



Advancing Stem Cell Science– CIRM’s Scientific Scope and Programs

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Senior Vice President, Research and Development

Presentation to CFAOC
February 20, 2013

CIRM's Vision and Strategy

Mission

“To support and advance stem cell research and regenerative medicine under the highest ethical and medical standards for the discovery and development of cures, therapies, diagnostics, and research technologies to relieve human suffering from chronic disease and injury”

Deliver (2016+)

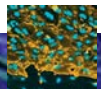
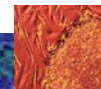
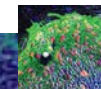
- Facilitate commercialization of therapies
- Advance therapies to patients
- Enable business model for stem cell-based therapies

Focus (2011-2016)

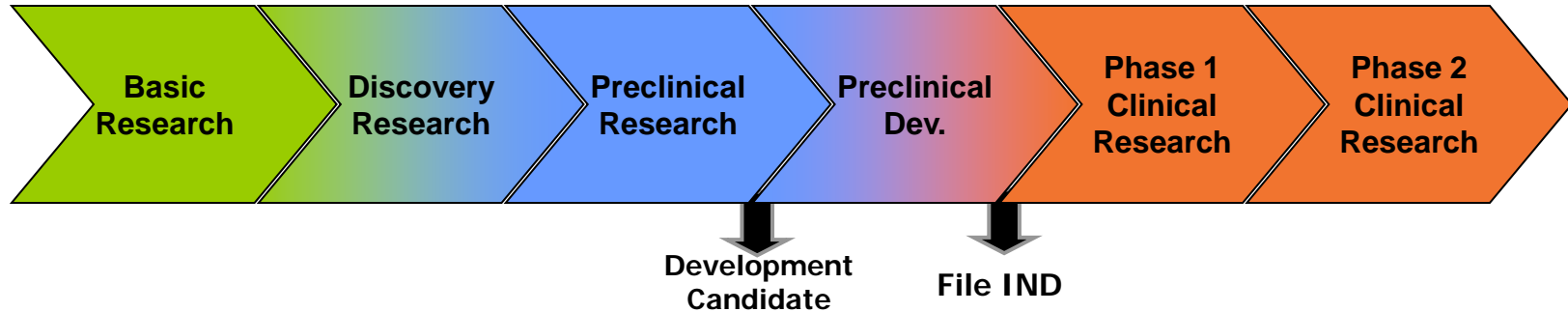
- Prioritize projects and investments
- Drive clinical trials for patients to generate preliminary evidence of therapeutic benefit
- Develop partnerships

Explore (2004-2010)

- Fund broad number of diseases and projects
- Establish foundation for leadership in stem cell research



Where have the \$ been invested? CIRRM's research funding commitment



Infrastructure: Facilities & Cores - \$343.0 MM

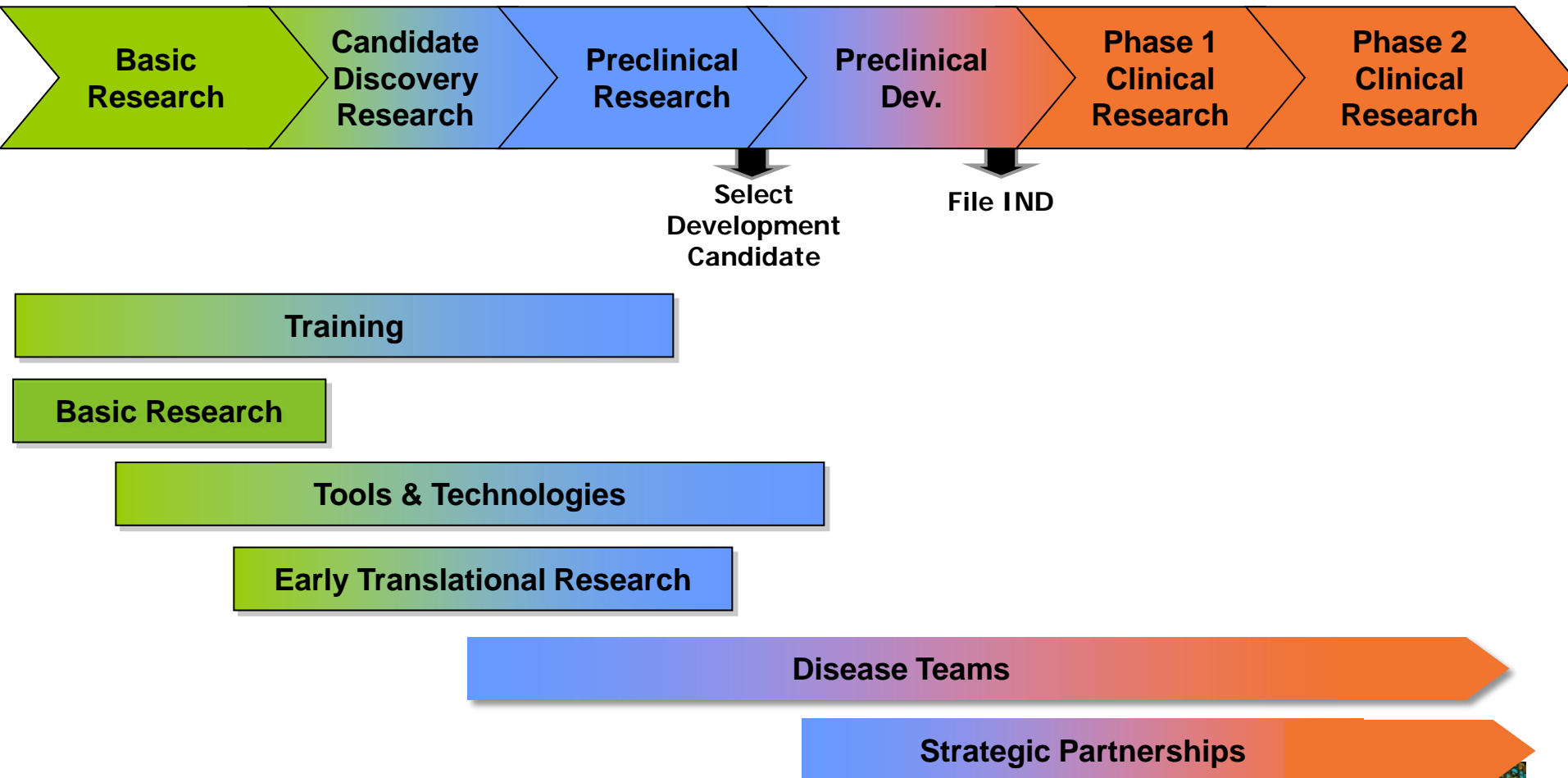
Infrastructure: Intellectual - \$379.0 MM

Pipeline: Foundational Research - \$337.1 MM

Pipeline: Translational Research - \$675.0 MM



CIRM's core programs provide a pathway spanning scientific advances to therapies



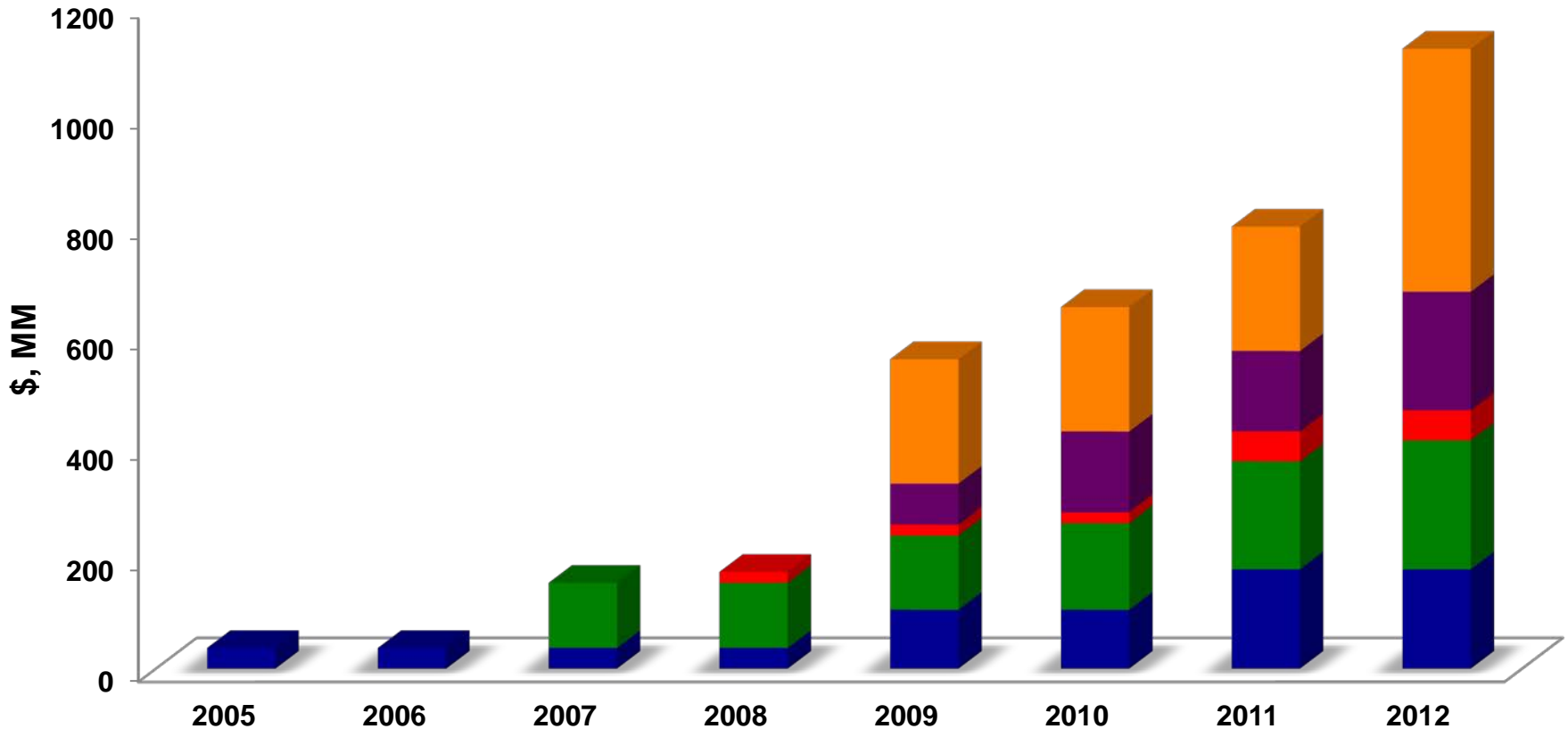
CIRM activities towards our mission



- Over 560 research and facilities awards to over 60 institutes and companies
- 12 new institutes and centers of regenerative medicine
- Over 1200 major scientific papers published
- Over 130 new major stem cell researchers in California
- 77 translational/development programs
 - 51 Early Translation programs, 24 Disease Teams, 2 Strategic Partnership programs
- \$1.7 B awarded



Cumulative ICOC approved funding in core programs



■ Training ■ Basic Research ■ Tools & Technology ■ Early Translation ■ Disease Teams

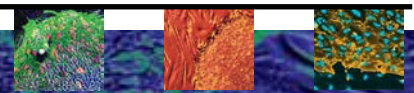
Not shown - Facilities \$270.9 M ICOC approved 2008 (\$518.9M from institutions);

Shared Labs \$72M ICOC approved (\$50.5M in 2007, and \$21.5M for 3 year extension 2011)

Breakdown: CIRM Training & Bridges Program Initiatives



RFA (Year Approved by ICOC)	# of Awards	Funds Approved by ICOC (MM)
Training	33	\$130.9
Training I (2005)	16	\$38.9
Training II (2008)	17	\$45.2
Training Extensions (2011)	17 (from Training II)	\$46.8
Bridges	16	\$50.6
Bridges I (2008)	16	\$24.0
Bridges Extensions (2011)	16 (from Bridges I)	\$26.6
Totals	49	\$181.5



CIRM Training & Bridges Programs

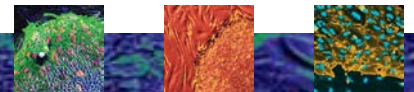


Training: Predoctoral candidates , post doctoral and clinical fellows

- Mentored laboratory stem cell research
- Course work: Stem cell biology – application to health and disease; ethical legal and social aspects of stem cell research
- To date: 635 CIRM Scholars at 18 institutions, 300 labs

Bridges: Undergraduate, Master's degree candidates especially from CSU and community colleges

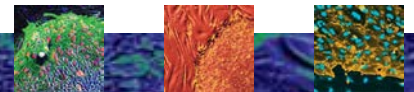
- Shared Lab Stem Cell Techniques course
- Mentored internships stem cell research in laboratories in research-intensive universities and biotech companies
- To date: 482 interns from 16 institutions
- Survey 2011: 52% of 163 interns had jobs; 26% enrolled or accepted into graduate, professional programs



Training Program I: CIRM Scholar



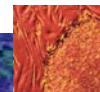
- Ann Zovein, MD
 - UCLA Training Program
 - Trained as a clinical fellow under Dr. Luisa Iruela-Arispe from 2006-2009
 - Current Position: Assistant Professor of Pediatrics and CVRI at UCSF
 - Awarded the Burroughs Wellcome Career Award for Medical Scientists



CIRM Bridges Program Intern

Ms. Laughing Bear Torrez

- CSU San Bernardino Bridges Program
- Bridges internship at UC Riverside with Dr. Duncan Liew
 - First author on a paper on the derivation of neural progenitor and retinal cells from pluripotent stem cells
- Earned Masters degree.
- Honored as college's outstanding graduating student
- Current Position: predoctoral student at Stanford University in the Stem Cell Biology and Regenerative Medicine Ph.D. program



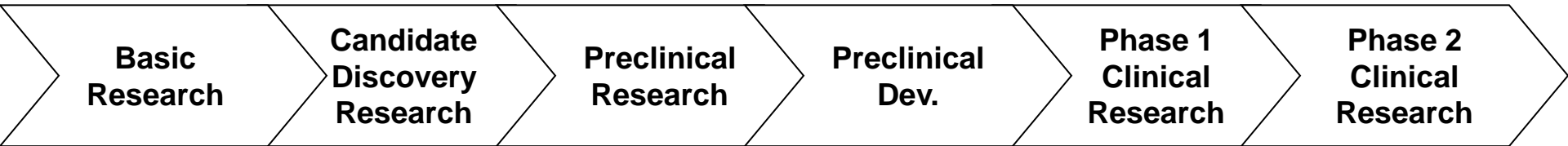
Breakdown: CIRM Basic Research Initiative



RFA (Year Awarded by ICOC)	# of Awards	ICOC Approved Funding (MM)
SEED (2007)	73	\$45.3
Comprehensive (2007)	28	\$72.0
Basic Biology	83	\$113.5
Basic Biology I (2009)	12	\$16.3
Basic Biology II (2010)	16	\$22.4
Basic Biology III (2011)	27	\$37.8
Basic Biology IV (2012)	28	\$38.0
Totals	183	\$231.8



Basic Research Program



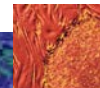
Select
Development
Candidate

File IND

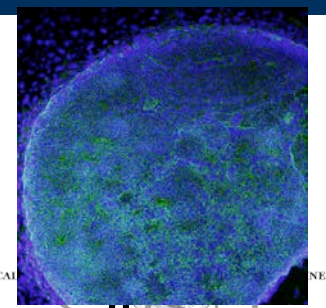
SEED Awards

Comprehensive Awards

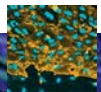
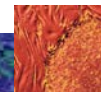
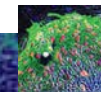
Basic Biology I, II, III, IV



Basic Research Program Focus: Human Stem Cells



- Supports basic research on **human** stem/progenitor cells
 - 164 Principle Investigators
- Attract researchers new to human stem cell research:
SEED program:
 - Attract investigators new to embryonic stem cell research into the field to conduct research on the biology, derivation and application of hESC and their derivatives
 - 31/72 (42%) SEED investigators received 38 other CIRM research grant(s)
 - 12 received a Basic Biology award
 - 9 received New Faculty), New Cell Lines (2) or Stem Cell Transplantation Immunology (1) awards
 - 11 PIs received 14 ‘applied’ awards - 1 Tools and Technologies, 2 New Cell Lines, 9 Early Translational, 2 Disease Team Research awards



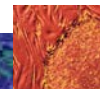
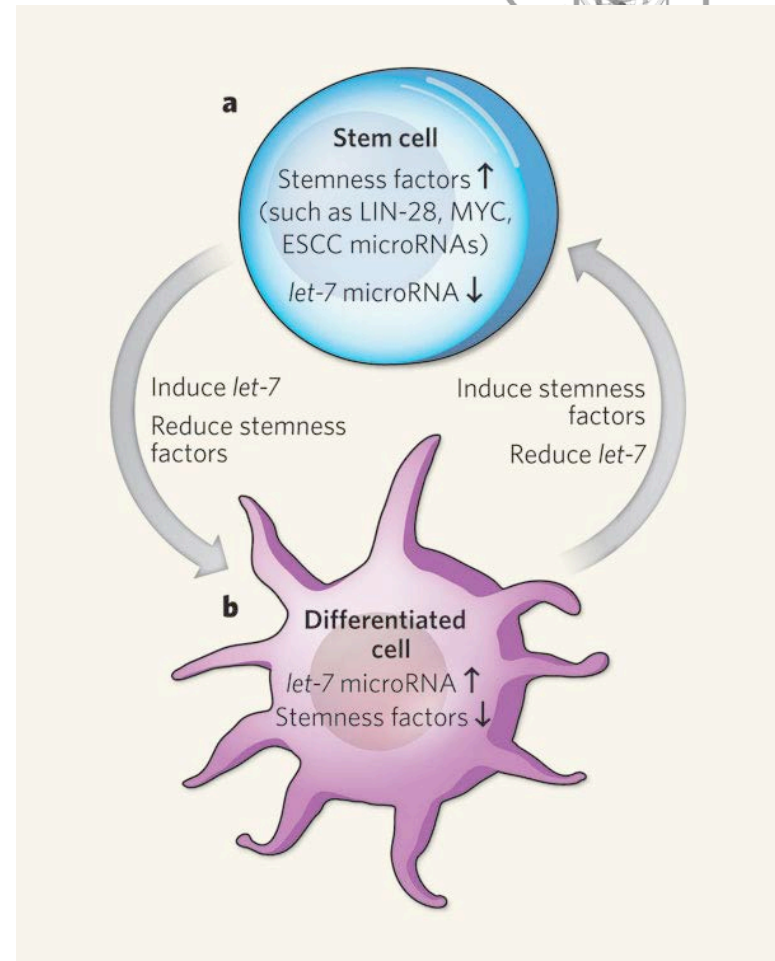
CIRM-Supported Research Highlights

PI: Dr. Robert Blelloch
(UCSF)
SEED grant



- Discovered that two distinct microRNA (ESCC and Let-7 families) play opposing roles in regulation of self-renewal genes
- Provided novel insights into cellular mechanisms that orchestrate stem cell self-renewal

Melton, C, Judson, R.L., Blelloch, R. (2010)
Opposing microRNA families regulate self-renewal in mouse embryonic stem cells.
Nature 463, 621-626.



CIRM-Supported Research Highlights

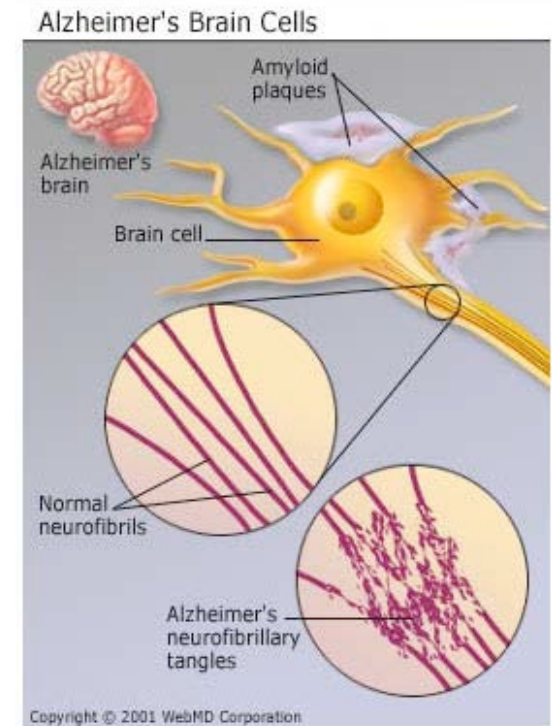


PI: Dr. Lawrence Goldstein
(UCSD)
Comprehensive grant



- generated iPSCs from Alzheimer's Disease patients and differentiated these cells into neurons
- derived neurons displayed aberrant properties typical of Alzheimer's Disease
- provides a novel system for studying the disease and for developing a platform for drug screening

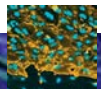
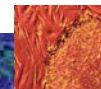
Israel, M.A., et al. (2012) Probing sporadic and familial Alzheimer's disease using induced pluripotent stem cells. **Nature** 382, 216-220.



Breakdown: CIRM Tools & Technology Initiative



RFA (Year Approved by ICOC)	# of Awards	ICOC Approved Funds (MM)
Tools & Technology I (2008)	23	\$19.8
Tools & Technology II (2011)	20	\$34.7
Total	43	\$54.5



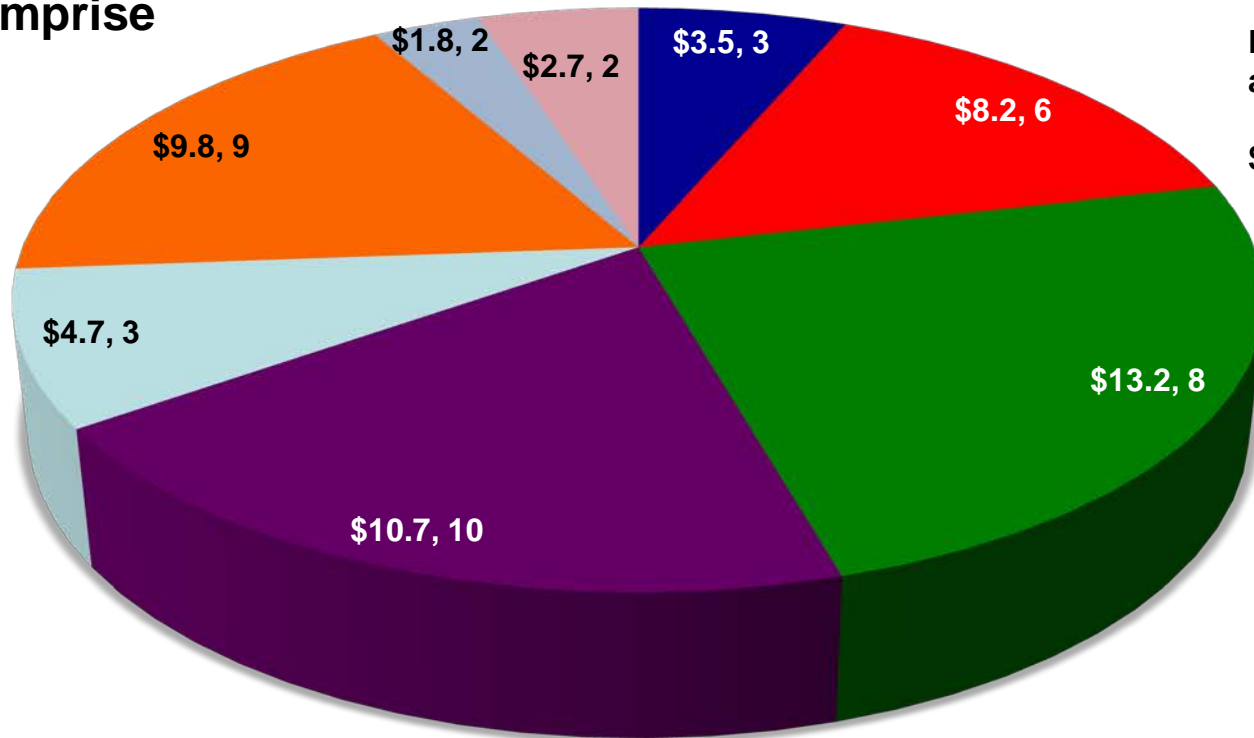
Breakdown: CIRM Tools & Technology Initiative



43 Awards comprise
\$54.5 MM

Pie slices are labeled
as follows:

\$ MM, # of Programs



Markers & Assays

Screening

Disease Modeling

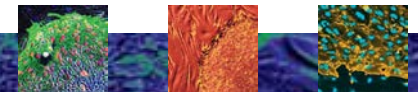
Cell Line Development

Tissue Engineering

Imaging

BioProcess

Cell Delivery Devices

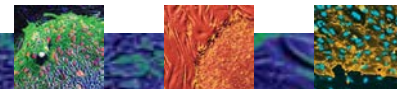
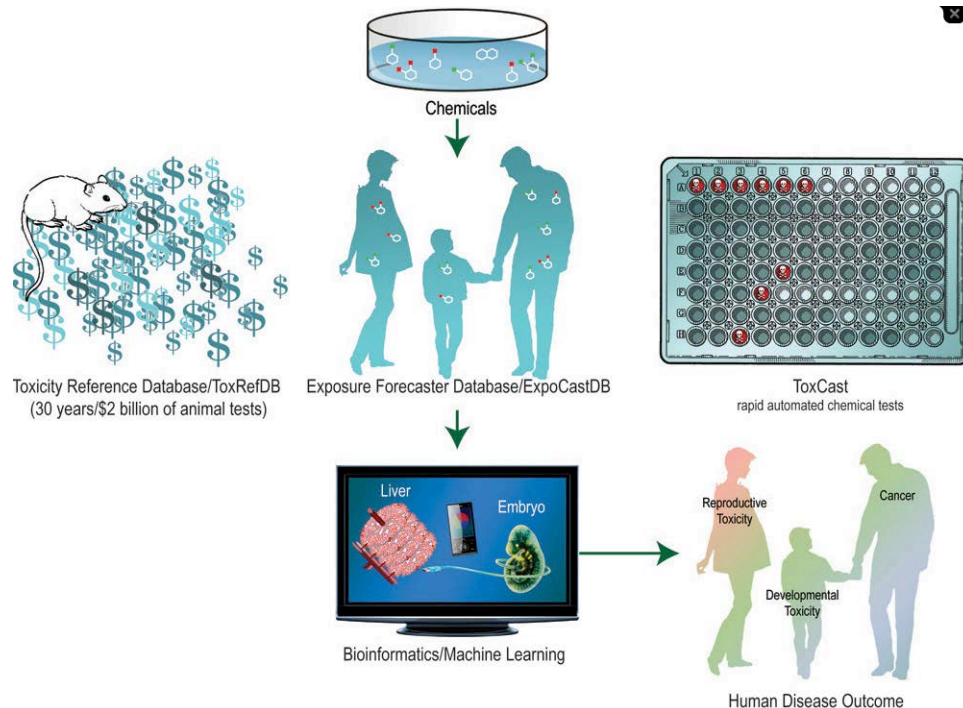


Tools & Technologies Research Highlights

RT1-01143: McDonough, Vala Sciences Inc.

Contributed to technology development of an instrument -kinetic imaging cytometer (KIC) - enabling high throughput measurement of electrical behavior of heart cells and subtypes in mixed populations of cells.

- Won contract from Environmental Protection Agency to screen up to 10,000 chemicals as part of their ToxCast program
- Collaboration with VistaGen: Vala will use its KIC platform in conjunction with VistaGen's human pluripotent stem cell derived cardiomyocytes for screening new drug candidates for potential heart toxicities

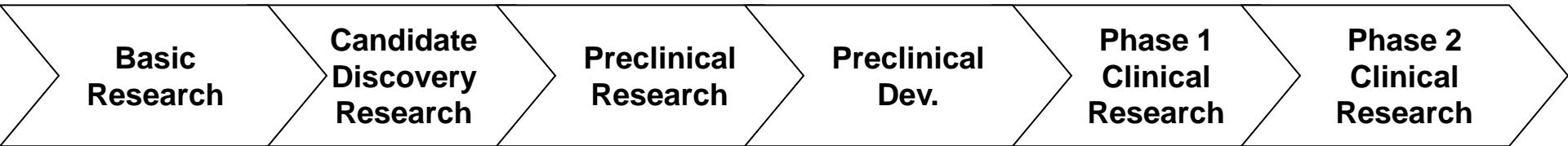


Breakdown: CIRM Early Translation Initiative

RFA	Program Period	Grants Awarded, #				Funds Committed, MM			
		B*	DCF	DC	Total	B*	DCF	DC	Total
ET I	2009 - 2013	7	---	9	16	\$29.5	---	\$43.9	\$73.4
ET II	2011 - 2014	---	9	12	21	---	\$16.7	\$54.7	\$71.4
ET III	2012 - 2015	---	11	10	21	---	\$19.6	\$49.8	\$69.4
TOTAL		7	20	31	58	\$29.5	\$36.3	\$148.4	\$214.2



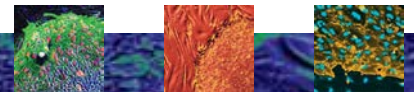
Early Translation Awards



Bottleneck Awards

DCF Awards

DC Awards



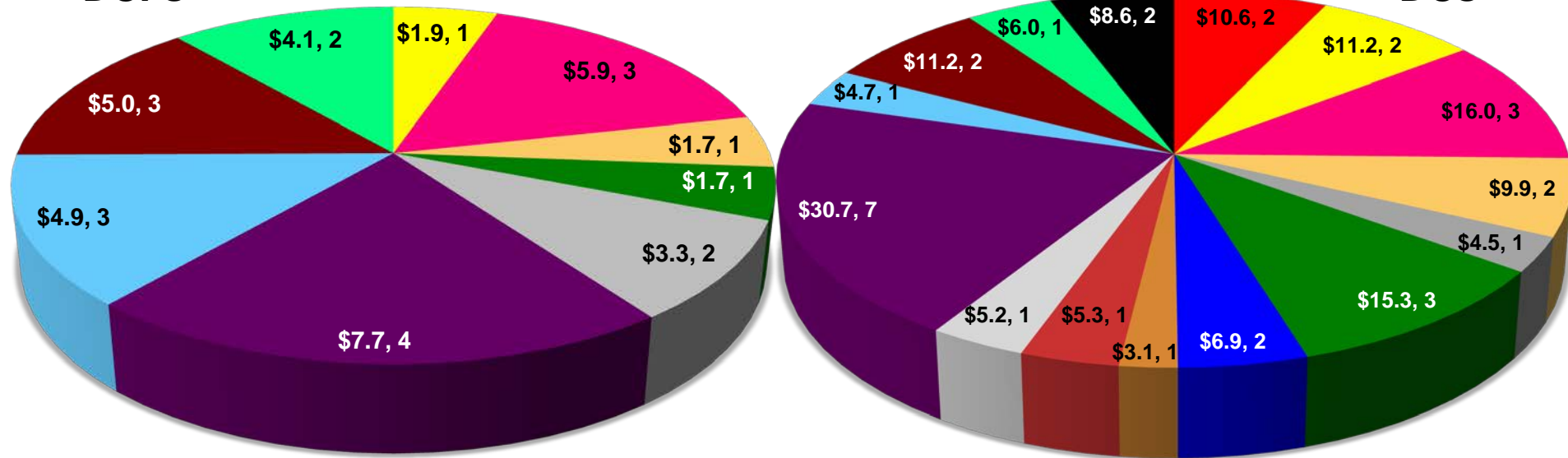
CIRM Early Translation Program
















51 Early Translation Programs, funding commitment of \$185.4 MM

Pie slices are labeled as follows:
\$ MM, # of Programs

DCFs

DCs



-  Blood Disorders
-  Bone Disorders
-  Cardiovascular Disorders
-  Cartilage Disorders
-  Endocrine Disorders
-  Eye Disorders
-  Hematologic Cancers
-  HIV/AIDS
-  Kidney/Urinary Disorders
-  Liver Disorder
-  Neurodegenerative Disorders
-  Neurologic Injuries
-  Pediatric Neurological Disorders
-  Skeletal Muscle Disorders
-  Solid Cancers



Early Translation Research Outcomes

Early Translation ➡ Disease Team



TR2-01272 DR2A-05739

- Klassen, UCI
- Disease: Retinitis Pigmentosa
- Approach: Allogeneic retinal progenitor cells



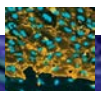
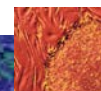
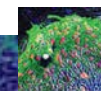
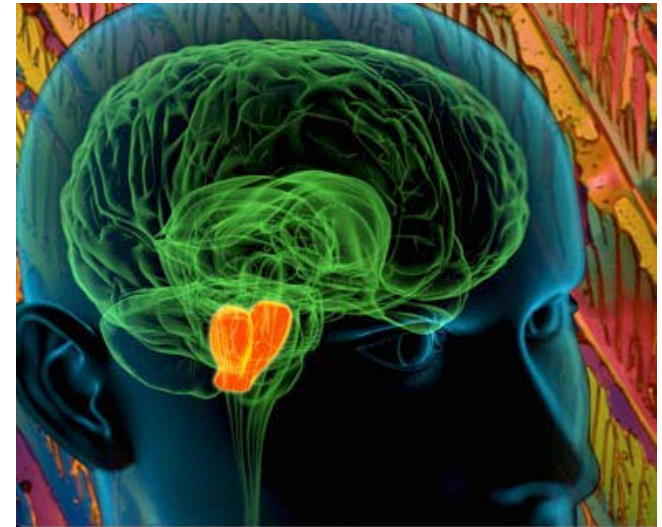
Early Translation Research Highlights: TR1-01246: Langston, The Parkinson's Institute



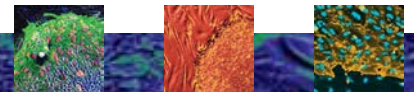
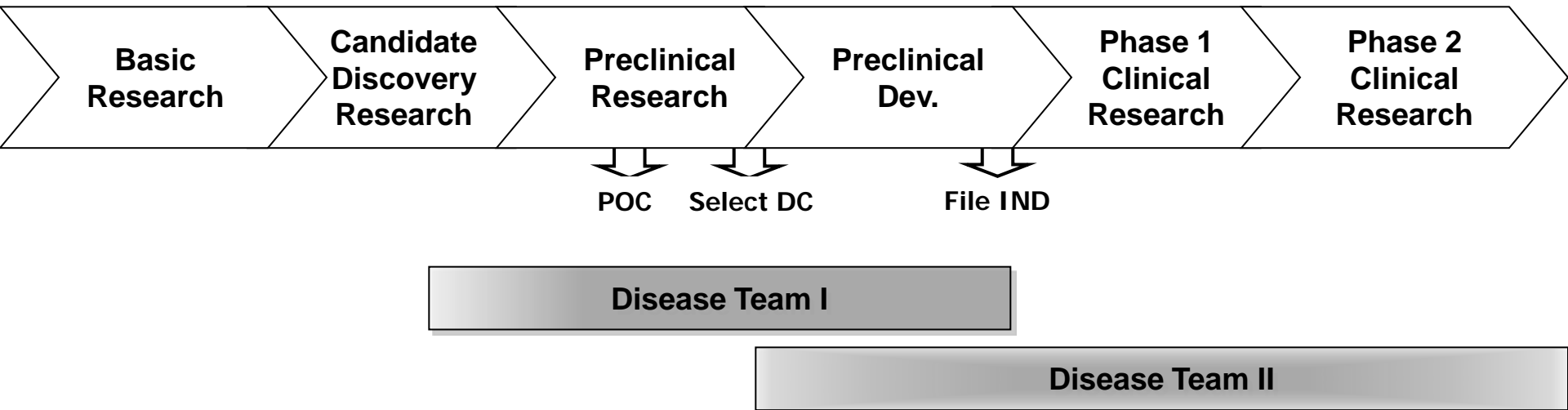
Goal : develop a model for Parkinson's Disease (PD) in a lab dish using patient derived lines as a model to study disease mechanisms

Outcomes:

- iPSC-derived neurons from PD patients with causative mutations in either the LRRK2 or alpha synuclein genes show greater susceptibility to cellular toxins
- Resource for PD iPSC lines
- Has led to multiple new collaborations, industry and academic, public and private.
- Leveraged new funding both public and private (~\$700,000 to date)



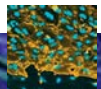
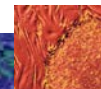
Disease Team Research Awards



CIRM Disease Teams Initiative: Target End Goals



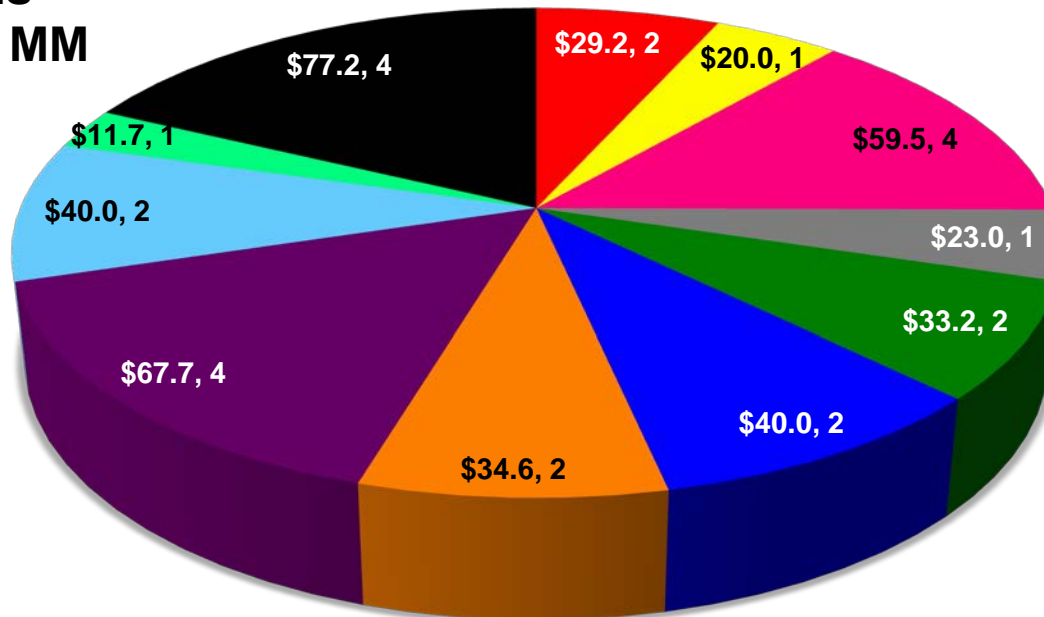
RFA (Year Awarded by ICOC)	# of INDs	\$ (MM) towards IND	# of Early Stage Clinical Trials	\$ (MM) towards Early Stage Clinical Trials
Disease Team I (2009)	14	\$228.0	0	\$0
Disease Team II (2012)	3	\$60.0	8	\$148.1
TOTALS	17	\$288.0	8	\$148.1



CIRM Disease Teams Initiative














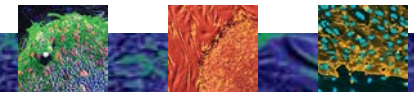
25 Disease Teams
comprise \$436.1 MM



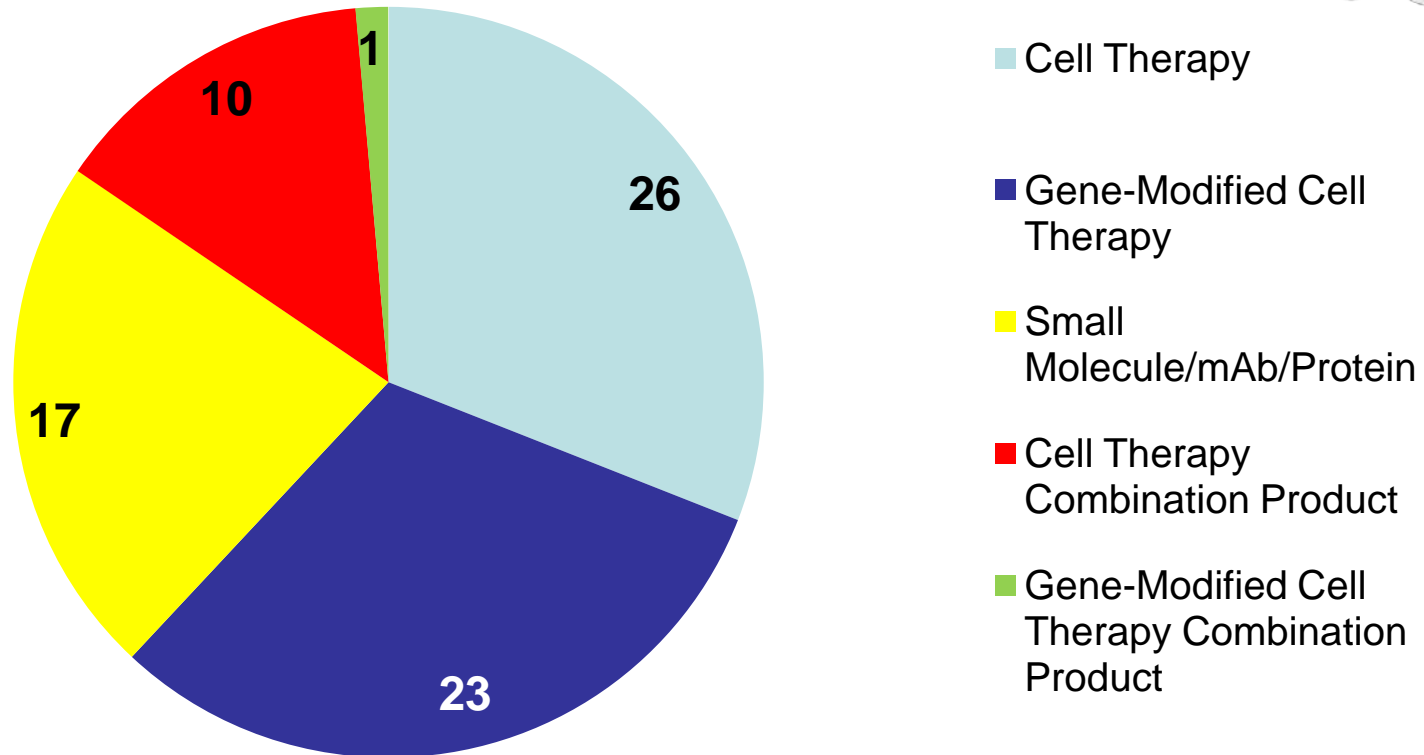
Pie slices are labeled as follows:

\$ MM, # of Programs

- | | | |
|---|---|---|
|  Blood Disorders |  Bone Disorders |  Cardiovascular Disorders |
|  Endocrine Disorders |  Eye Disorders |  Hematologic Cancers |
|  HIV/AIDS |  Neurodegenerative Disorders |  Skin Disorder |
|  Neurologic Injuries |  Solid Cancers | |



Therapeutic Modality

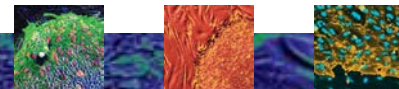


Therapeutic modality of CIRM translational portfolio current as of October, 2012
13 DTI – 5 allogeneic, 4 autologous (1 iPS), 2 Mab, 2 small molecules
11 DTII – 7 allogeneic, 2 autologous, 1 Mab, 1 small molecule
2 SPI – 1 allogeneic, 1 autologous



Driven by science and evidence needed on regulatory pathway

- Prior to award
 - mutually agreed upon Go, no go and progress milestones, success criteria
- During the conduct of research
 - Interactive ongoing discussions between CIRM scientists and funded research team
 - Updates on interval progress on bi-annual to quarterly basis and overall annual progress updates
 - clinical development advisor meetings yearly/ key milestones (DT1s have been assessed in 2011 at 12-18 month milestone, now at 24-30 month milestone)
- CIRM/FDA webinars, educational roundtables, conferences, seminars



CIRM's Disease Teams, addressing major unmet clinical needs, are moving towards the clinic



DEVELOPMENT
CANDIDATE

FILE IND

Diabetes (1)

Neurological Dis (2)

Eye Disease (1)

Cardiac Disease (1)

HIV/AIDS (2)

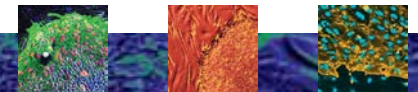
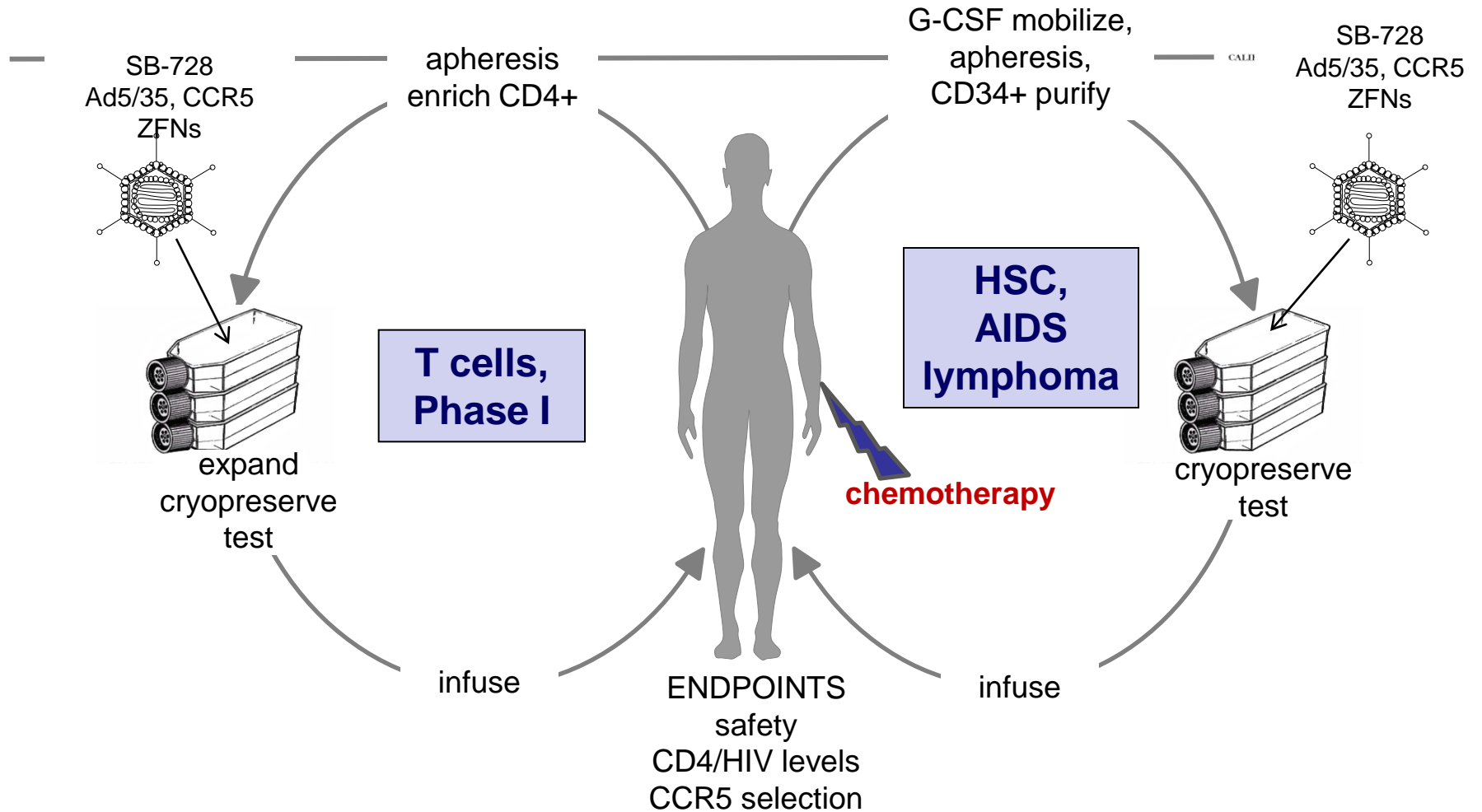
Cancer (4)

Blood Disorders (1)

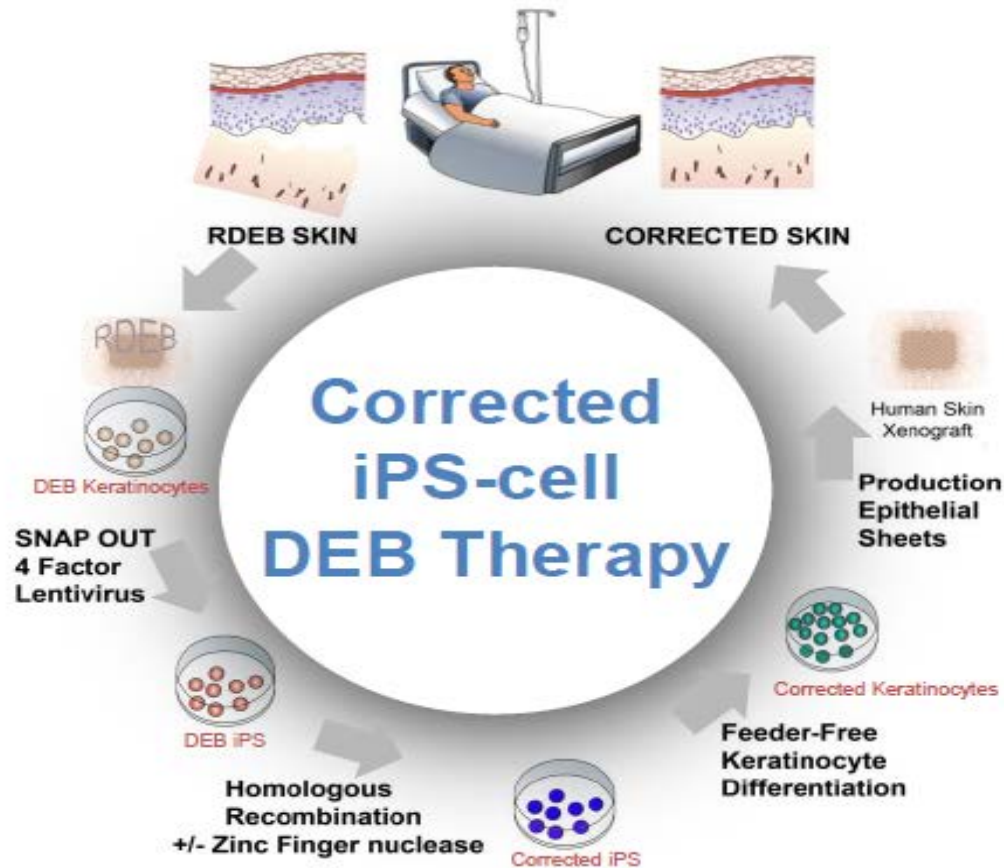
Skin Disease (1)



Example – moving to the clinic in HIV/AIDS

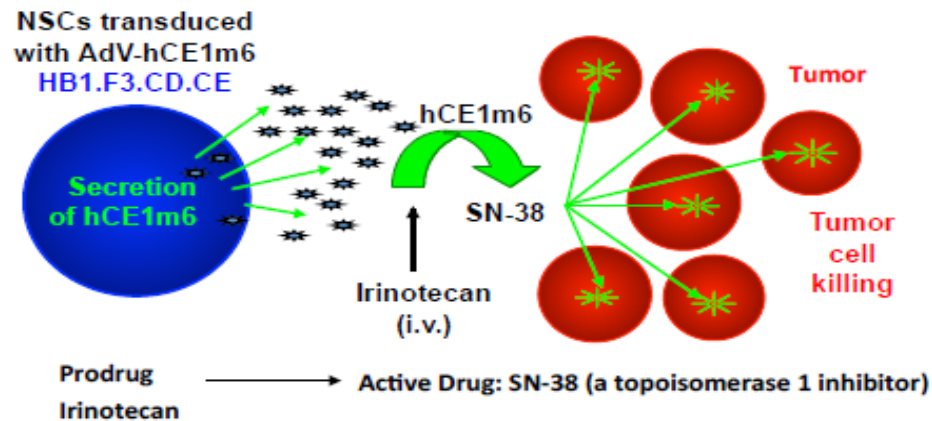


Example: Moving to the clinic in rare genetic disorder dystrophic epidermolysis bullosa



Example: Moving to the clinic in cancer

CIRM DT Cell Therapy/Therapeutic Candidate:
CE-expressing HB1.F3.CD NSCs to locally convert prodrug CPT-11 to SN-38 in recurrent glioma patients



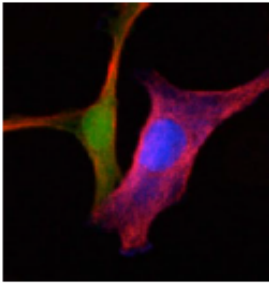
Optimize NSC distribution to tumor cells

- ✓ NSC Delivery Route: intracerebral vs. intravenous
- ✓ NSC Dose: high/low
- ✓ NSC Tracking: SPIO labeling for MRI imaging

Optimize CE/CPT-11 efficacy

- ✓ CE variant selection: rCE vs. hCE1m6
- ✓ Optimize adeno transduction of NSCs
- ✓ CPT-11 dose regimens

Example: Spinning out a company



TheraBiologics Inc.

Karen S. Aboody, MD
Founder, Chief Scientific Officer & Director

A clinical stage biopharmaceutical company developing a neural stem cell platform for targeted cancer treatment

Cancer Targeted Drug Delivery™

Tom Smart, MBA
Chair, Board of Directors

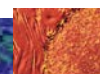
Alexander J. Annala, PhD
Chief Operating Officer & Director

Rex Moats, PhD
Director

TBX-01: NSC.CD + 5-FC → 5-FU active drug

TBX-02: NSC.CE + CPT-11 → SN-38 active drug

- **GMP Scale-up & Optimization**
- **Phase II – III Target Product Profile Development & Clinical Trials**



Summary of DT highlights

- Over half of the DT1s successfully advanced through their pre-IND meeting with FDA, towards an approvable IND
- 1 clinical trial to start in 2013, expect 1 to 2 more in 2013
- Anticipate 5 clinical trials by end of 2014
- 5 have collaborative funding partners; 1 has collaboration with disease foundation; 2 have companies as PI or co-PI; 2 have founded companies
- 21 invention disclosures, 24 active/pending patent applications
- 18 scientific publications

