CPCI

Consortium for Pediatric Cellular Immunotherapy

2nd Annual Meeting
October 7 – 8, 2019
Seattle

Children's Hospital Colorado
Children's Hospital LOS ANGELES
Children's National Health System
Seattle Children's HOSPITAL • RESEARCH • FOUNDATION
UCSF Benioff Children's Hospital Oakland

Welcome!


NIH
National Center
for Advancing
Translational Sciences

Welcome Back

What a difference a year makes!

U01 General Objectives

- Accelerate the development of novel cellular immunotherapies for pediatric disease, including cancer, infection, and immune tolerance

- Develop and disseminate resources to enhance the development and implementation of novel cellular immunotherapy
  - Establish collaborations across the CTSA network
  - Train clinical, manufacturing, research, and regulatory teams

- Expand patient access to novel cellular immunotherapy

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 1
Key Accomplishments
At a Glance

Established Governance and Committee Structure

Steering Committee

- Membership: Chair (Dr. Bollard) and Co-Chair, Voting Member from each site
- Responsibilities: Provide scientific oversight and prioritization; oversee operations
- Term Limits: 5 years

Protocol Review Committee

- Membership: Chair (Dr. Verneris); CTU Manager; Statistician; Site Investigators (2); Clinical Research Assistant or Research RN (2); Patient Advocate
- Responsibilities: Critically review, critique, and rate protocols in the areas of scientific merit, feasibility, and study design
- Term limits: 3 years, staggered starting at Year 2

Patient Advocacy Committee

- Membership: Chair (Dr. Walters), Site Investigators (2); Site's CTSA Institute of Special Populations reps (2); Patient Advocates (2)
- Responsibilities: Ensure input from families and participants on all aspects of the therapeutic development process
- Term Limits: 3 years, staggered starting at Year 2

External Advisory Board

- *Membership: Leslie Kean, Michael Konstan, Catriona Jamieson*
- *Responsibilities: Annual performance review*

Training and Evaluation

- Multi-site implementation of PLAT-02 at 3 Consortium sites (SCH, CHLA, BCHO)
  - Development and implementation of clinical trial tools and training materials
  - On-site training (SCH → CHLA and BCHO)
- Engaging junior faculty on committees and working groups
- Collaboration with ITHS Education Program – Arti Shah, Director
- Established evaluation program with key metrics – Julie Elworth

CPCI
Consortium for Pediatric Cellular Immunotherapy

SA1: Expand Manufacturing Capabilities of Cellular Immunotherapy Products

- Define and align best practices across cGMP facilities
- Expand distribution of cellular therapeutics to sites of patient care
- Expansion of available cGMP facilities across CTSA
- **Key 2018 Outcomes**
  - **Site training materials for PLAT-02 implementation**
  - **cGMP working group established and completed GAP analysis of cell therapy product(s) shipping**

CPCI
Consortium for Pediatric Cellular Immunotherapy

SA2: Expand the Clinical Development of Cell-Based Immunotherapy for Pediatric Disease

- Establish the training and infrastructure to promote development and implementation of clinical immunotherapy trials in pediatric patients
- Utilize clinical trial designs that account for the unique constraints of rare disease-focused clinical trials in pediatric populations
- Ensure equitable access for all participants who may directly or indirectly benefit from cellular immunotherapies clinical trials
- **Key 2018 Outcomes**
  - **Implemented two multi-center trials across Consortium**
    - **PLAT-02 (NCT 0202 8455) at SCH, CHLA, BCHO**
    - **ACES (NCT 03475212) at CNMC, SCH, CHLA, CHC**

CPCI
Consortium for Pediatric Cellular Immunotherapy

SA3: Expedite the Assessment of Key Biologic Correlates Uniquely Associated with Cellular Immunotherapy

- Develop reproducible sample collection and process standards for use across consortium trials
- Apply a web-based data integration platform for the integration, analysis visualization, and sharing of data across sites
- Establish outcome measures to assess safety, efficacy, and promote rapid translation of findings
- **Key 2018 Outcomes**
  - **Labkey service platform employed across PLAT-02 sites to support correlative studies**

CPCI
Consortium for Pediatric Cellular Immunotherapy

SA4: Facilitate Sustainable Access to the Most Promising Cellular Immunotherapies for Children

- Sustain through extramural grant funding and pharmaceutical collaborations
- Establish an organizational model to develop a sustainable infrastructure
- **Key 2018 Outcomes**
  - **Model of sustainability – CureWorks established, including three consortium sites – SCH, CHLA, CNMC**

CPCI
Consortium for Pediatric Cellular Immunotherapy

Agenda

Monday, October 7, 2019

- Monday Morning
  - Aim 1 Presentation
  - Aim 2 Presentation
  - Aim 3 Presentation
- Monday Afternoon
  - EAB Overview
  - EAB – Aim 1
  - EAB – Aim 2
  - EAB – Aim 3
  - EAB – Aim 4
  - Committee Meetings
  - Report-Out

Tuesday, October 8, 2019

- Tuesday Morning
  - Aim 4 Presentation
  - Meeting Summary and Action Items
  - Scientific Talk
  - Building Cure Tour

CPCI

Consortium for Pediatric Cellular Immunotherapy

Aim 1

Catherine Lindgren
Michael Jensen

CPCI
Consortium for Pediatric Cellular Immunotherapy

Aim Overview

Develop the infrastructure to expand manufacturing capabilities of cellular immunotherapy products developed for treatment of pediatric disease

CPCI
Consortium for Pediatric Cellular Immunotherapy

Sub-Aims

- Define and align best practices across cGMP facilities
- Expand distribution of cellular therapeutics to sites of patient care
- Expansion of available cGMP facilities across CTSA

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 1 Accomplishments

- Established working group
- Achieved Consortium consensus around best practices for shipping/receiving cell therapy starting material and products
    - Gap analysis completed in 4/5 Consortium sites
    - Best practices table completed
- Delivered cell therapy products delivered to 3/5 Consortium sites (X # products)
    - CNHS: 8 shipments to CHLA, 1 shipment to UCSF, 3 shipments to CHC
    - SCH: 11 shipments to CHLA, 3 shipments to BCHO
- Visited one consortium site for shipping/receiving training
- Provided vendor information to Consortium site to assist in development of new cGMP facility

CPCI
Consortium for Pediatric Cellular Immunotherapy

Working Group Members

- Julie Annis
  - *Supervisor, BMT Laboratory - CHLA*
- Jonathan Esensten, MD, PhD
  - *Medical Director, Regulatory T Cell Manufacturing Group - UCSF*
- Terry Fry, MD
  - *Director, Cancer Immunotherapy – CU*
- Patrick Hanley, PhD
  - *Director, GMP for Immunotherapy - CNHS*
- Ashley Leinbach
  - *Project Manager, Regulatory T Cell Group – UCSF*
- Catherine Lindgren
  - *Senior Director, Therapeutic Cell Production Core - SCRI*

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 1 Barriers

- Availability of consortium team for monthly calls
- Time constraints to produce work products by consortium members
- Time needed for group to learn about each consortium site cGMP facility, develop working relationship, and establish trust between consortium members for sharing proprietary cGMP SOPs and documents

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 2 Goals

- Disseminate best practices for shipping/receiving cell therapy starting material and final products by publishing manuscript in Cytotherapy
  - To include practical experience-based insights
  - To include training strategies and their pros/cons for external clinical sites (on-site training, videos, written training, check lists, questionnaires)
- Share information among working group for proficiency/competency testing of cGMP manufacturing personnel at Consortium sites (FACT)
- Increase in number of cell therapy products distributed among Consortium clinical trial sites

CPCI
Consortium for Pediatric Cellular Immunotherapy

Metrics for Year 2 Goals

- # hits on Cytotherapy shipping/receiving paper
- # hits on CTSA page of best practices shipping/receiving
- # clinical products sent to other consortium sites
- # of SOPs, forms, worksheets, or labels exchanged between sites
- # of ad hoc communications between working groups

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 3 - 5 Goals

- Disseminate best practices for annual competency/proficiency training of cGMP manufacturing personnel as required by FACT
- Expand cell product distribution for multi-site trials
- Open relevant clinical trials at various manufacturing sites
- Develop a robust training plan based on best practices and publish as a white paper

CPCI
Consortium for Pediatric Cellular Immunotherapy

Planned Outputs

Best practices for shipping/receiving cell therapy starting material and final products

manuscript in Cytotherapy

Grant to support training of staff in manufacturing and quality roles.

CPCI

Consortium for Pediatric Cellular Immunotherapy

Discussion Points

- How can we fund an in-person 2 day cGMP working group meeting?

CPCI
Consortium for Pediatric Cellular Immunotherapy

Aim 2

Julie Park

CPCI

Consortium for Pediatric Cellular Immunotherapy

Aim Overview

Expand the clinical development of cell-based immunotherapy for pediatric disease

CPCI
Consortium for Pediatric Cellular Immunotherapy

Sub-Aims

- Establish the training and infrastructure to promote development and implementation of clinical immunotherapy trials in pediatric patients
- Utilize clinical trial designs that account for the unique constraints of rare disease-focused clinical trials in pediatric populations
- Ensure equitable access for all participants who may directly or indirectly benefit from cellular immunotherapies clinical trials

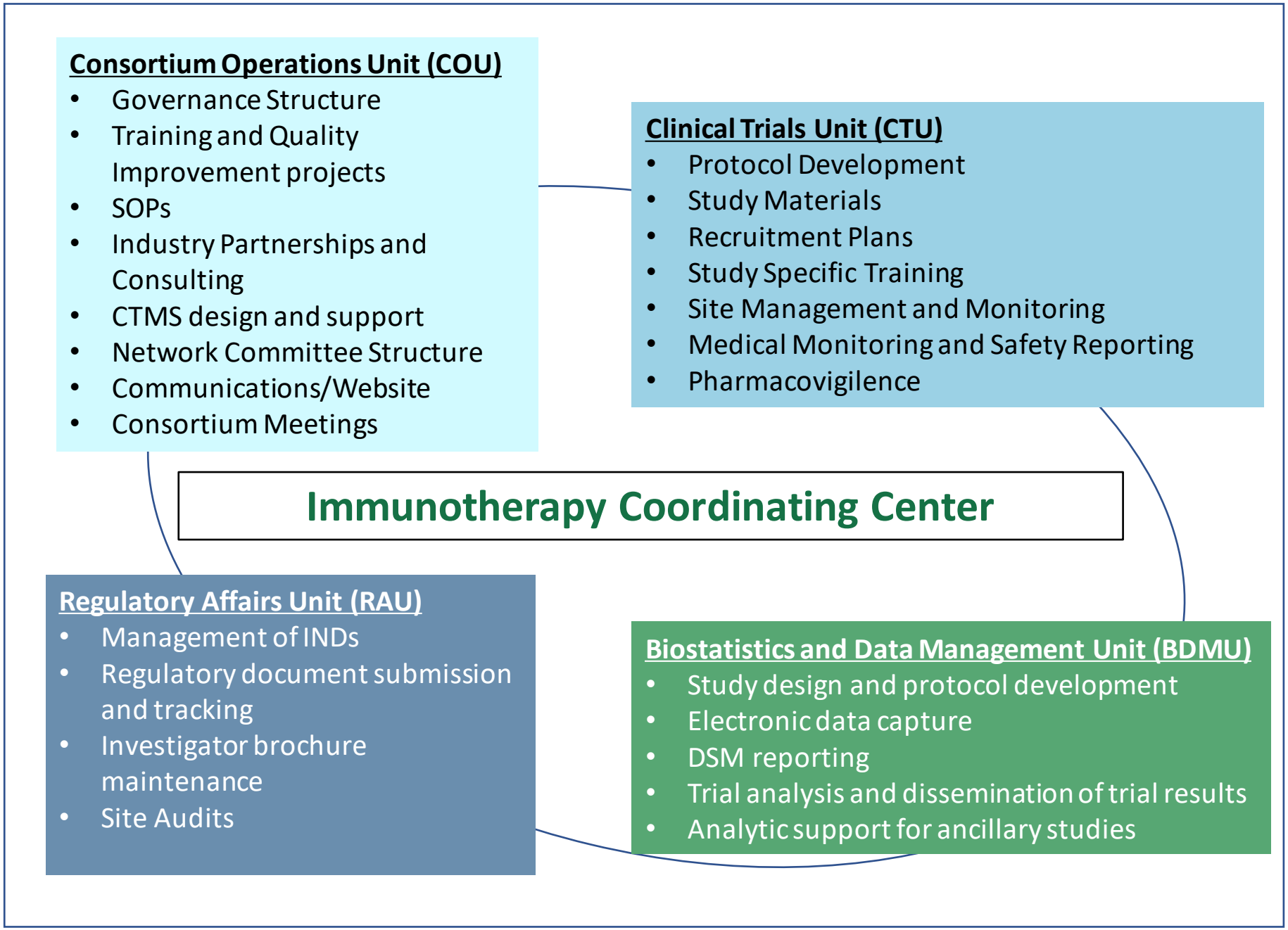
CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 1 Accomplishments

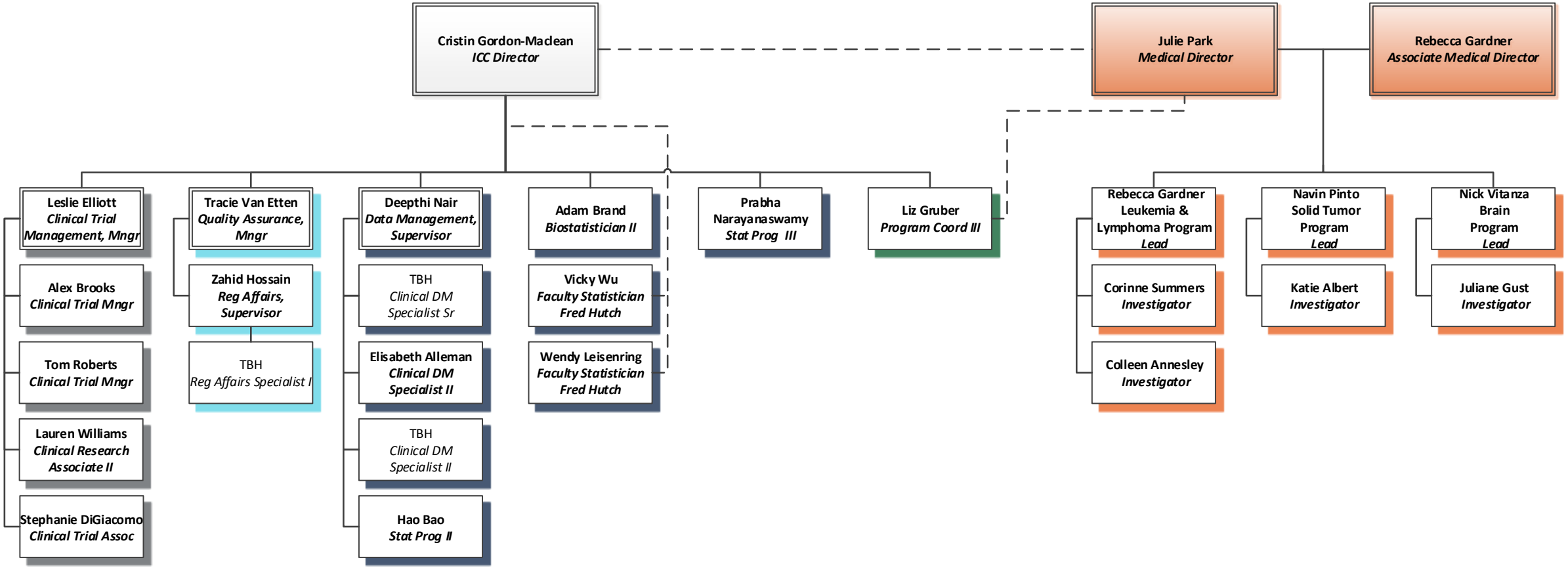
- Established Protocol Review Committee and Patient Advocacy Committee
- Expanded the Immunotherapy Coordinating Center
- Established statistical and data management structure
    - Developed statistical tools (Statistical Analysis Plan Templates)

- Opened two trials across Consortium (PLAT02 and ACES)
- Conducted oversight of trial compliance
    - PRA and ICC monitoring unit
- Finalized plans for CIRB through Seattle Children's IRB
- Developed project planning tool that will allow Consortium to visualize interdependencies in clinical trial management

CPCI
Consortium for Pediatric Cellular Immunotherapy


Consortium Operations Unit (COU)
• Governance Structure
• Training and Quality Improvement projects
• SOPs
• Industry Partnerships and Consulting
• CTMS design and support
• Network Committee Structure
• Communications/Website
• Consortium Meetings
Clinical Trials Unit (CTU)
• Protocol Development
• Study Materials
• Recruitment Plans
• Study Specific Training
• Site Management and Monitoring
• Medical Monitoring and Safety Reporting
• Pharmacovigilence
Immunotherapy Coordinating Center
Regulatory Affairs Unit (RAU)
• Management of INDs
• Regulatory document submission and tracking
• Investigator brochure maintenance
• Site Audits
Biostatistics and Data Management Unit (BDMU)
• Study design and protocol development
• Electronic data capture
• DSM reporting
• Trial analysis and dissemination of trial results
• Analytic support for ancillary studies

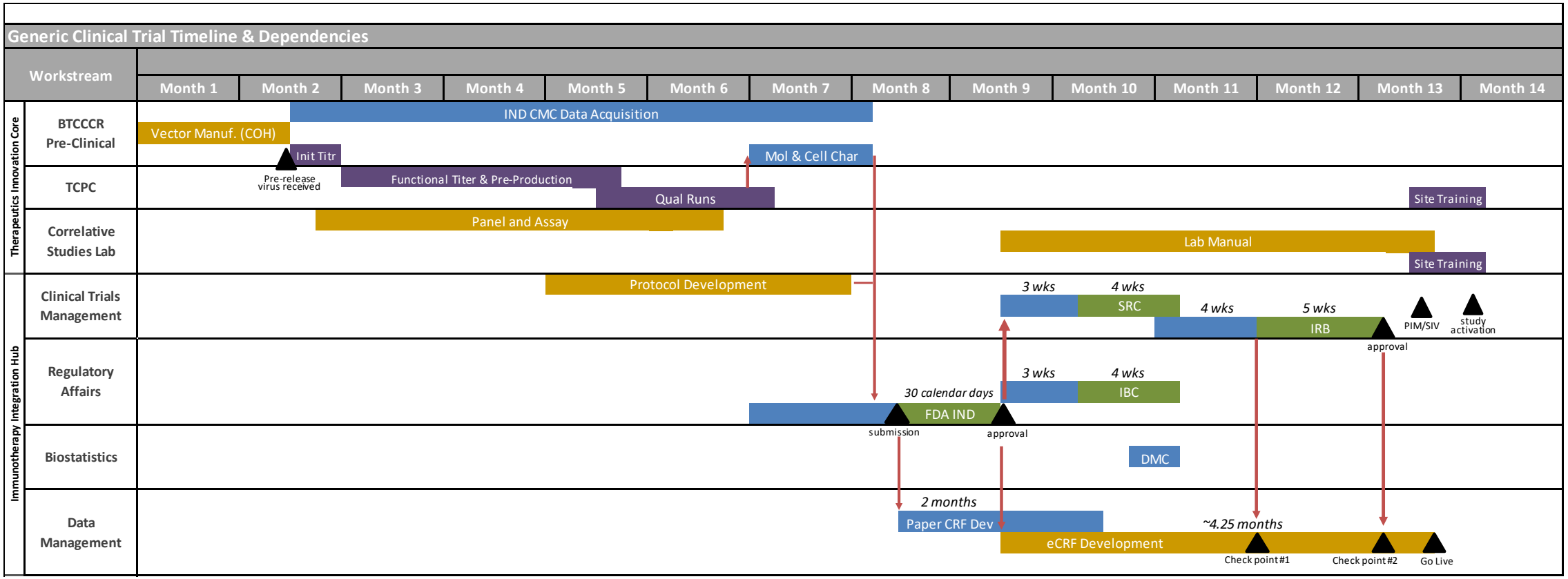
ICC Organizational Chart



CPCI

Consortium for Pediatric Cellular Immunotherapy

Swim Lanes



Plan/Dev | Test/Tr | Prep | Approval | Dependency | Major Milestone

Key Dependencies

1. SRC submission requires approval from FDA (IND)
2. IRB submission requires IND approval, SRC approval, DSMB charter and CRFs

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 2 Goals (beyond PRC and PAC)

- Establish tools needed to efficiently and effectively develop and implement clinical trials
  - CRF Global Library
  - Implementation of standardized toxicity grading
- Establish standards for monitoring and share clinical trial monitoring plans
- Utilize central IRB (SCRI) for implementation of PLAT-06

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 3 - 5 Goals

- Evaluate accuracy of standardized timelines
- Expand protocol templates beyond cancer
- Evaluate use of training tools and compliance to protocol
- Expand utilization of cIRB

CPCI
Consortium for Pediatric Cellular Immunotherapy

Protocol Review Committee

Michael Verneris

CPCI

Consortium for Pediatric Cellular Immunotherapy

Year 1 Accomplishments

- Assembled committee
- Held multiple interactive meetings
- Discussed opportunity for cellular therapy educational video
- Considered opportunity for sharing SOP around vaccinations

CPCI
Consortium for Pediatric Cellular Immunotherapy

Committee Members

- Alexis Brooks
  - *Clinical Trial Manager, ICC - SCRI*
- Dana Dornsife
  - *Founder and Chair - Lazarex Cancer Foundation*
- Leslie Elliott
  - *Manager, Clinical Trial Management Unit, ICC - SCRI*
- Rebecca Gardner, MD
  - *Pediatric Hematologist-Oncologist - SCRI*
- Michael Keller, MD
  - *Pediatric Immunologist – CNHS*
- Jennifer Michlitsch, MD
  - *Pediatric Hematologist-Oncologist - BCHO*

CPCI
Consortium for Pediatric Cellular Immunotherapy

Committee Members (cont)

- Julie Park, MD
  - *Bushnell, Towne and Wilkerson Endowed Chair in Pediatric Neuroblastoma; Medical Director, ICC - SCRI*
- Bonnie Ramsey, MD
  - *Director, Center for Clinical and Translational Research; Associate Director, Pediatric Clinical Research Center - SCRI*
- Agne Taraseviciute, MD
  - *Pediatric Hematologist-Oncologist – CHLA*
- Michael Verneris, MD
  - *Pediatric Hematologist-Oncologist – CHC*
- Vicky Wu, PhD
  - *Assistant Member, Clinical Research Division; Assistant Member, Public Health Services Division - FHCRC*

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 1 Barriers

One goal of the committee is to assist in protocol review and prioritization, but at present, there are no protocols submitted to the committee, thus the focus on other related opportunities

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 2 Goals

- Develop shared projects on cellular therapy
  - Projects could include:
    - Treatment approaches/guidelines
    - Protocols/clinical trials
  - Caveat: different cellular therapy products offered at each institutions and varied approaches

- Share SOPs and supportive care guidelines
  - Management of:
    - Revaccination
    - CRS
    - ICANS
    - What patients should go to BMT? When?
  - Can these become training modules for cellular therapy research specified in the grant?

- ? Protocol planning tool (tasks, timelines, resources needed)

CPCI
Consortium for Pediatric Cellular Immunotherapy

Discussion Points

- How do we deal with Consortium heterogeneity?
  - Types of cell therapy products being delivered
  - Various institutional protocol temples and IRB nuances
- How to bring true value to this aim?
  - What is missing in our field and how to contribute
  - What are the outstanding questions that this group can address

CPCI
Consortium for Pediatric Cellular Immunotherapy

Patient Advocacy Committee

Mark Walters
Anurag Agrawal

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 1 Accomplishments

- Recruitment of committee members broadly representing patients/families, disease advocacy, ethics, and health equity
- Standing bimonthly meetings
- Development of mission statement with priorities
- Subsequent project development within aim/sub-aim

CPCI
Consortium for Pediatric Cellular Immunotherapy

Committee Members

- Anurag Agrawal, MD
  - *Pediatric Hematologist-Oncologist - BHCO*
- Lourdes Baezconde-Garbanati, PhD
  - *Director, Community Outreach and Engagement; Associate Dean, Community Initiatives, Keck SOM - USC*
- Tumaini Coker, MD, MBA
  - *Research Director, Center for Diversity and Health Equity - SCRI*
- Dana Dornsife
  - *Founder and Chair - Lazarex Cancer Foundation*
- Paibel Aguayo-Hiraldo, MD
  - *Pediatric Hematologist-Oncologist - CHLA*

CPCI
Consortium for Pediatric Cellular Immunotherapy

Committee Members (cont)

- Lauren Jerkins, MD
  - *Pediatric Hematologist-Oncologist - CNHS*
- Amy Keating, MD
  - *Pediatric Hematologist-Oncologist - CHC*
- Adam Lamble, MD
  - *Pediatric Hematologist-Oncologist - SCRI*
- Diana Merino, PhD
  - *Science Policy Analyst - Friends of Cancer Research*
- Mark Walters, MD
  - *Director, Blood and Marrow Transplantation Program - BHCO*

CPCI
Consortium for Pediatric Cellular Immunotherapy

Mission Statement

Ensure cellular therapy trial development includes discussion and strategies to ensure equitable access, with input by families about what is important to them

CPCI
Consortium for Pediatric Cellular Immunotherapy

Subsequent Questions

- How best to use/empower family/patient involvement in study development?
- How to harness existing CTSI resources to improve patient/family involvement/empowerment?
- How to promote and ensure equal access to participation?

Potential Strategies to Prioritize

- How best to use/empower family/patient involvement in study development?
  - Survey of patients/families to understand barriers to accessing cellular therapy→development of focus groups
- How to harness existing CTSI resources to improve patient/family involvement/empowerment?
  - Question for EAB, but each site also has been asked to query local CTSI to better understand existing resources
- How to promote and ensure equal access to participation?
  - Landscape analysis of current CMS coverage→collaborative advocacy work

Committee Planned Responsibilities

- Sub-Aim 3: Ensure equitable access of all participants who may directly or indirectly benefit from cellular immunotherapies clinical trials
  - Describe current gaps in access to cellular therapies at participating sites
  - Understand barriers from provider and patient/family perspective
    - Development of focus groups to address
  - Analyze current access to FDA approved product and clinical trials
    - Potential advocacy/position paper
  - What tools would be beneficial to improve access and ensure uniformity of information disseminated to patients/families?
  - Understand the ethical challenges with cellular therapies

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 1 Barriers

- How best to engage existing structures within our organizations?
  - ISP
  - CCHE
  - CTSI
- What resources/tools can they provide us that is helpful?
- Is there overlap between other committees?

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 2 Goals

Project Timeline: Retrospective Review of Patients Accessing Cellular Therapies

	July 2019	Aug 2019	Sept 2019	Oct 2019	Nov 2019	Dec 2019	Jan 2020	Feb 2020	Mar 2020	Apr 2020	May 2020
IRB Submission											
IRB Approval											
Data Collection											
Data Analysis											
Manuscript Preparation											
Manuscript Submission + Revisions											

CPCI

Consortium for Pediatric Cellular Immunotherapy

Year 2 Goals

Project Timeline: Patient/Family Survey Re: Perspectives on Accessing Cellular Therapies (PLAT-02)

	July 2019	Aug 2019	Sept 2019	Oct 2019	Nov 2019	Dec 2019	Jan 2020	Feb 2020	Mar 2020	Apr 2020	May 2020	June 2020
Review Draft Survey and Finalize												
IRB Submission												
IRB Approval												
Data Collection												
Data Analysis												
Manuscript Preparation												
Manuscript Submission + Revisions												

CPCI

Consortium for Pediatric Cellular Immunotherapy

Year 2 Goals

- Insurance coverage landscape analysis
- Provider survey
- How to access families who do not participate in trials
- Engagement with NCATS for additional grant opportunities for correlative or supplemental studies to the primary U01 award
- Further exploration of how institutional resources can be leveraged, building towards goals for years 3-5

CPCI
Consortium for Pediatric Cellular Immunotherapy

Metrics for Year 2 Goals

- Completion of:
  - Retrospective review
  - Patient/family and provider surveys
  - Landscape analysis

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 3 - 5 Goals

- Development of focus groups to further understand the barriers
- Furthering advocacy work to ensure equal access
- Development of educational tools which allow:
  - Wider dissemination of trial information
  - More uniform messaging in regard to study aims, risks/benefits
- Further grant exploration

CPCI
Consortium for Pediatric Cellular Immunotherapy

Planned Outputs

Manuscripts for the retrospective review and surveys

New **grant opportunities** linked to the parent U01 (Ben Wilfond) and others

- Potential **advocacy collaborations**
  - Kids v. Cancer
  - Children's Cause for Cancer Advocacy
  - Greg Reaman at FDA

CPCI
Consortium for Pediatric Cellular Immunotherapy

Discussion Points

- How best to engage existing structures within our organizations?
  - ISP
  - CCHE
  - CTSI
- What resources/tools can they provide us that is helpful?
- Is there overlap between other committees?
- Additional aims for years 3-5?

CPCI
Consortium for Pediatric Cellular Immunotherapy

Aim 3

Ashley Wilson

CPCI

Consortium for Pediatric Cellular Immunotherapy

Aim Overview

Enhance rigorous assessment of key biologic correlates uniquely associated with cellular immunotherapy mechanism(s) of action in conjunction with safety and outcome metrics

CPCI
Consortium for Pediatric Cellular Immunotherapy

Sub-Aims

- Develop reproducible sample collection and process standards for use across Consortium trials
- Apply a web-based data platform for the integration, analysis visualization and sharing of data across sites
- Establish outcome measures to assess safety, efficacy and promote rapid translation of findings

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 1 Accomplishments

- Established Correlative Working Group (CWG)
- Completed gap analysis comparing specimen collection, shipping and processing practices at 4/5 Consortium sites
- Defined assay capacity at each site
- **While there is some variability in processes at sites (mostly study-specific), reproducible processes are feasible**

CPCI
Consortium for Pediatric Cellular Immunotherapy

Working Group Members

- Hisham Abdel-Azim, MD, MS
  - *Pediatric Hematologist-Oncologist - CHLA*
- Hema Dave, MD, MPH
  - *Pediatric Oncologist - CNHS*
- Kimberly Jordan, PhD
  - *Assistant Director, Human Immunology & Immunotherapy Initiative - CU*
- Ashley Wilson, PhD
  - *Manager, Human Immunotherapy Correlative Studies - SCRI*

CPCI
Consortium for Pediatric Cellular Immunotherapy

Gap analysis of specimen collection, shipping and processing practices (Sub-Aim 1)

- Overview of specimen types
- Serum vs. plasma isolation
- PB/BMA shipment practices
- Isolation of MCs and Cryo
- Multi-site assay capacity
- Protocol deviation tracking

	Seattle Children's	CNMC	CHLA	UC Denver
Specimens Processed / Analyzed				
Peripheral Blood (PB)	Yes	Yes	Yes	Yes
Bone Marrow Aspirate (BMA)	Yes	No, but biobank has a protocol	Yes	No
Cerebrospinal Fluid (CSF)	Yes	Yes, neuro-onc group processes CSF	Yes	No
Tissue biopsies	Yes	No	Yes	Yes, blocks processed by pathology
Collection Practices: Serum vs. Plasma Isolation				
PB Serum Isolation	Yes	No	Yes	Yes
If yes, tube type?	Red top	N/A	Study-specific	Red top
Initial spin speed / time / temp	1000xg / 15 minutes / ambient	N/A	Study-specific	500xg / 10 minutes / ambient
Aliquot serum	2mL into an intermediate tube	N/A	Study-specific	Yes, into intermediate tube
Final speed / time / temp	10,000xg / 10 minutes / 4C	N/A	Study-specific	500xg / 10 minutes / ambient
Frozen aliquots	0.45mL, up to 4 aliquots	N/A	Study-specific	250uL aliquots
Long-term storage temp	-80C	N/A	Study-specific	-80C
PB Plasma Isolation	No	Yes	Yes	Yes
If yes, tube type?	N/A	Green top	Study-specific	Purple top/EDTA, green top, yellow top
Initial spin speed / time / temp	N/A	1500xg / 15 minutes / ambient	1000xg / 10 minutes / ambient	500xg / 10 minutes / ambient
Aliquot PB plasma	N/A	N/A	Transfer into an intermediate tube	Yes, into intermediate tube
Final speed / time / temp	N/A	N/A	1200xg / 10 minutes / ambient	500xg / 10 minutes / ambient
Frozen aliquots	N/A	0.5-1.5mL, up to 3 aliquots	Yes	250uL aliquots
Long-term storage temp	N/A	-80C	-80C	-80C
BMA Plasma Isolation	Yes	No	Yes	No
If yes, tube type?	EDTA	N/A	Study-specific	N/A
Initial spin speed / time / temp	400xg / 10 minutes / RT	N/A	Study-specific	N/A
Aliquot pBMA plasma	1mL to intermediate tube	N/A	Study-specific	N/A
Final speed / time / temp	10,000xg / 10 minutes / 4C	N/A	Study-specific	N/A
Frozen aliquots	0.11mL, up to 4 aliquots	N/A	Study-specific	N/A
Long-term storage temp	-80C	N/A	Study-specific	N/A
Specimen Shipment Practices				
Ambient temperature shipments	PB/BMA	PB	PB/BMA	PB
4C shipments	diluted CSF (using Nanocool)	Study-specific	Study-specific	Study-specific
Dry ice shipments	frozen CSF	Study-specific	PB may be on dry ice if pre-processed	Study-specific
Qualified courier	FedEx or local courier	FedEx or local courier	FedEx or local courier	FedEx or local courier, in person delivery
Shipping labels/instructions included	Yes	Varies by protocol	Yes	Varies by protocol
Expiration day/time included	Yes	Varies by protocol	Yes	Varies by protocol
Mechanism for stakeholder feedback	Yes, 24/7 email inbox monitored	Yes, CRA/PI communication	Yes, CRA/PI communication	Yes, CRA/PI communication
Initial Specimen Processing Alignment				
Isolation of mononuclear cells (MCs)	Ficoll	Lymphocyte Separation Medium (Ficoll)	Ficoll	Lymphocyte Separation Medium (Ficoll)
Dilue in PBS to begin	Yes	Yes	Yes	Yes
Spin speed / time / temp	830xg / 20 minutes / ambient	1200xg / 10 minutes / ambient	400xg / 30 minutes / ambient	800xg / 15 minutes / ambient
Collect MC layer	Yes	Yes	Yes	Yes
Centrifugation of MCs	250xg / 10 minutes / ambient	400xg / 5 minutes / ambient	400xg / 10 minutes / ambient	500xg / 10 minutes / ambient
RBC Lysis	Yes, if necessary	Yes, if necessary	Yes, if necessary	Yes
Count cells	Yes	Yes	Yes	Yes
Cryopreservation of MCs	Yes	Yes	Yes	Yes
Method	Mr. Frosty temps, then -80C	Mr. Frosty temps, then -80C	Mr. Frosty temps, then -80C	Mr. Frosty temps, then -80C
Freezing media	CryoStor (has 10% DMSO)	FBS + 10% DMSO	FBS + 10% DMSO	FBS + 10% DMSO
Documentation worksheets/forms	Yes	Yes	Yes	Yes
Post-collection incubation limits	3 day limit for PB specimens for flow	Need to establish	Need to establish	<5 day limit for plasma for cytokine
Assay Capacity				
Multi-parameter flow	Yes	Yes	Yes	Yes
qPCR	Yes	Mainly TCR sequencing	Yes	Yes
Gene expression profiling	Yes, NanoString	Yes, in collaboration with others	Yes, in collaboration with others	In progress, considering NanoString
Immunohistochemistry	Yes, in collaboration with others	In progress, building in-house capability	Yes, in collaboration with others	Yes, Vectra/IHC in-house
Genomic/epigenetic profiling	Yes, in collaboration with others	Yes, in collaboration with others	Yes, in collaboration with others	No
Cytokine/chemokine analysis	Luminex	Luminex	Multiplex	MSD
Chromium/cytotoxicity assays	Yes, IncuCyte in progress	Yes	No	No
Deviation Tracking				
Submission/reporting workflow	Yes, formal process in place	Yes, only for major issues	Yes, only for major issues	Yes, but informal

Identification of specimen types most commonly processed at Consortium sites

	SCH	CNMC	CHLA	UC Denver
Specimens Processed / Analyzed				
Peripheral Blood (PB)	Yes	Yes	Yes	Yes
Bone Marrow Aspirate (BMA)	Yes	No, but biobank has a protocol	Yes	No
Cerebrospinal Fluid (CSF)	Yes	Yes, neuro-onc group processes CSF	Yes	No
Tissue biopsies	Yes	No	Yes	Yes, blocks processed by pathology

Serum or plasma isolation varies by Consortium site and requirements are mainly study or protocol-specific

	SCH	CNMC	CHLA	UC Denver
Collection Practices: Serum vs. Plasma Isolation				
PB Serum Isolation	Yes	No	Yes	Yes
If yes, tube type?	Red top	N/A	Study-specific	Red top
Initial spin speed / time / temp	1000xg / 15 minutes / ambient	N/A	Study-specific	500xg / 10 minutes / ambient
Aliquot serum	2mL into an intermediate tube	N/A	Study-specific	Yes, into intermediate tube
Final speed / time / temp	10,000xg / 10 minutes / 4C	N/A	Study-specific	500xg / 10 minutes / ambient
Frozen aliquots	0.45mL, up to 4 aliquots	N/A	Study-specific	250uL aliquots
Long-term storage temp	-80C	N/A	Study-specific	-80C
PB Plasma Isolation	No	Yes	Yes	Yes
If yes, tube type?	N/A	Green top	Study-specific	Purple top/EDTA, green top, yellow top
Initial spin speed / time / temp	N/A	1500xg / 15 minutes / ambient	1000xg / 10 minutes / ambient	500xg / 10 minutes / ambient
Aliquot PB plasma	N/A	N/A	Transfer into an intermediate tube	Yes, into intermediate tube
Final speed / time / temp	N/A	N/A	1200xg / 10 minutes / ambient	500xg / 10 minutes / ambient
Frozen aliquots	N/A	0.5-1.5mL, up to 3 aliquots	Yes	250uL aliquots
Long-term storage temp	N/A	-80C	-80C	-80C
BMA Plasma Isolation	Yes	No	Yes	No
If yes, tube type?	EDTA	N/A	Study-specific	N/A
Initial spin speed / time / temp	400xg / 10 minutes / RT	N/A	Study-specific	N/A
Aliquot pBMA plasma	1mL to intermediate tube	N/A	Study-specific	N/A
Final speed / time / temp	10,000xg / 10 minutes / 4C	N/A	Study-specific	N/A
Frozen aliquots	0.11mL, up to 4 aliquots	N/A	Study-specific	N/A
Long-term storage temp	-80C	N/A	Study-specific	N/A

MC isolation and cryopreservation protocols are closely aligned between sites

	SCH	CNMC	CHLA	UC Denver
Initial Specimen Processing Alignment				
Isolation of mononuclear cells (MCs)	Ficoll	Lymphocyte Separation Medium (Ficoll)	Ficoll	Lymphocyte Separation Medium (Ficoll)
Dilue in PBS to begin	Yes	Yes	Yes	Yes
Spin speed / time / temp	830xg / 20 minutes / ambient	1200xg / 10 minutes / ambient	400xg / 30 minutes / ambient	800xg / 15 minutes / ambient
Collect MC layer	Yes	Yes	Yes	Yes
Centrifugation of MCs	250xg / 10 minutes / ambient	400xg / 5 minutes / ambient	400xg / 10 minutes / ambient	500xg / 10 minutes / ambient
RBC Lysis	Yes, if necessary	Yes, if necessary	Yes, if necessary	Yes
Count cells	Yes	Yes	Yes	Yes
Cryopreservation of MCs	Yes	Yes	Yes	Yes
Method	Mr. Frosty temps, then -80C	Mr. Frosty temps, then -80C	Mr. Frosty temps, then -80C	Mr. Frosty temps, then -80C
Freezing media	CryoStor (has 10% DMSO)	FBS + 10% DMSO	FBS + 10% DMSO	FBS + 10% DMSO
Documentation worksheets/forms	Yes	Yes	Yes	Yes
Post-collection incubation limits	3 day limit for PB specimens for flow	Need to establish	Need to establish	<5 day limit for plasma for cytokine

Assay capacity was defined to determine what analytics can be performed across sites to assess safety and efficacy of cellular therapies

	SCH	CNMC	CHLA	UC Denver
Assay Capacity				
Multi-parameter flow	Yes	Yes	Yes	Yes
qPCR	Yes	Mainly TCR sequencing	Yes	Yes
Gene expression profiling	Yes, NanoString	Yes, in collaboration with others	Yes, in collaboration with others	In progress, considering NanoString
Immunohistochemistry	Yes, in collaboration with others	In progress, building in-house capability	Yes, in collaboration with others	Yes, Vectra/IHC in-house
Genomic/epigenetic profiling	Yes, in collaboration with others	Yes, in collaboration with others	Yes, in collaboration with others	No
Cytokine/chemokine analysis	Luminex	Luminex	Multiplex	MSD
Chromium/cytotoxicity assays	Yes, IncuCyte in progress	Yes	No	No

Year 1 Barriers

- Establishing CWG members
- Complexity of clinical protocols and study-specific requirements

CPCI
Consortium for Pediatric Cellular Immunotherapy

Year 2 Goals

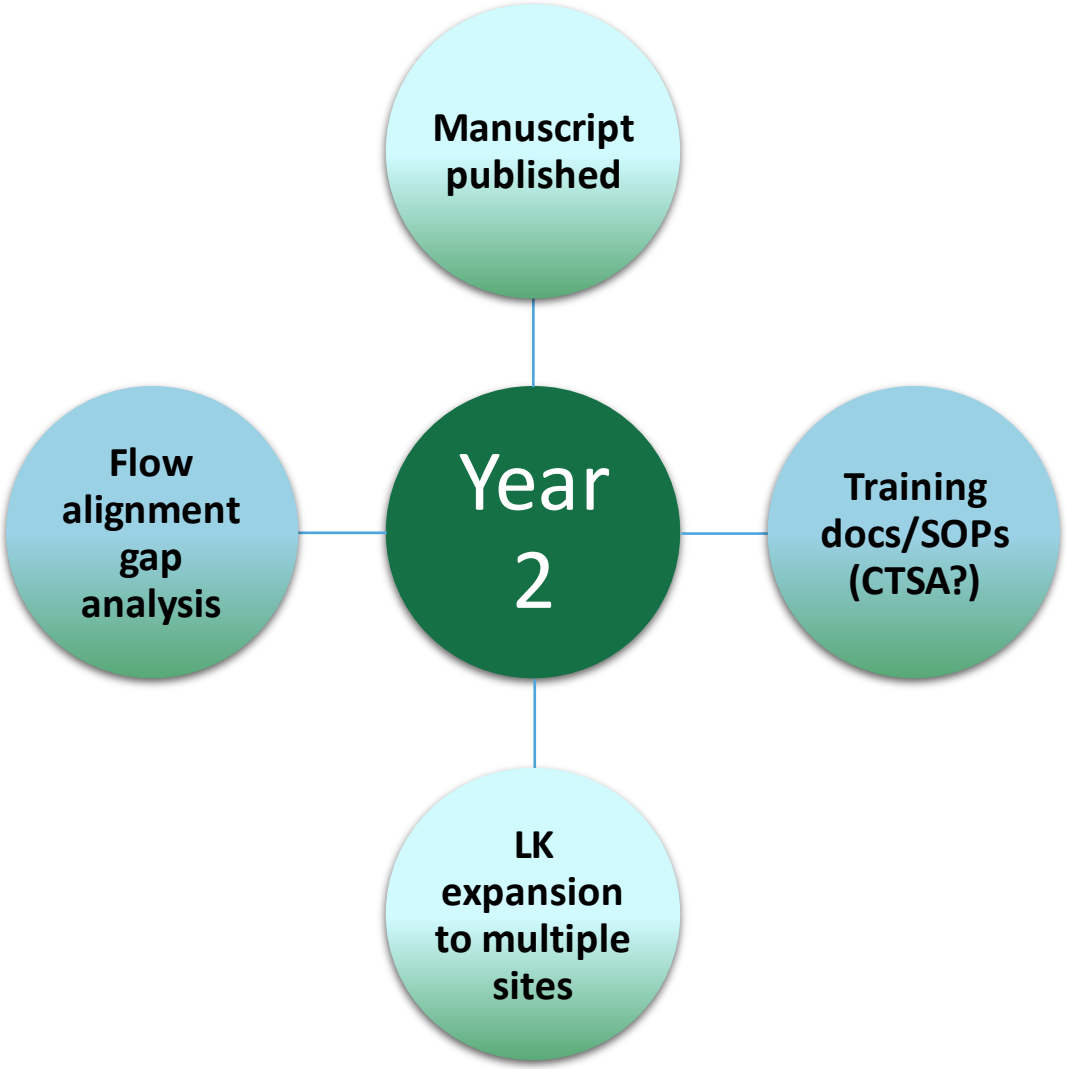
Sub-Aim(s)	Goals

1/3	• **Publish manuscript**
	  • Gap analyses (processing best practices & flow assay alignment)
	  • SCH flow comparison study data (other datasets?)

2	• Implement & expand LK from Seattle to multiple sites
3	• Take lessons learned and develop training materials for flow assay

CPCI
Consortium for Pediatric Cellular Immunotherapy

Metrics for Year 2 Goals



CPCI
Consortium for Pediatric Cellular Immunotherapy

Flow assay gap analysis (in progress in Year 2)

	Seattle Children's	CNMC	CHLA	UC Denver
Flow Staining Alignment (whole blood)				
Cytometer	BD Fortessa	MACS Quant (simple), BC Cytoflex (full pa	BD FACSCalibur, Fortessa, FACSCanto, LS	BD Fortessa
Lysis (Y/N?)	Y	Y	Y	Y
Temperature criteria	Room temp/IC at 4degC	Room temp/IC at 4degC	Room temp	Room Temp/IC at 4degC
Collection tube criteria	EDTA	Green top (heparin tubes)	EDTA or heparin	EDTA or heparin
Overnight incubation vs. same-day processing	Both	Both	Both	Both
Incubation limits for flow assay	≤ 72 hours	Nothing set (but don't go past 72 hours)	≤ 48 hours (up to 72 hrs for certain app)	Nothing set (but usually within 24 h)
Fresh vs. frozen	Both	FU samples are mostly done frozen	Both (with fresh only in certain applications)	Usually frozen or fixed-frozen
Panel validation strategy	Yes	Titrating Abs, running FMOs, use HDs	Yes	FMOs, ab titration with counterstains, HD
Gating strategy defined/templates used	Yes	Yes	Yes, example in immunophenotyping SOP	Yes, but flexible
Minimum number of cells		Collect by volume (min. 350,000 cells for	Try to collect 20K events, max 50K, stain	Collect 50k or higher (complex panels 200
Immunophenotyping markers				
T cells	CD3, CD4, CD8	CD3, CD8, CD4	CD3, CD4, CD8	CD3, CD4, CD8
B cells	CD19, CD22	CD19	CD19	CD19
Monocytes	CD14	CD14		CD11c, CD14, CD16, CD11b
NK cells		CD56, CD57, CD16 (NK/NKT)	CD56, CD16	CD56, CD16
Treg	CD4+CD25+Foxp3+	CD4+CD25+CD127dim	CD4+CD25+CD127dim	CD3, CD4, FOXP3, CD25hi, CD127dim/neg
Memory/differentiation markers				
T-Naïve	CD45RO-CD62L+CCR7+	CD45RO-CD62L+CCR7+	CD45RA+CD45RO-	CD45RO-, CD45RA+, CCR7+
T-MSC	CD45RA+CD62L+CCR7+CD27+	CD45RA+CD62L+CCR7+CD27+		
T-CM	CD45RO+CD62L+CCR7+	CD45RO+CD62L+CCR7+		CD45RA-, CD45RO+, CCR7+
T-EM	CD45RO+CD62L-CCR7-	CD45RO+CD62L-CCR7-		CD45RA-, CD45RO+, CCR7-
T-Effector	CD45RO-CD62L-CCR7-	CD45RA+CD45RO-CD62L-CCR7-		CD45RA+, CD45RO-, CCR7-
B-Naïve			CD19+IGD+CD27-	CD19+, IgD+, CD27-
B-non-switched			CD19+IGD+CD27+	CD19+, IgD+, CD27+
B-switched			CD19+IGD-CD27+	CD19+, IgD-, CD27+
Activation/exhaustion markers (is it part of standardized flow? Yes/No)				
4-1BB	Yes	Yes		No
CD69	No		Yes	No
OX40 (CD134)	No		Yes	No
CD25	Yes	Yes	Yes	Yes
PD-1	Yes	Yes		Yes
LAG3	Yes	Yes		Yes
TIM3	Yes	Yes		Yes
CTLA-4	Yes	Yes		Yes
Perforin (IC)	No	Yes		No (we use granzyme B)
IFNg (IC)	Yes	Yes		Yes
TNFa (IC)	Yes	Yes		Yes
IL-2 (IC)	Yes	Yes		Yes
**CD62L is cleaved on frozen samples				We also use Tbet/EOMES

CAR T cell and antigen detection flow comparison study between SCH labs

- 75 total samples collected at SCH were used for comparison analysis
- Study and Sample Type profile of the analyzed samples and difference in stain date between the two labs

Core panel markers: *Different clones used by each lab

CD3
CD4*
CD8
CD19*
CD22*
EGFRt
Her2tG
Viability

	Number of Samples			
Study	**Total**	**PB**	**BMA**	**CSF**
PLAT-02	19	9	5	5
PLAT-03	48	39	6	3
PLAT-05	8	2	6	0
Sum	75	50	17	8

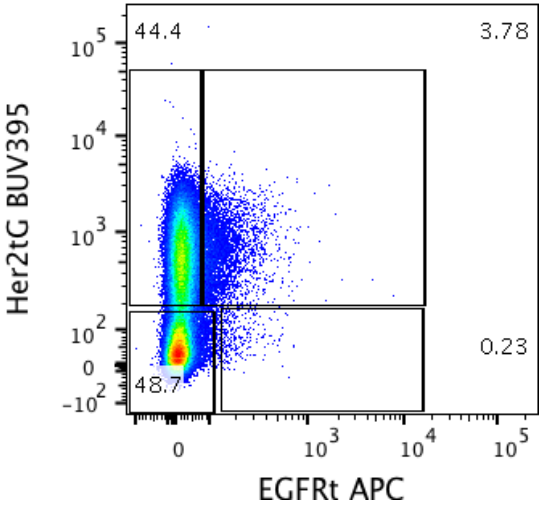
Stain Date Difference	**Number of Samples**
CM 1D before	36
CM 2D before	0
CM 3D before	1
Same day	32
CM 1D after	3
CM 2D after	3

Note: No significant impact was detected when separating samples by stain date.

Limits of Detection (LOD)

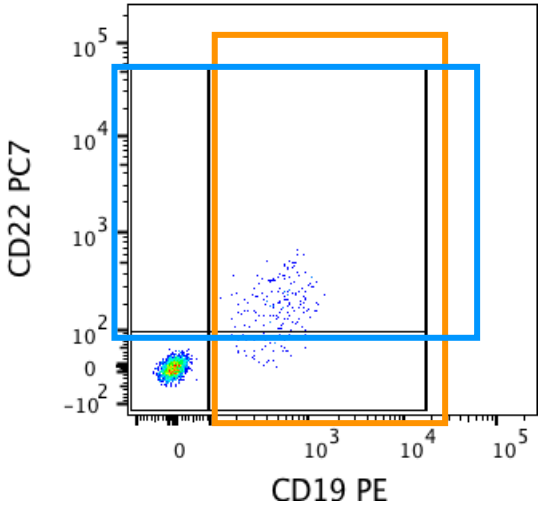
Each lab determined their own assay-specific LOD values for the 4 INDIVIDUAL engineered cell populations detected in their staining panel.

LOD (%Lymph)	CM	CSL (PB)	CSL (BMA)	CSL (CSF)
CD3+ EGFRt+ Her2tG+	0.005	0	0	0
CD3+ EGFRt+ Her2tG-	0.02	0.02	0.02	0.83
CD3+ EGFRt- Her2tG+	0.004	0.03	0.03	0.1
CD3+CD19+	0.15	0.1	0.2	0.07



The TOTAL CD19 or CD22 value is used to determine antigen detection.
EX: The sum of the CD19+CD22- and CD19+CD22+ populations is used to determine total CD19 detection.

For antigen detection, LOD is set at 1% of the lymphocyte population and is not assay or lab-specific.



Antigen Detection/Functional Persistence Status

Determined the agreement/disagreement between the two labs for **overall CD19 and CD22** antigen detection in **all** samples.

For PLAT **functional persistence**, evaluated only **study-specific** samples where the persistence status of the CAR is based on detection of that particular antigen.

Functional persistence is defined as lack of antigen detection regardless of CAR detection.

	All samples		Study-Specific Reporting	
	CD19 Detection	CD22 Detection	antiCD19-CAR Persistence	antiCD22-CAR Persistence
Agree	74	68	74	7
CM+CSL-	1	7	1	1
CM-CSL+	0	0	0	0
Total	75	75	75	8
	All studies	All studies	All studies	PLAT-05

PB T1.D7: CM stained 1D before

PB PreA: CM stained 1D before

Individual CAR Population Detection

Determined the agreement/disagreement between the two labs for **individual CAR population** detection in the **study-specific** samples.

	Study-Specific Reporting		
	EGFRt+Her2tG+ Detection	**EGFRt-Her2tG+ Detection**	**EGFRt+Her2tG- Detection**
Agree	7	6	62
CM+CSL-	0	0	3
CM-CSL+	1	2	10
Total	8	8	75
	PLAT-05	PLAT-05	PLAT-02, -03, -05

PB D28: **CSL** CAR+, CM CAR-; CM stained 1D before

BMA D21: **CSL** CAR+, CM CAR-; same day stain
BMA D21: **CSL** CAR+, CM CAR-; CM stained 1D after

CD3+CD19+ T APC Detection

Determined the agreement/disagreement between the two labs for T APC detection in the **PLAT-03** samples.

CD3+CD19+	**# of Samples**
Total samples compared	48
Agreed on detection of CD3+CD19+	46
Disagreed on detection of CD3+CD19+	2

BMA ~T2.D14: **CSL** TAPC-, CM TAPC+; CM stained 1D before
PB T2.D1: **CSL** TAPC+, CM TAPC-; same day stain

Year 3 - 5 Goals

Year 3

- Implement training at multiple sites (1/3)
- Build LK best practice documents/SOPs (2)
- Develop a statistical analysis plan (3)
- Create standards for CSF processing and profiling (3)

Year 4

- Compare samples between sites to evaluate efficacy of training (1/3)
- Implement multi-directional use of LK at sites (2)

Year 5

- Audit use of SOPs (1/3)
- Monitor/update SOPs based on feedback from multi-site use of LK (2)
- Develop control samples to monitor assay performance across sites (3)

Planned Outputs

Manuscript highlighting specimen processing best practices and flow assay alignment (include SCH sample comparison data)

Abstracts/presentations at CTSA conferences

Training documents and **SOPs** generated from lessons learned to be shared with Consortium sites

CPCI
Consortium for Pediatric Cellular Immunotherapy

Discussion Points

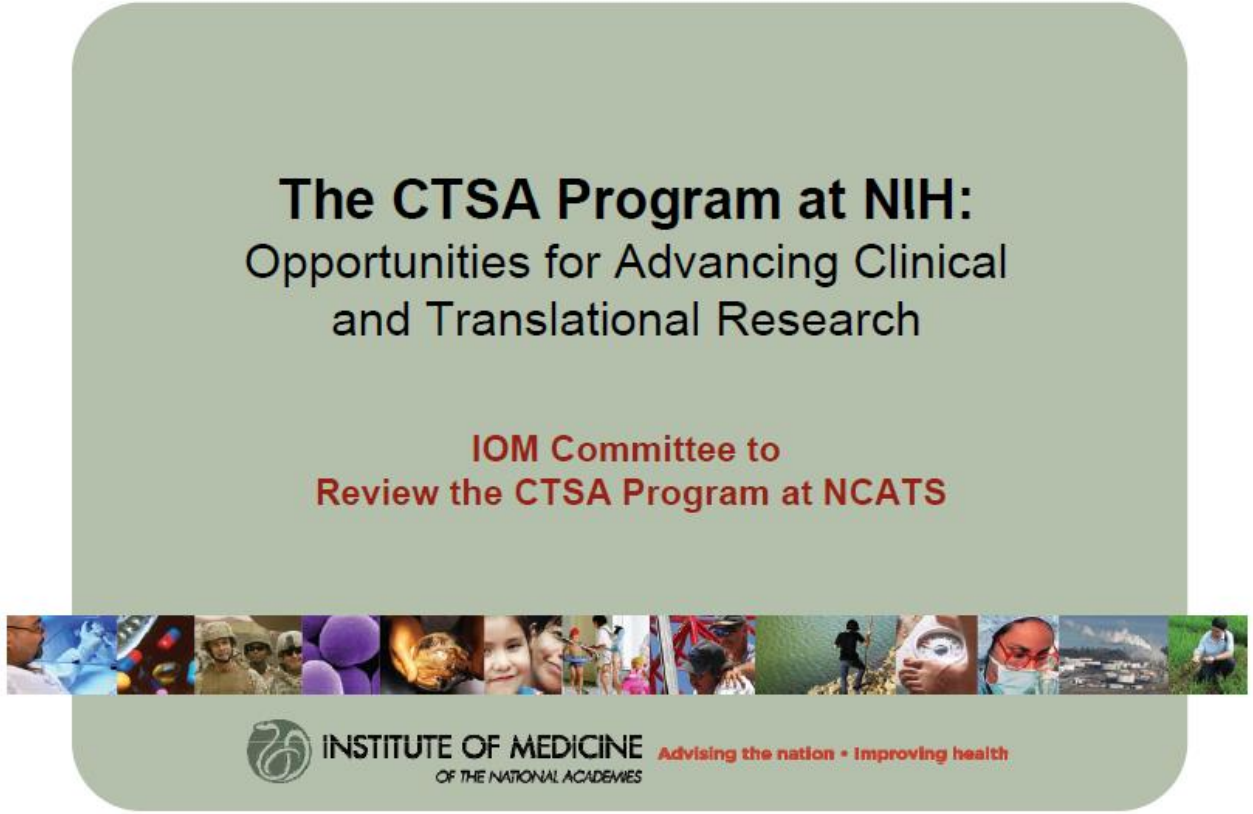
- How can we use the work performed to enrich our science?
- How do we utilize CTSA resources and conferences to disseminate findings?
- Is there value in reducing the complexity of clinical protocols by standardizing correlative collection practices (e.g. serum vs. plasma isolation)?

CPCI
Consortium for Pediatric Cellular Immunotherapy

The NCATS CTSA Collaborative Innovation Awards Program

P.J. Brooks, Ph.D.

Program Director, Office of Rare Diseases Research
National Center for Advancing Translational Sciences (NCATS) , NIH



"The committee recommends that the CTSA Program establish an innovations fund to promote collaborative pilot studies and other innovative initiatives. The activities supported through this fund should engage a combination of CTSA institutions and a variety of possible entities and stakeholders."

http://www.nationalacademies.org/hmd/Reports/2013/The-CTSA-Program-at-NIH-Opportunities-for-Advancing-Clinical-and-Translational-Research.aspx

Released June 25, 2013

The CTSA Program Collaborative Innovation Awards

- Goal: incentivize and enable cross-CTSA institution collaborations
- Develop innovations to address critical systemic roadblocks to translational efficiency that can only be addressed by combining expertise resident at different CTSA institutions

  - Critical to enabling systems change and allowing the CTSA “whole to be greater than the sum of the parts”

https://grants.nih.gov/grants/guide/pa-files/PAR-18-244.htm

https://grants.nih.gov/grants/guide/pa-files/PAR-18-245.html

FY20 NCATS CTSA Program Collaborative Suite of Awards

		Eligibility	Review Type	Purpose
Foster research collaboration to **develop, demonstrate and disseminate** innovative, experimental approaches to overcoming translational science roadblocks.	Collaborative Innovation Award (R21)	2 or more CTSA Program hubs	External Peer Review	Collaborative Innovation – High Risk/ High Reward
	Collaborative Innovation Award (U01)	3 or more CTSA Program hubs	External Peer Review	Collaborative Innovation
Provide support for the **demonstration, and/or dissemination, and/or implementation** of translational science projects that have been tested and validated at a specific hub or institution.	Competitive Revision (Administrative Supplement)	1 or more CTSA Program hubs	External Peer Review	Demonstration and/or Dissemination and/or Implementation

NIH National Center for Advancing Translational Sciences

2016 CCIA Projects

- A National IPS Cell Network with Deep Phenotyping for Translational Research
- Disseminating Curative Biological Therapies for Rare Pediatric Diseases
- Early Check: A Collaborative Innovation to Facilitate Pre-Symptomatic Clinical Trials in Newborns
- Leveraging Existing Registry Resources to Facilitate Clinical Trials
- Improving Patient-Reported Outcome Data for Research Through Seamless Integration of the PROMIS Toolkit into EHR Workflows
- Strengthening Translational Research in Diverse Enrollment (STRIDE)
- Transformative Computational Infrastructures for Cell-Based Biomarker Diagnostics

2017 CCIA Projects

- Development, Implementation and Assessment of Novel Training in Domain-Based Competencies
- Investigating Teleconsent to Improve Clinical Research Access in Remote Communities
- Measure Development to Accelerate the Translation of Evidence Based Clinical Guidelines into Practice
- Modulation of Gut-Brain Axis Using Fecal Microbiome Transplant Capsules in Cirrhosis
- Open Health Natural Language Processing Collaboratory
- Translating Research Into Practice: A Regional Collaborative to Reduce Disparities in Breast Cancer Care

2018 CCIA Projects

- A Platform Trial Design to Accelerate Translational Therapies in a Canine Disease Model of ALS
- Accelerate Cellular Immunotherapy Development for Treatment of Life-Threatening Childhood Disorders
- TEAMSS – Transforming Expanded Access to Maximize Support & Study
- Harnessing Human Brain and Liver Microphysiological Systems for Testing Therapeutics for Metastatic Melanoma
- Harnessing the Power of CTSA-CDRN Data Networks: Using Social Determinants of Health, Frailty and Functional Status to Identify At-Risk Patients and Improve Risk Adjustment
- Impact of Breast Milk on Infant Gut Microbiome
- Increasing Access to Clinical Microbiome Specimens via a Living μBiome Bank
- Peer-based Retention Of people who Use Drugs in Rural Research (PROUD-R2)
- Precision Medicine in the Diagnosis of Genetic Disorders in Neonates
- TCR and BCR Deep Sequencing to Distinguish Autoimmune Recurrence from Allograft Rejection
- Effects of apoE-Enhancing Compounds on Alzheimer's Disease Phenotypes *In Vivo*
- Transforming Exercise Testing and Physical Activity Assessment in Children: New Approaches to Advance Clinical Translational Research in Child Health

Disseminating Curative Biological Therapies for Rare Pediatric Diseases Across the CTSA Program

- Problem :
  - Stem-cell directed *ex vivo* gene therapy using lentiviral vectors (LVs) can be highly effective, and in some cases curative
  - Initiating clinical trials is a daunting challenge for new/young investigators
    - In part due to biosafety issues related to LVs
  - Especially for Ph.D.s with innovative technologies

Boston Children's Hospital

Ucla

Cincinnati Children's
changing the outcome together

Growing Gene and Cell Therapy Cooperative (GGACT)

Investigational New Drug (IND) Application

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

National Center for Advancing Translational Sciences

NCATS U01 TR001814

Disseminating Curative Biological Therapies for Rare Pediatric Diseases Across the CTSA Program

MEDICAL COLLEGE OF WISCONSIN | CTSI

David A. Wilcox PhD

Associate Professor
Institution: Medical College of Wisconsin
Department: Pediatrics
Division: Hematology and Oncology - Pediatrics
Program: Oncology

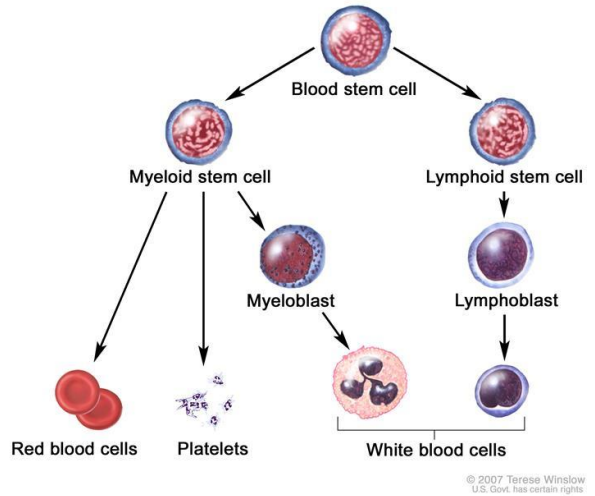
Member of the Cancer Center

nature COMMUNICATIONS

Article | Open Access | Published: 19 November 2013

Platelet-targeted gene therapy with human factor VIII establishes haemostasis in dogs with haemophilia A

Lily M. Du, Paquita Nurden, Alan T. Nurden, Timothy C. Nichols, Dwight A. Bellinger, Eric S. Jensen, Sandra L. Haberichter, Elizabeth Merricks, Robin A. Raymer, Juan Fang, Sevasti B. Koukouritaki, Paula M. Jacobi, Troy B. Hawkins, Kenneth Cornetta, Qizhen Shi & David A. Wilcox



Gene Therapy Trial for Platelet Derived Factor VIII Production in Hemophilia A

Timeline:

Applied for CCAGT support	Nov 2016
GGACT support started	April 2017
IND submitted	May 2019
FDA letter to proceed	June 2019

ClinicalTrials.gov Identifier: NCT03818763

Recruitment Status : Not yet recruiting
First Posted : January 28, 2019
Last Update Posted : July 4, 2019

Information provided by (Responsible Party):
Parameswaran Hari, Medical College of Wisconsin

National Center for Advancing Translational Sciences

Disseminating Curative Biological Therapies for Rare Pediatric Diseases Across the CTSA Program

- Key Points
  - Leveraging knowledge for translation from across CTSA program
  - Collaboration and team science to go from lab to clinic
  - Generalizable solution ; not limited to gene therapy

National Center for Advancing Translational Sciences

Newborn Screening: More than a Spot on a Card - A Public Health System

- Over 4 million babies are screened each year across the United States
- Saved lives through the identification of infants at risk for disorders for which early intervention and treatments have the potential to reduce morbidity and mortality
- Screening – blood spot on filter paper in nursery at birth
  - Hearing Screening and Pulse Oximetry for Critical Congenital Heart disease

<u>Mandatory (Opt-out) system</u>

Early Check: A Collaborative Innovation to Facilitate pre-symptomatic clinical trials in newborns

- Accelerate the acquisition of data to support decisions about adding new conditions to the Recommended Uniform Screening Panel (RUSP)
  - Gauge parents' interests for "opt-in" screening for new conditions
  - Test potential for large-scale screening in a state public health lab
  - Understand early natural history of "screen positive" infants
  - Identify infants who could participate in pre-symptomatic treatment trials
  - Two "use case" diseases: Fragile X and Spinal Muscular Atrophy (SMA)
- Provide the foundation for an envisioned future in which states offer screening for a voluntary panel of non-RUSP conditions
- Address the "Catch-22" of newborn screening

RTI INTERNATIONAL

Duke UNIVERSITY

WAKE FOREST UNIVERSITY

Early Check

Search | En español | Contact Us | JOIN NOW

What is Early Check | How It Works | For Health Care Providers | Newsroom

The Early Check test can find babies with rare health problems before the symptoms show up.

When babies are born in North Carolina, they get a heel prick to test for certain health conditions. This is called regular newborn screening. Early Check is a research study that offers two extra tests for **fragile x syndrome and spinal muscular atrophy**. These are rare but serious health conditions.

Why should you join?

- **Knowledge is power.** Taking part in Early Check can help you know whether your baby has either of these health conditions. In the rare case that your baby has a condition, the sooner you know, the better.
- **The tests are free and painless.** The Early Check tests don't require any extra blood to be drawn from your baby. They use blood that is already taken through a standard heel prick after birth. You can sign up for Early Check online without a doctor.
- **You can make a difference.** By taking part in Early Check, you'll help us find treatments for these rare health conditions and improve the lives of babies everywhere.

SEE HOW IT WORKS.

Find out if you're eligible for Early Check

Has your baby been born yet?

NOT YET | YES

Are you a health care provider?

HERE'S WHAT YOU NEED TO KNOW

JOIN NOW

Because it's easy to say yes for your baby's health.

National Center for Advancing Translational Sciences

Led by RTI INTERNATIONAL

With Partners: NCPH North Carolina State Laboratory of Public Health; Duke University; Wake Forest School of Medicine; The University of North Carolina at Chapel Hill

Contact Us
support@earlycheck.org
+1 (866) 881-2715

Launched October 15, 2018

Precision Medicine in the Diagnosis of Genetic Disorders in Neonates

MPIs: Drs. Jonathan Davis and Jill Maron

Floating Hospital for Children at Tufts Medical Center Boston, MA

National Center for Advancing Translational Sciences

Study Overview:

- **Multicenter, prospective study involving 400 high-risk infants with signs/symptoms consistent with a possible genetic disorder**
  - **Tufts, Mt. Sinai, San Diego, Cincinnati, Pittsburgh, UNC**

- **Enrolled subjects will undergo genetic testing on two distinct platforms:**
  - **Rapid Whole Genomic Sequencing (rWGS)**

    AND
  - **Targeted Next Generation Sequencing Panel (TNGS)**
    - **TNGS is comprised of 1,722 monogenetic disorders known to have a neonatal/childhood onset**

Study Objectives

- **To estimate the diagnostic yield of the TNGS and rWGS testing in identifying genetic disorders of unknown etiology**
- **To assess the clinical and economic utility of genomic sequencing in newborns suspected of having a genetic disorder**

News & Events

Stories & Publications

- Features and Briefs
- Scientific Publications
- NCATS E-Newsletter

Media Resources

NCATS-Supported Research Reduces Time to Diagnosis for Seriously Ill Children with Genetic Diseases

Seriously ill children with genetic diseases, particularly infants in intensive care units for whom every hour and day is critical, might now be diagnosed and treated far more quickly than in the past.

Dr. Stephen Kingsmore, President and CEO of Rady Children's Institute for Genomic Medicine

SHARE

RESEARCH ARTICLE | GENETIC DIAGNOSIS

Diagnosis of genetic diseases in seriously ill children by rapid whole-genome sequencing and automated phenotyping and interpretation

Michelle M. Clark[1], Amber Hildreth[1,2,3], Sergey Batalov[1], Yan Ding[1], Shimul Chowdhury[1], Kelly Watkins[1], Katarzyna El...
+ See all authors and affiliations

Science Translational Medicine 24 Apr 2019:
Vol. 11, Issue 489, eaat6177
DOI: 10.1126/scitranslmed.aat6177

Article | Figures & Data | Info & Metrics | eLetters | PDF

A streamlined genetic diagnosis pipeline

Science Translational Medicine
Vol 11, Issue 489
24 April 2019
Table of Contents

ARTICLE TOOLS
Email
Print
Request Permissions
Citation tools
Download Powerpoint
Save to my folders
Alerts
Share

RELATED CONTENT
RESEARCH RESOURCE

https://ncats.nih.gov/pubs/features/rapid-diagnosis-genetic-diseases-children

Connect With NCATS

https://ncats.nih.gov/connect

Website: ncats.nih.gov

Facebook: facebook.com/ncats.nih.gov

Twitter: twitter.com/ncats_nih_gov

YouTube: youtube.com/user/ncatsmedia

E-Newsletter: https://ncats.nih.gov/enews

National Center for Advancing Translational Sciences

CPCI

Consortium for Pediatric Cellular Immunotherapy

Annual Meeting Wrap Up

Children's Hospital Colorado

Children's Hospital LOS ANGELES

Children's National Health System

Seattle Children's HOSPITAL • RESEARCH • FOUNDATION

UCSF Benioff Children's Hospital Oakland

Aim 1: Year 2 Goals

- Disseminate best practices for shipping/receiving cell therapy starting material and final products by publishing manuscript in Cytotherapy
  - To include practical experience-based insights
  - To include training strategies and their pros/cons for external clinical sites (on-site training, videos, written training, check lists, questionnaires)
- Share information among working group for proficiency/competency testing of GMP manufacturing personnel at Consortium sites (FACT)
- Increase in number of cell therapy products distributed among Consortium clinical trial sites

CPCI
Consortium for Pediatric Cellular Immunotherapy

Aim 1: Planned Outputs

Best practices for shipping/receiving cell therapy starting material and final products

manuscript in Cytotherapy

Grant to support training of staff in manufacturing and quality roles.

FACT proficiency training – manuscript year 3?

Engage CTSA education/training

CPCI

Consortium for Pediatric Cellular Immunotherapy

Aim 2: Year 2 Goals

- Develop shared projects on cellular therapy
  - Protocols template
- Share SOPs and supportive care/management guidelines
  - Revaccination
  - Management of CRS and ICANS vs uniform use of CTCAE terminology
- Develop supportive care training modules for cellular therapy research
  - Management of CRS/ICANS?
  - Engage CTSA Educator
- Protocol planning tool (tasks, timelines, resources needed)
  - Project Manager to present timeline data at Steering Committee meeting
- Biobanking protocol template
  - Subgroup?
- LTFU protocol
  - Year 3?

CPCI
Consortium for Pediatric Cellular Immunotherapy

Protocols - Year 3

- PLAT-05
- PLAT-06
  - Supportive care guidelines and associate immune recovery correlative aim
- COG EBV Cell therapy
  - Correlative science/Lab Key use

CPCI
Consortium for Pediatric Cellular Immunotherapy

PAC: Year 2 Goals

Project Timeline: Retrospective Review of Patients Accessing Cellular Therapies

	July 2019	Aug 2019	Sept 2019	Oct 2019	Nov 2019	Dec 2019	Jan 2020	Feb 2020	Mar 2020	Apr 2020	May 2020
IRB Submission											
IRB Approval											
Data Collection											
Data Analysis											
Manuscript Preparation											
Manuscript Submission + Revisions											

CPCI

Consortium for Pediatric Cellular Immunotherapy

PAC: Year 2 Goals

Project Timeline: Patient/Family Survey Re: Perspectives on Accessing Cellular Therapies (PLAT-02)

	July 2019	Aug 2019	Sept 2019	Oct 2019	Nov 2019	Dec 2019	Jan 2020	Feb 2020	Mar 2020	Apr 2020	May 2020	June 2020
Review Draft Survey and Finalize												
IRB Submission												
IRB Approval												
Data Collection												
Data Analysis												
Manuscript Preparation												
Manuscript Submission + Revisions												

CPCI

Consortium for Pediatric Cellular Immunotherapy

PAC Planned Outputs

Manuscripts for the retrospective review and surveys

New **grant opportunities** linked to the parent U01 (Ben Wilfond) and others

- Potential **advocacy collaborations**
  - Kids v. Cancer
  - Children's Cause for Cancer Advocacy
  - Greg Reaman at FDA

CPCI
Consortium for Pediatric Cellular Immunotherapy

Aim 3: Year 2 Goals

Sub-Aim(s)	Goals

1/3	• **Publish manuscript**
	  • Gap analyses (processing best practices & flow assay alignment)
	  • SCH flow comparison study data (other datasets?)

2	• Implement & expand LK from Seattle to multiple sites – **COG EBV cell protocol correlative studies**
3	• Take lessons learned and develop training materials for flow assay

CPCI
Consortium for Pediatric Cellular Immunotherapy

Aim 3: Planned Outputs

Manuscript highlighting specimen processing best practices and flow assay alignment (include SCH sample comparison data)

Abstracts/presentations at CTSA conferences

Training documents and **SOPs** generated from lessons learned to be shared with Consortium sites

Correlative studies for COG EBV cell therapy trial, LabKey integration?

CPCI
Consortium for Pediatric Cellular Immunotherapy

Aim 4 – Year 2

- Grant applications?
- CureWorks expansion
- Scientific meeting through CureWorks?

CPCI
Consortium for Pediatric Cellular Immunotherapy

Additional Items

- Structure/participation of Steering Committee Call
  - All PI and sub-PI
  - All aim leads
  - ICC leadership
  - CTSA evaluator/CTSA education
  - SCRI Grants
- Where/How would pre-concepts be presented
  - Included in roles/responsibilities Steering Committee
- Annual Meeting 2020
  - Format
  - Participants
  - Location/Overlap with CIPO Sept 2020?
- Key Personnel Replacement for Troy Torgerson

CPCI
Consortium for Pediatric Cellular Immunotherapy

CPCI

Consortium for Pediatric Cellular Immunotherapy