL GANGLION PROGENITORS

RGP TRANSPLANTATION IMPROVES HOST RGC SURVIVAL IN MICROBEAD/MOUSE GLAUCOMA MODEL

23



RGPs enhance pSTR amplitude in glaucoma mice

pSTR is the most sensitive indicator of RGC function in the mouse

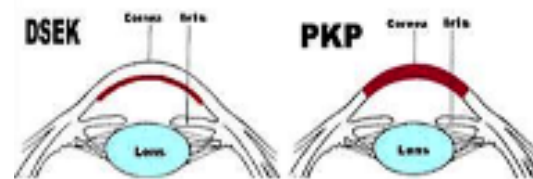
CORNEAL ENDOTHELUM

CORNEAL REPAIR: CORNEAL ENDOTHELIUM DERIVED FROM hESCs

25

Corneal endothelial cells (CECs) can be generated from hESCs that closely resemble normal adult CECs

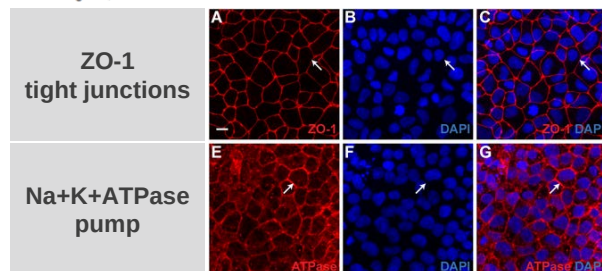
- 10 million people with corneal blindness
- Cornea the most transplanted organ (1/3 due to endothelial failure)
- Solutions: Tx of whole cornea “Penetrating Keratoplasty”
More popular: Tx corneal endothelium & Descemet’s membrane (DSEK)



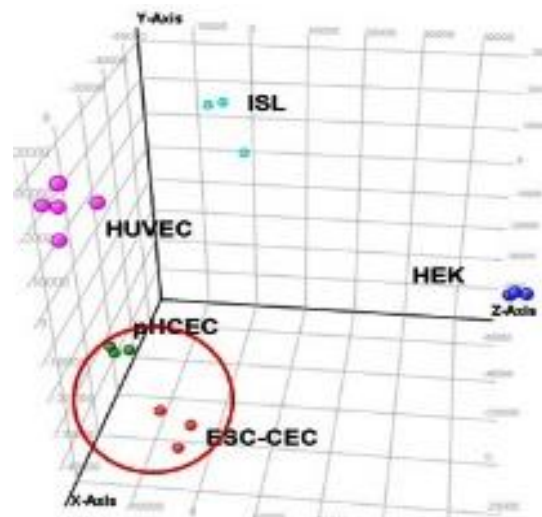
RESEARCH ARTICLE

Efficient Generation of Human Embryonic Stem Cell-Derived Corneal Endothelial Cells by Directed Differentiation

Kathryn L. McCabe¹, Noelia J. Kunzevitzky^{2,3,4}, Brian P. Chiswell^{1*}, Xin Xia⁴, Jeffrey L. Goldberg^{2,4,5}, Robert Lanza^{1*}



hESC-CEC resemble normal CEC



Global gene analysis: hESC-CEC & adult-CECs almost identical



AGENDA

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I Introduction

II Ophthalmology program (Retinal pigment epithelium, Photoreceptor progenitors, Retinal ganglion progenitors and Corneal endothelium)

III **Application in other fields (Hemangioblast-derived MSCs and Vascular progenitors)**

IV Joint research with academia in Japan



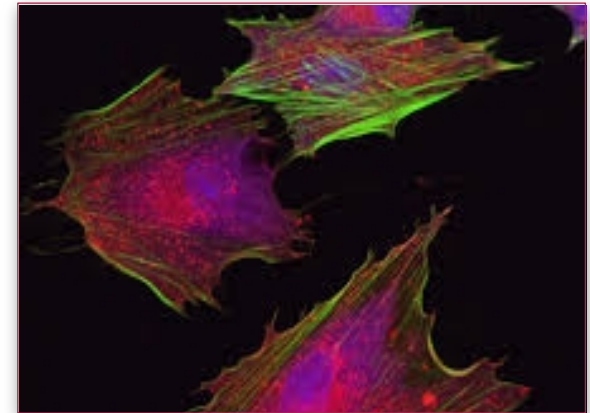
HMCs

HEMANGIOBLAST-DERIVED MESENCHYMAL STEM CELLS (HMCs)

28

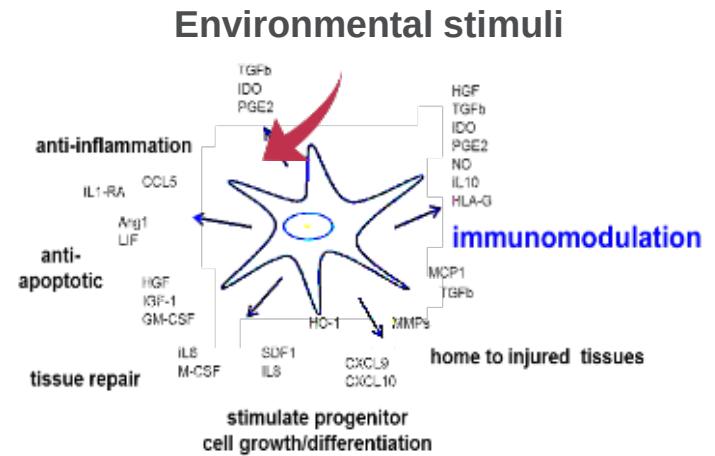
HMCs more youthful (30,000X greater expansion than BM-MSCs) and potent than tissue-derived MSCs. Proof-of-concept demonstrated in six pre-clinical models

- Developed an efficient method of HMC generation
- HMCs are immunomodulatory/no need for immunosuppression
- Cells persist transiently/minimal risk of tumorigenicity
- Platform technology (therapeutic potential shown in 6 different indications)



HMCs superior to other clinically used MSCs

- Greater therapeutic potency vs. BM & CB MSCs
- Better migratory properties vs. BM & CB MSCs
- Reduced IL6 levels vs BM & CB MSCs
- Unlimited (and non-variable) cell source



HMCs (BUT NOT BM-MSCs) DRAMATICALLY REDUCE CLINICAL SYMPTOMS IN EAE MODEL OF MS

29

Cell
PRESS

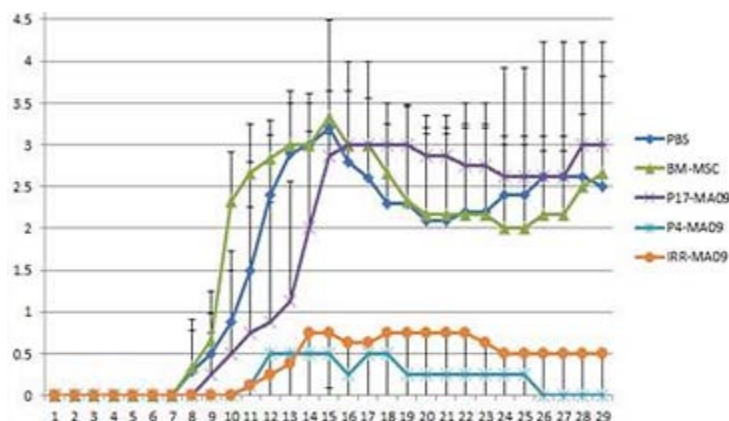
Stem Cell Reports
Article

ISSCR

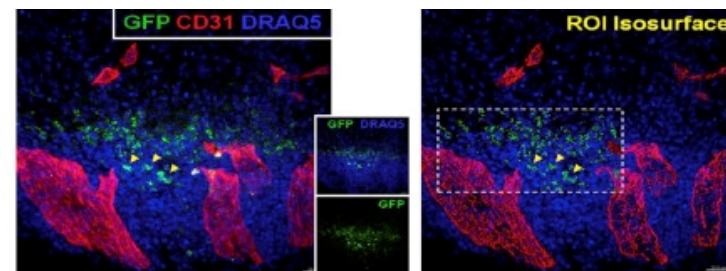
OPEN ACCESS

Human ESC-Derived MSCs Outperform Bone Marrow MSCs in the Treatment of an EAE Model of Multiple Sclerosis

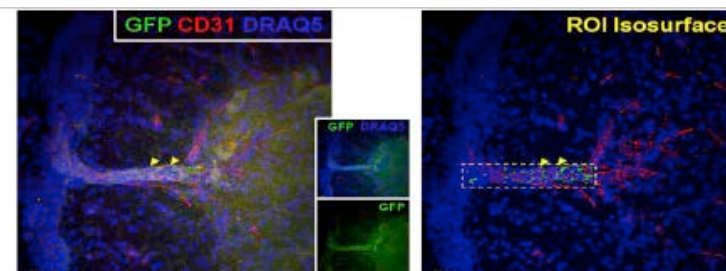
Xiaofang Wang,^{1,2,7} Erin A. Kimbrel,^{3,7} Kumiko Ijichi,⁴ Debayon Paul,⁵ Adam S. Lazorchak,² Jianlin Chu,³ Nicholas A. Kouris,³ Gregory J. Yavanian,³ Shi-Jiang Lu,³ Joel S. Pachter,⁵ Stephen J. Crocker,⁴ Robert Lanza,^{3,*} and Ren-He Xu^{1,2,6,*}



hES-MSC
(Envy-GFP+)
Day 14



BM-MSC#5
(GFP+)
Day 14



- HMCs dramatically reduce clinical symptoms of EAE
 - both prophylactic and therapeutic inhibition
- *In vitro* inhibition of T-cell function
- Differential cytokine expression (HMCs vs BM-MSCs)
- Differential ability to migrate into damaged tissues (hESC-MSCs vs BM-MSCs)

astellas

EAE: experimental autoimmune encephalomyelitis

Lanza and colleagues, Stem Cell Reports 2014 Jun 6;3(1):115-30. doi: 10.1016/j.stemcr.2014.04.020. eCollection 2014.

HMCs HAVE POTENT THERAPEUTIC EFFECT IN ANIMALS WITH LUPUS AND CROHN'S DISEASE

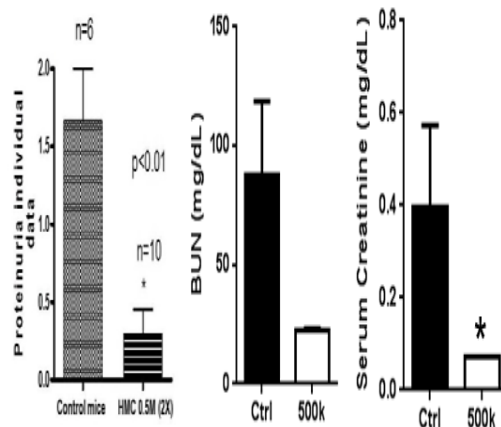
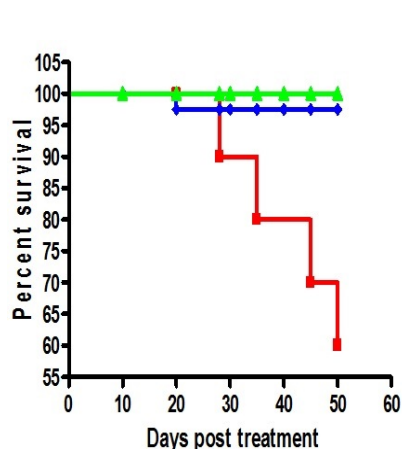
30

SCIENTIFIC
REPORTS

nature

Human embryonic stem cell-derived mesenchymal cells preserve kidney function and extend lifespan in NZB/W F1 mouse model of lupus nephritis

Austin Thiel, Gregory Yavanian, Maria-Dorothea Nastke, Peter Morales, Nicholas A. Kouris, Erin A. Kimbrel & Robert Lanza

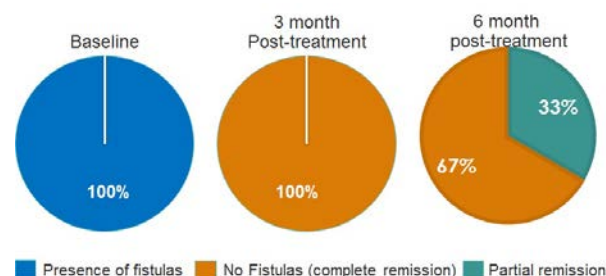


Research Article

For reprint orders, please contact: reprints@futuremedicine.com

Regenerative
Medicine

Treatment of perianal fistulas with human embryonic stem cell-derived MSCs: a canine model of human fistulizing Crohn's disease

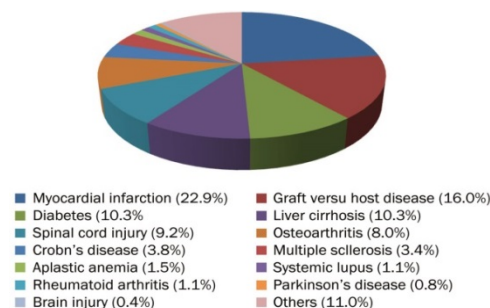


POTENTIAL THERAPEUTIC APPLICATIONS FOR MSCs

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- >100 autoimmune diseases
- Multiple Sclerosis
- Osteoarthritis
- Lupus
- Aplastic Anemia
- Crohn's Disease/IBS
- Chronic Pain
- Limb Ischemia
- Heart Failure/MI
- Stroke
- Graft-versus-host Disease
- Spinal Cord Injury
- Liver Disease
- Kidney Disease
- Emphysema/Pulmonary Diseases
- Wound healing (ulcers/decubitus/burns)
- HSC engraftment/irradiated cancer patients
- Eye diseases (uveitis, retinal degeneration, glaucoma)

Percentages of diseases now treated with MSCs



hES/hiPS-MSCs are ideal for clinical translation

- No need for immunosuppression
- Persist transiently
- Can be irradiated

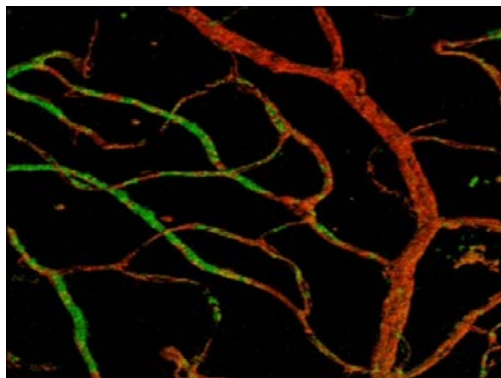
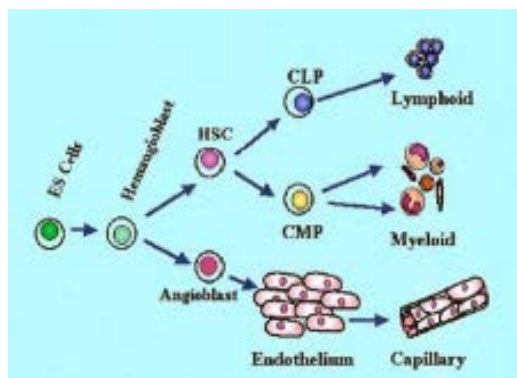
VASCULAR PROGENITORS

Vascular progenitor cells generated from PSCs repair vascular injury

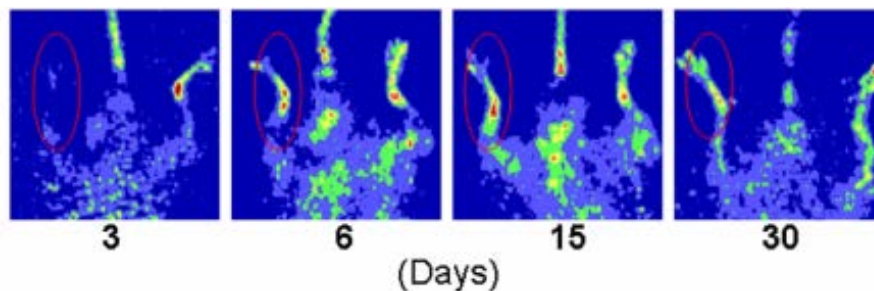
nature **methods**

Generation of functional hemangioblasts from human embryonic stem cells

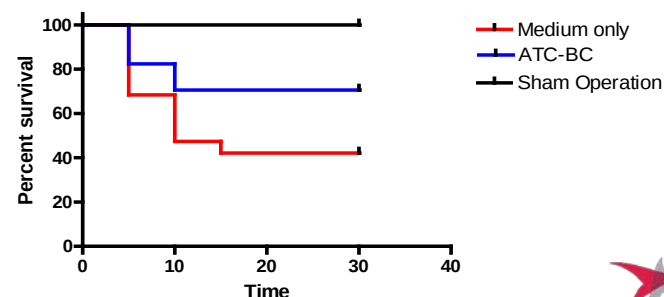
Shi-Jiang Lu¹, Qiang Feng¹, Sergio Caballero², Yu Chen³, Malcolm A S Moore³, Maria B Grant² & Robert Lanza¹



Hemangioblasts restore blood flow to ischemic limbs and cut mortality rate after severe MI in half



Survival of Data 1: Survival proportions



AGENDA

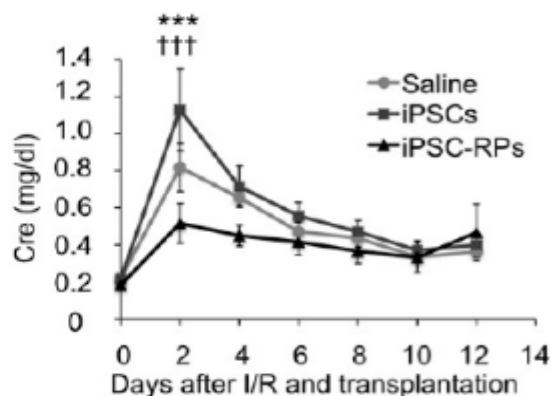
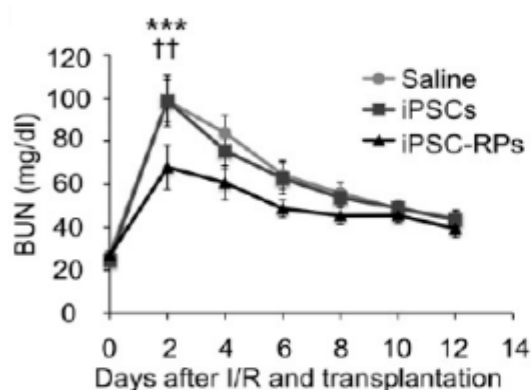
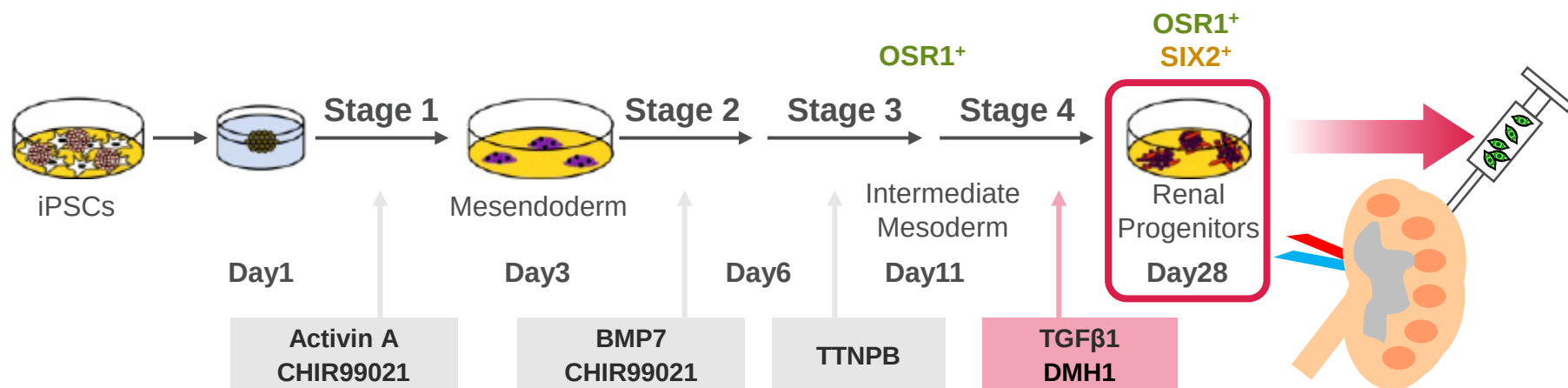
34

- I Introduction
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(Retinal pigment epithelium, Photoreceptor progenitors, Retinal ganglion progenitors and Corneal endothelium)
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(Hemangioblast-derived MSCs and Vascular progenitors)
- IV **Joint research with academia in Japan**

COLLABORATION WITH PROF. OSAFUNE, CiRA, KYOTO UNIVERSITY ON CELL THERAPY FOR KIDNEY DISEASES

35

Explore the possibility to develop new cell-based therapies for renal diseases



Transplantation of human iPSC-derived renal progenitors ameliorated acute kidney injury (AKI) in mouse model



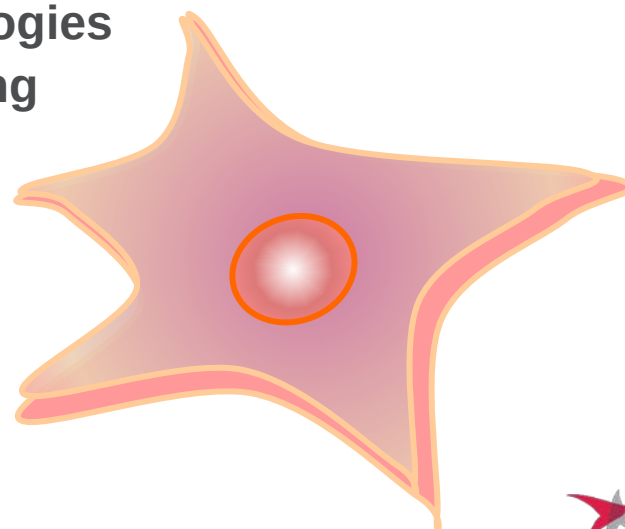
Osaka University and Astellas establish joint research chair for R&D on next-generation cell therapy

Osaka University



With a view developing fundamental technologies for next-generation cell therapies and bringing those technologies into practical use

- Develop cell sources
- Develop cell processing technologies
- Make cells highly functional
- Enhance therapeutic effects



Turn innovative science into value for patients by

**maximizing the potential of
regenerative medicine.**

CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING INFORMATION

In this material, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future performance of Astellas. These statements are based on management's current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas' intellectual property rights by third parties.

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