CPCI

Consortium for Pediatric Cellular Immunotherapy

4th Annual Meeting
October 11 – 12, 2021

Annual Meeting Welcome

October 11, 2021 | Bonnie Ramsey

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Consortium for Pediatric Cellular Immunotherapy

Welcome Collaborators

Special Guest | NCATS

PJ Brooks, PhD

Program Director
National Center for Advancing Translational Sciences
National Institutes of Health

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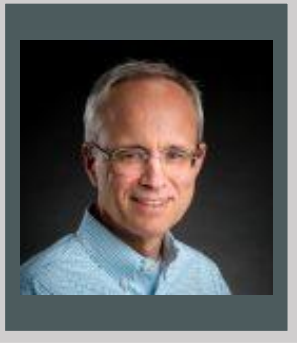
Special Guests | External Advisory Board



Stephen Gottschalk, MD | St. Jude Children's Research Hospital

Member, St. Jude Faculty
Chair, Department of Bone Marrow Transplantation & Cellular Therapy
Endowed Chair in Bone Marrow Transplantation & Cellular Therapy

Leslie Kean, MD, PhD | Dana-Farber/Boston Children's Cancer and Blood Disorder Center

Director, Stem Cell Transplant Center
Robert A. Stranahan Professor of Pediatrics, Harvard Medical School

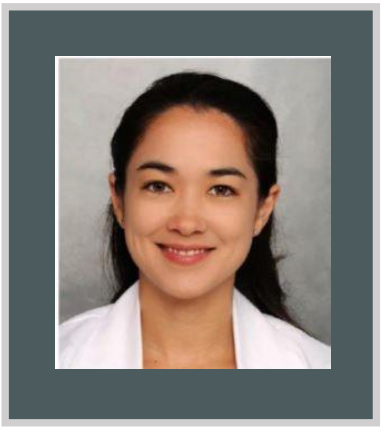
Michael Konstan, MD | Case Western Reserve University

Gertrude Lee Chandler Tucker Professor of Pediatrics, Department of Pediatrics, School of Medicine
Vice Chair for Clinical Research, Department of Pediatrics Division of Pulmonology Allergy and Immunology, School of Medicine
Vice Dean for Translational Research, School of Medicine
Principal Investigator, Clinical and Translational Science Collaborative, School of Medicine

Training & Mentoring

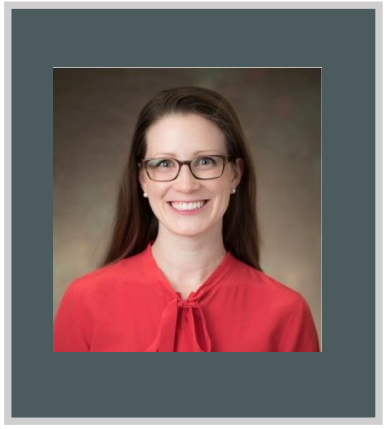
Bindu Hegde, PhD
UCSF

Chintan Parekh, MD
USC



Hannah Kinoshita, MD
GWU

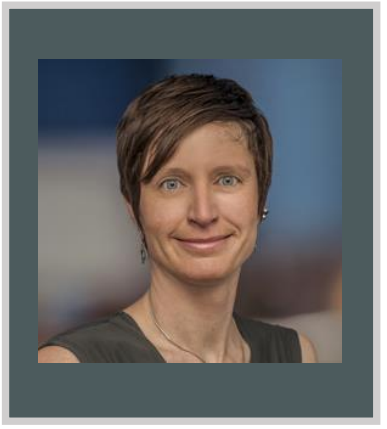
Nick Vitanza, MD
UW



Elizabeth Crouch, PhD
UCSF

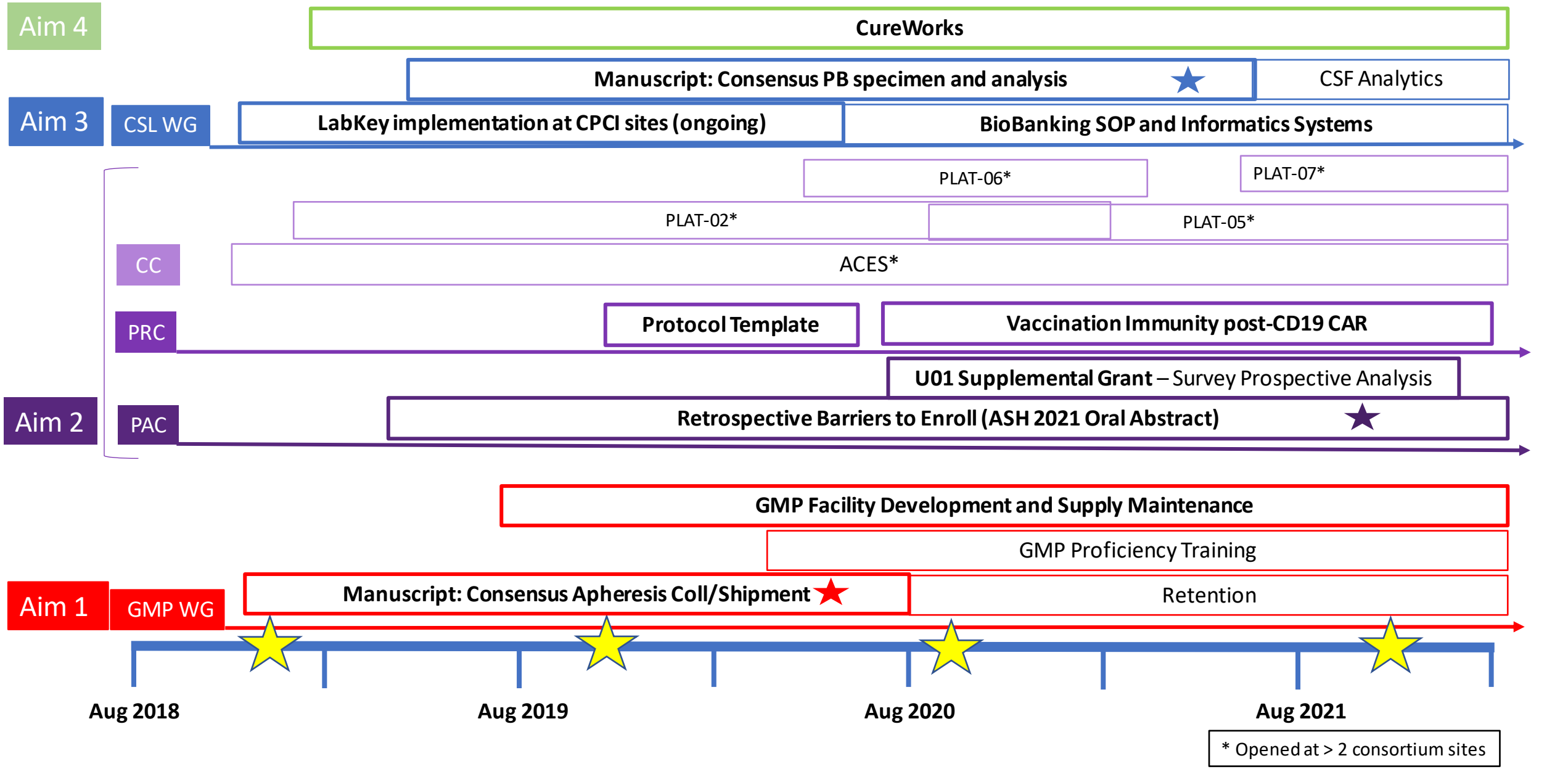
Russell Cruz, MD, PhD
GWU

Siddhartha Mitra, PhD
CU



Juliane Gust, MD, PhD
UW

Timelines/Notable Accomplishments



Website

CPCIsite

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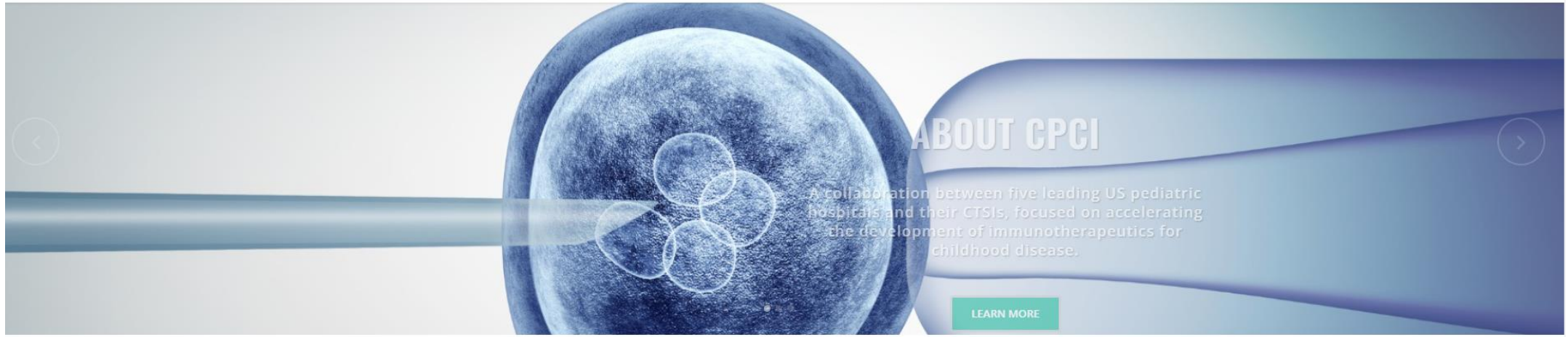
ABOUT | MAJOR INITIATIVES | EDUCATIONAL RESOURCES | CONSULTATIONS | CONTACT US



The promise of immune-directed cellular therapies is great – so are the challenges of translating the science into clinical trials which could lead to approved therapeutics for diseases states like auto-immunity, infection and cancer. In pediatric medicine, these translational challenges are exacerbated by the "orphan" scale of incidence, limited pediatric-dedicated cGMP production facilities and the low financial returns which make industry-sponsored research less likely.

The Consortium for Pediatric Cellular Immunotherapy is working to address these challenges by pooling its expertise and sharing its learnings with the broader community. By working together, we believe we can accelerate innovation in the field and bring these life-saving treatments to children more quickly and efficiently.


ABOUT THE CONSORTIUM


MAJOR INITIATIVES


EDUCATIONAL RESOURCES


CONSULTATIONS

Home Page

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PARTICIPATING SITES

Members of the Consortium include the following children's hospitals and their affiliated CTSIs:

Children's Hospital Los Angeles
About

SC CTSI
About

Children's National
About

CTSI Clinical and Translational Science Institute at Children's National
A PARTNERSHIP WITH THE GEORGE WASHINGTON UNIVERSITY
About

Children's Hospital Colorado
About

Colorado Clinical and Translational Sciences Institute (CCTSI)
About

Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION
About

ITHS Institute of Translational Health Sciences
ACCELERATING RESEARCH. IMPROVING HEALTH.
About

UCSF Benioff Children's Hospitals
About

UCSF Clinical & Translational Science Institute
About

ABOUT
Mission
Participating Sites
Committees & Working Groups

Participating Sites

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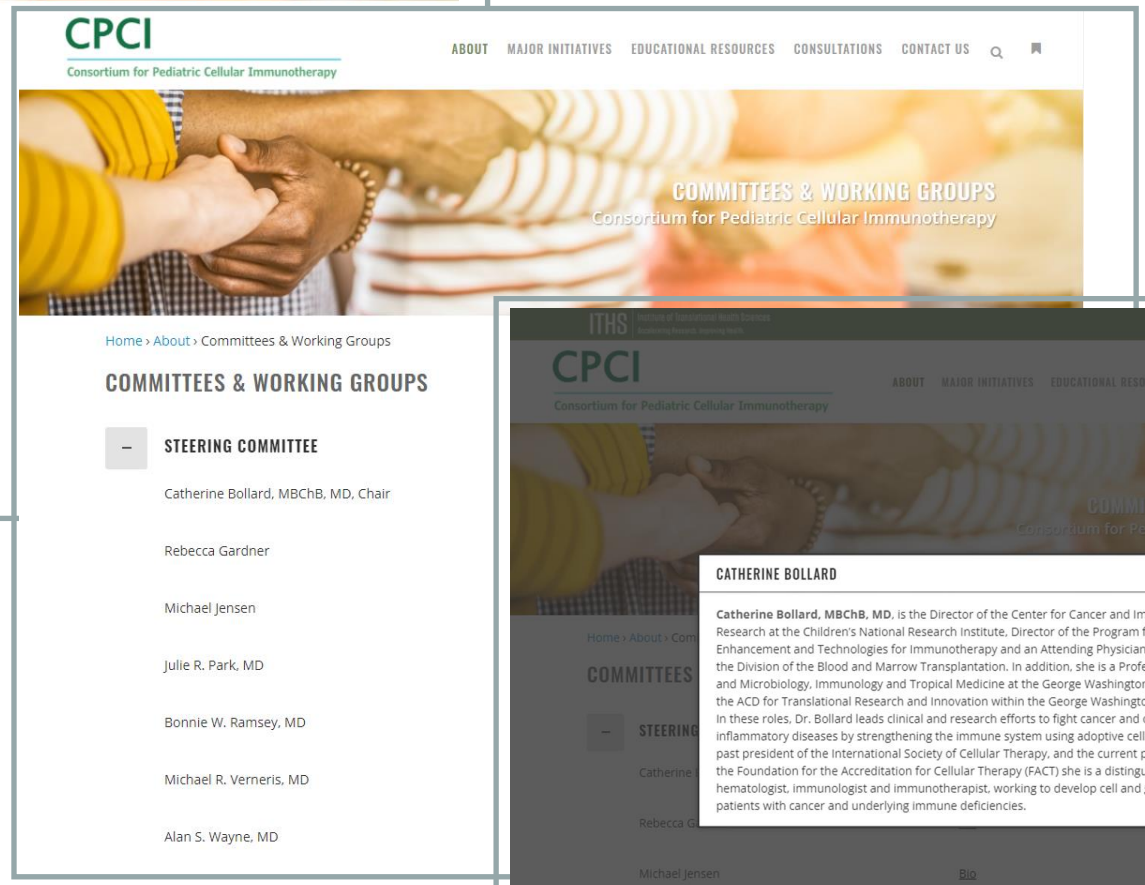

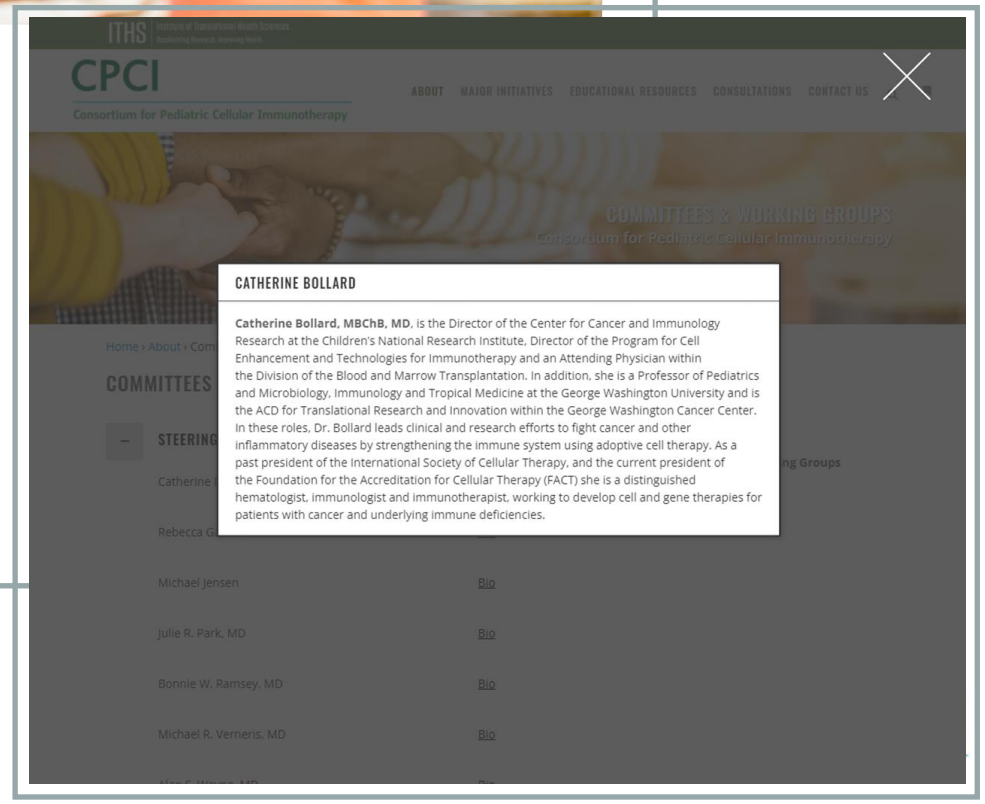

Committees & Working Groups

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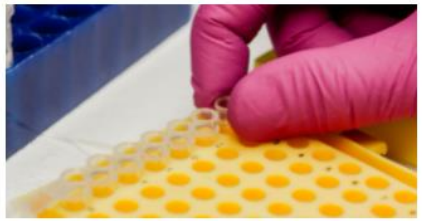
Home › Major Initiatives

MAJOR INITIATIVES

PATIENT ACCESS



CORRELATIVE STUDIES

CLINICAL TRIAL INFRASTRUCTURE

SUPPORTIVE CARE

MANUFACTURING

MAJOR INITIATIVES

- Patient Access
- Clinical Trial Infrastructure
- Manufacturing
- Correlative Studies
- Supportive Care

Major Initiatives

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Home › Major Initiatives › Patient Access

EXPANDING ACCESS TO CELL-BASED IMMUNOTHERAPEUTICS TO ENSURE HEALTH EQUITY.

A key challenge in treating pediatric populations with rare disease is ensuring equitable access of cellular immunotherapies to children, regardless of their site of primary medical care, racial, or socio-economic status. Clinical trial complexity may impede the enrollment of study participants if multiple clinical assessments or research visits are required, especially if study participants travel significant distances from their primary residence.

The Patient Advocacy Committee of the Consortium is actively working to understand the pediatric

MAJOR INITIATIVES

- **Patient Access**
- Clinical Trial Infrastructure
- Manufacturing
- Correlative Studies
- Supportive Care

Patient Access

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ABOUT MAJOR INITIATIVES EDUCATIONAL RESOURCES CONSULTATIONS CONTACT US

Home › Consultations › Request a Consultation

REQUEST A CONSULTATION

If your institution is interested expanding its expertise in pediatric immunotherapeutics, multi-site trials and/or cGMP manufacturing facilities and would benefit from the opportunity to speak with one of our Consortium members, complete the form below. Please provide a detailed description of your area of interest so that we can connect you with the appropriate Consortium member. Consultations are dependent on consultant availability and demand.

CONSULTATIONS

Request a Consultation

Consultations

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Agenda

8:15	**Aim 1 | cGMP Working Group**	*Christopher Brown & Stephanie Mgebroff*
9:00	**Break**	
9:15	**Aim 2 | Overview**	*Julie Park*
9:30	**Aim 2 | Protocol Review Committee**	*Mike Verneris & Rebecca Gardner*
10:30	**Break**	
10:45	**Aim 2 | Patient Advocacy Committee**	*Anurag Agrawal*
11:45	**Wrap Up**	*Julie Park*
12:00	**Adjourn**	

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Annual Meeting
Aim 1
cGMP Working Group

October 11, 2021 | Christopher Brown • Stephanie Mgebroff

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Aim Overview

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

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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

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Membership

• Julie Annis	*Supervisor, BMT Laboratory – CHLA*
• Christopher Brown	*Director GMP Cell Production - SCTx*
• Jonathan Esensten, MD, PhD	*Medical Director, Regulatory T Cell Manufacturing Group - UCSF*
• Roger Giller	*Medical Director Charles C. Gates Biomanufacturing Facility – 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 & Quality Assurance – SCRI*
• Stephanie Mgebroff	*Director Research Quality Control - SCTx*
• Matt Seefeldt	*Director of Cell Therapy Charles C. Gates Biomanufacturing Facility – CU*
• **Abeer Shibli, MT**	***Cell Therapy Lab Specialist - CNHS***
• Jay Tanna	*Quality Assurance Lead – CNHS*
• **Chandresh Undhad**	***Associate Director Quality Charles C. Gates Biomanufacturing Facility - CU***

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Accomplishments

- Articulated best practices for cGMP competency and proficiency programs
  - FAQ-style document,
  - Content-complete and awaiting web deployment
- Continued collaboration related to staff development pathways and retention strategies for cGMP personnel
  - Recurring discussion topic at monthly working group meetings

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Accomplishments

- Continued focus on COVID-19 supply chain issues
  - Standing agenda item at working group meetings
  - Escalation of relevant material shortages
  - Collaborative mitigation planning

- Numerous ad-hoc conversations among working group, including but not limited to
  - Significant figures & rounding rules
  - Microbiology lab collaboration
  - Deviation trending
  - Sterile media fill processing

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Q&A: Proficiency / Competency Best Practices

Q: Are staff trained and assigned to particular manufacturing processes and/or clinical trials? Are QC staff trained and assigned to particular studies and/or analytical tests?

A: This must be assessed based on the business needs of the team. Items to consider which impact this decision can include capacity, accrual rate, budgetary constraints, process complexity, overlap between similar processes, and the like. Important to ensure sufficient trained staff exist to meet projected "surge" capacity, and/or to have a plan in place for rapid cross-training if needed.

Q: For manufacturing, is there a difference in training in order for staff to be operators vs verifiers?

A: In general, while the same training overall is necessary, there are mixed preferences with respect to whether operation or verification is the first role performed by newly trained staff. This is in part dictated by the size of the team and the frequency of the processes in question. In some cases, supervisors or QA can perform some verifications (label preparation, calculations, etc).

Q: What are the consequences for failing to demonstrate competency?

A: Generally, retraining with counseling/coaching. This should generally be considered as ongoing education rather than a simple pass/fail. However, depending on the severity of the observation, more severe corrective action may be indicated, up to and including separation of employment.

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Y4 – Y5 Goals & Metrics

Deliverable	Proposed Completion Date	Comments
Articulate key operational considerations to facilitate third-party microbiology testing of early-phase cGMP production facilities	February 2022	
In-person working group meeting	May 2022	COVID-19 dependent
cGMP facility audits between two consortium sites	May 2022	COVID-19 dependent
Activate cGMP manufacturing at one additional site (USC)	May 2022	
Implement and continue to refine strategies for promoting retention and team engagement in at least 3 CPCI sites over the course of Y4	End of Y4	
Develop platform for the continued collaboration of the cGMP Working Group into Y5 and beyond	End of Y5	

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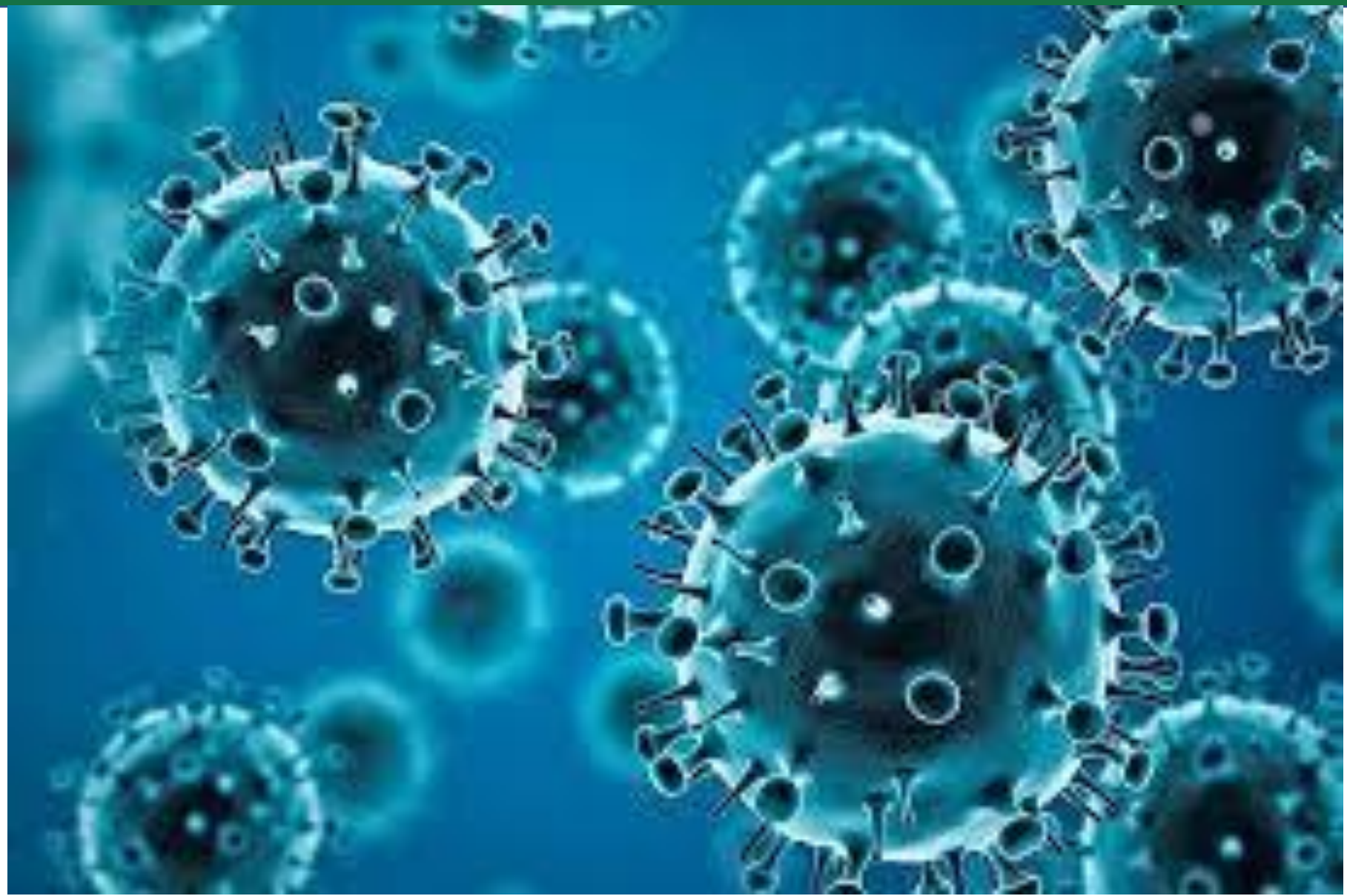
Barriers to Achieving Goals



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Annual Meeting Aim 2 Overview

October 11, 2021 | Julie Park

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Consortium for Pediatric Cellular Immunotherapy

Aim Overview

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

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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

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Accomplishments

- Clinical trial infrastructure provides tools, SOPs and learnings to CPCI
- Provide CPCI institutions access to cellular therapy clinical trials
- Implementation of Salesforce as an interface to schedule and track apheresis and manufacture

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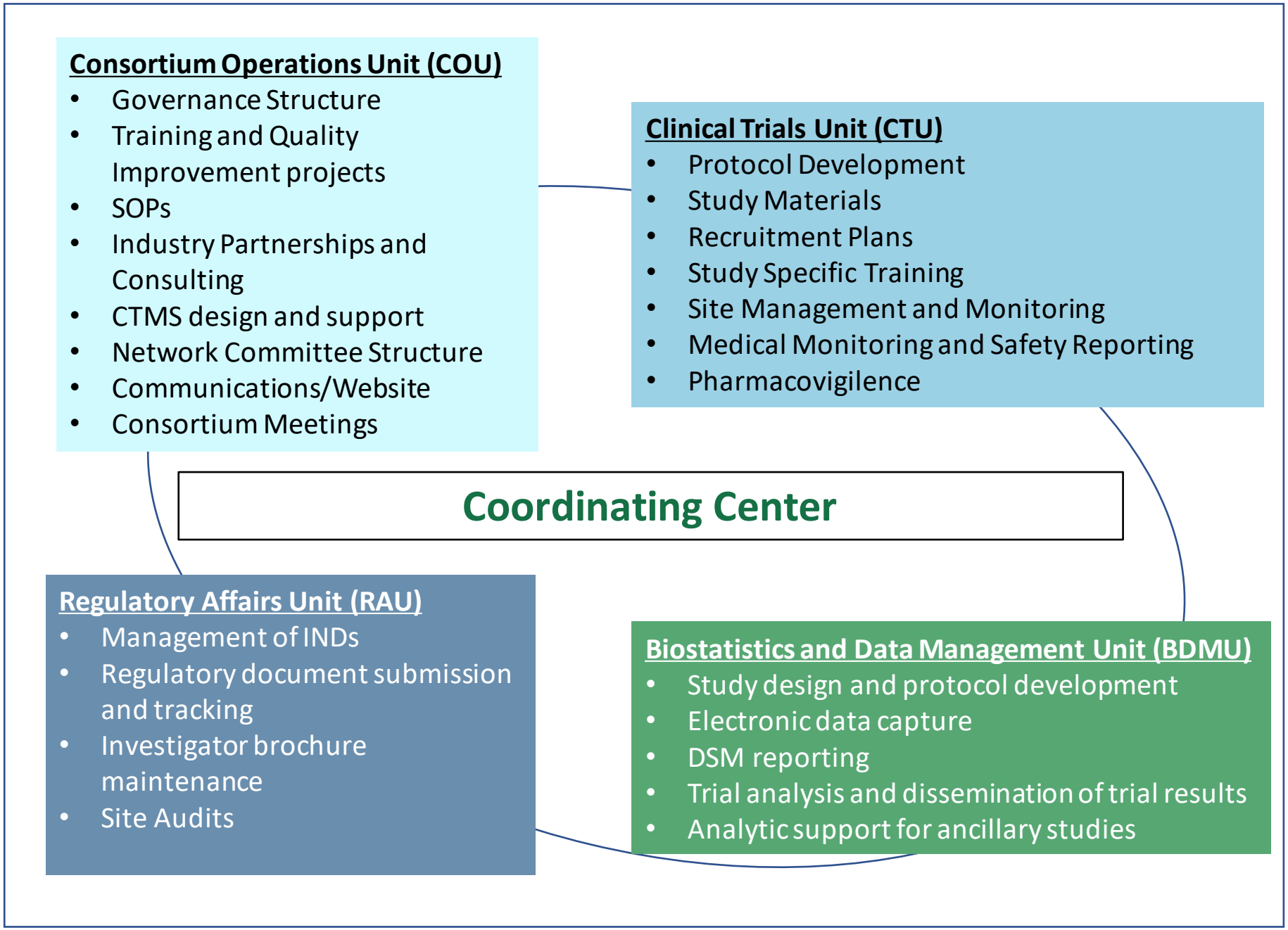
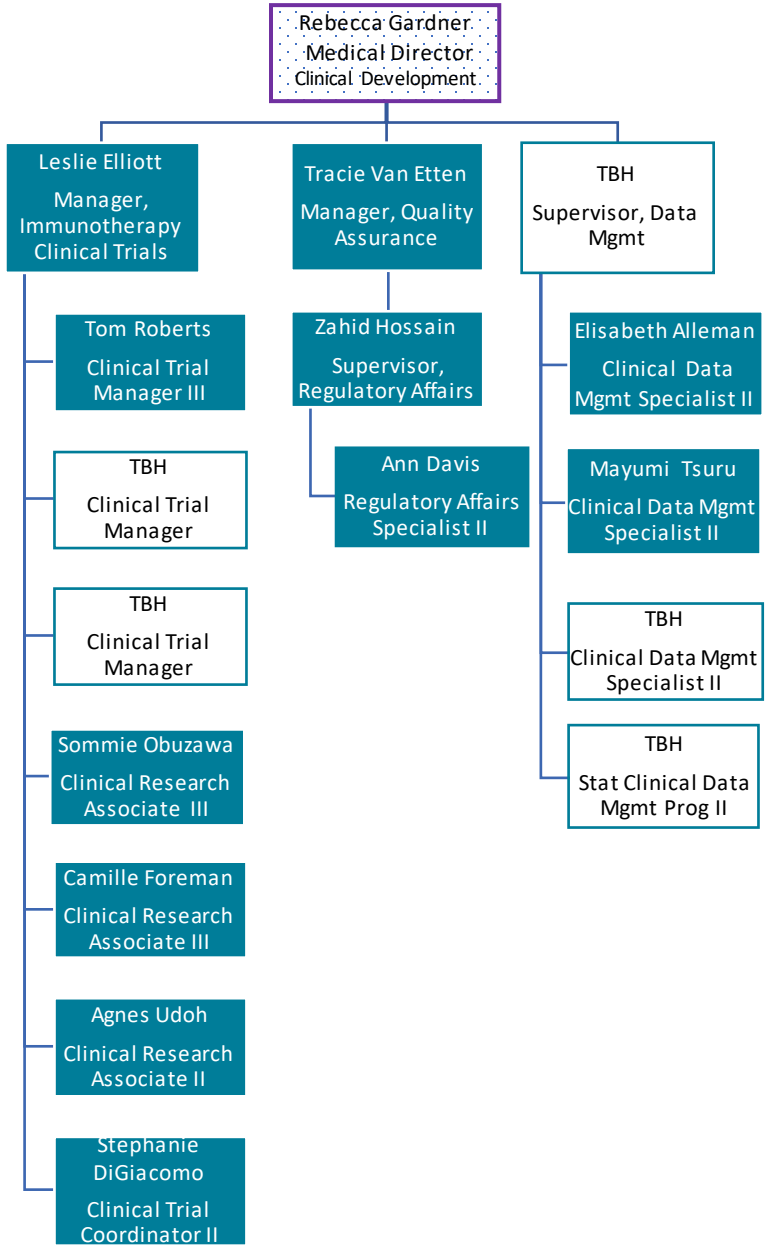
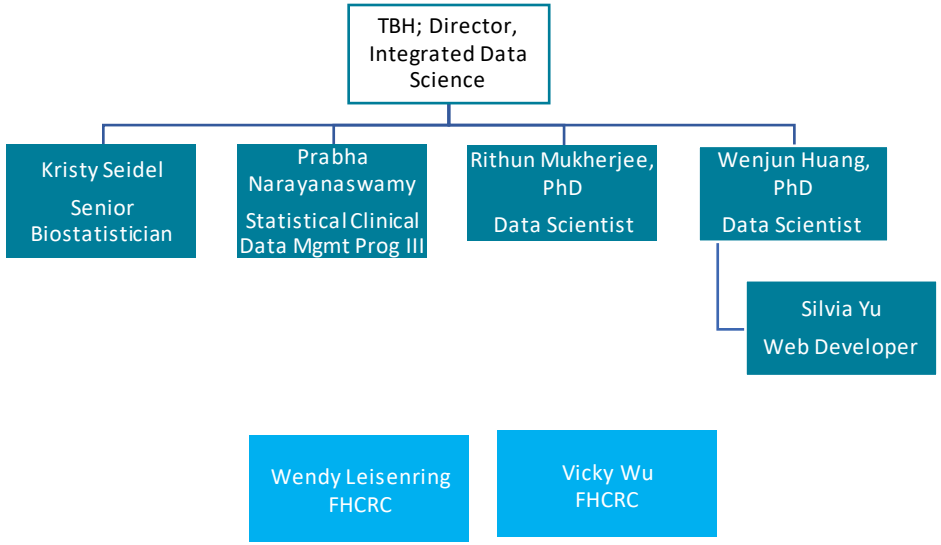

Consortium Operations Unit (COU)
• Governance Structure
• Training and Quality Improvement projects
• SOPs
• Industry Partnerships and Consulting
• CTMS design and support
• Network Committee Structure
• Communications/Website
• Consortium Meetings
Clinical Trials Unit (CTU)
• Protocol Development
• Study Materials
• Recruitment Plans
• Study Specific Training
• Site Management and Monitoring
• Medical Monitoring and Safety Reporting
• Pharmacovigilence
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

Clinical Trials Infrastructure





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Clinical Trials

Name	NCT.gov	Site	Status
PLAT-02	NCT02028455	CHLA, SC, U-BCHO	Phase 2 leukemia completed 12/2019, open for lymphoma, closed to accrual February 2021
ACES	NCT03475212	CHC, CHLA, CNMC, SC, UCSF	Open to accrual
PLAT-05	NCT03330691	CNMC, SC, CHLA, U-BCHO	Open to accrual
PLAT-06	NCT03684889	CHLA, SC, U-BCHO	Accrual halted, January 2021
PLAT-07	NCT04571138	SC, CHLA	Open to accrual

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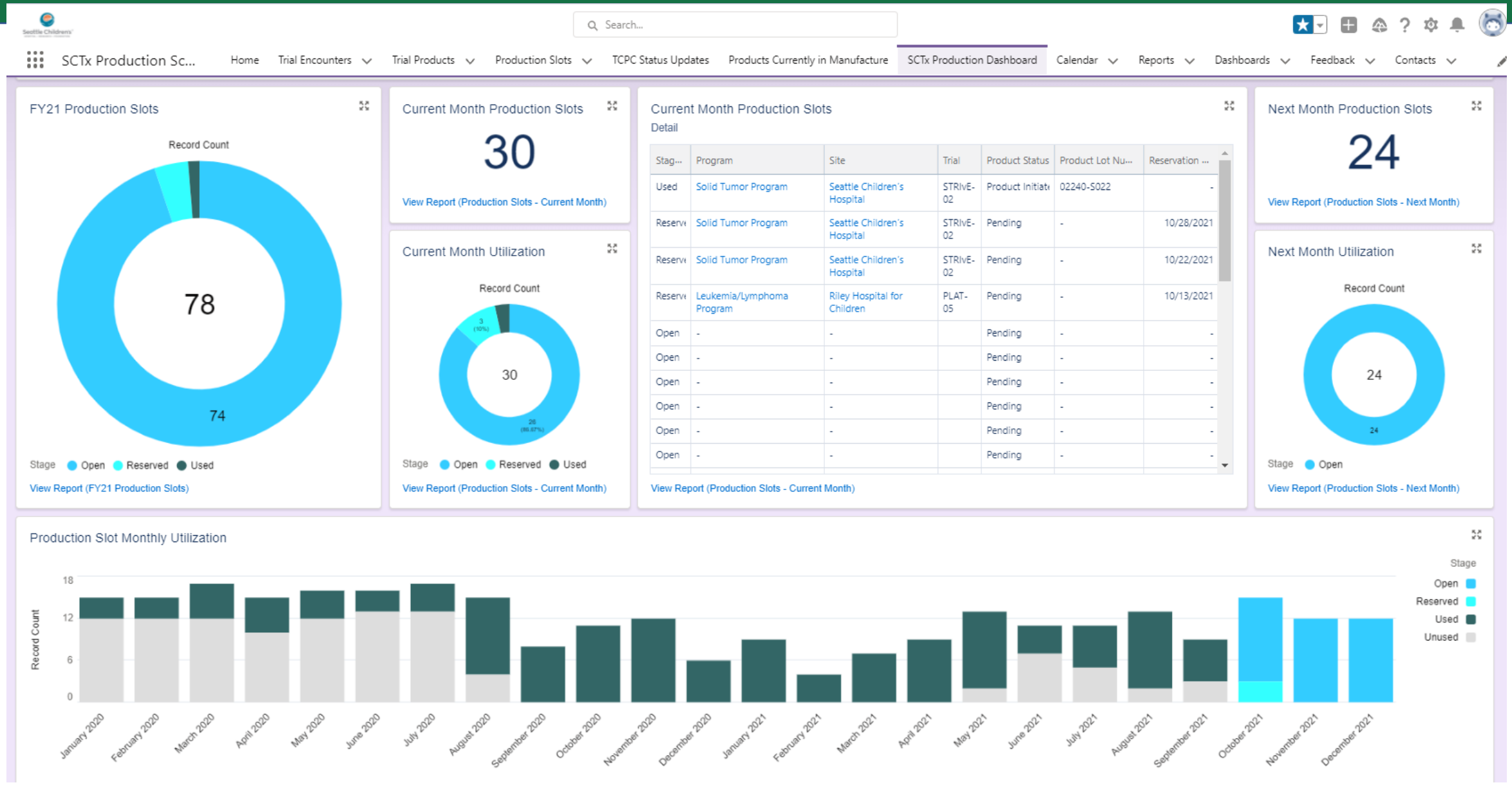
Salesforce – Cell Therapy Production



Y4 – Y5 Goals & Metrics

- Continued clinical trial development with focus on non-cancer indications
  - Stay tuned for Scientific Lecture tomorrow
  - COVID-19 specific T cell therapy (CNMC, M. Keller)
- Share analytic tools
  - Statistical analytic plan templates
  - Trial design examples (3+3, Up Down Escalation, Boin)
  - More to come from PRC

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Annual Meeting
Aim 2
Protocol Review Committee

October 11, 2021 | Michael Verneris • Rebecca Gardner

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Consortium for Pediatric Cellular Immunotherapy

Membership

Paibel Aguayo-Hiraldo, MD	*Pediatric Hematologist-Oncologist – CHLA*
Karin Chen, MD	*Pediatric Immunologist – SCH*
Dana Dornsife	*Founder and Chair - Lazarex Cancer Foundation*
Leslie Elliott	*Manager, Clinical Trial Management, ClinDev SCTx*
Rebecca Gardner, MD	*Pediatric Hematologist-Oncologist – SCH*
Emily Hsieh, MD	*Pediatric Hematologist-Oncologist – CHLA*
Michael Keller, MD	*Pediatric Immunologist – CNHS*
Jennifer Michlitsch, MD	*Pediatric Hematologist-Oncologist - BCHO*
Julie Park, MD	*Pediatric Hematologist-Oncologist – SCH*
Michael Verneris, MD	*Pediatric Hematologist-Oncologist – CHC*
Vicky Wu, PhD	Bio-*Statistician - FHCRC*

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Accomplishments

- PrevCAR trial Moving to Regulatory Submission
- Protocol Template available on SharePoint
- Immunization Guidelines available on SharePoint

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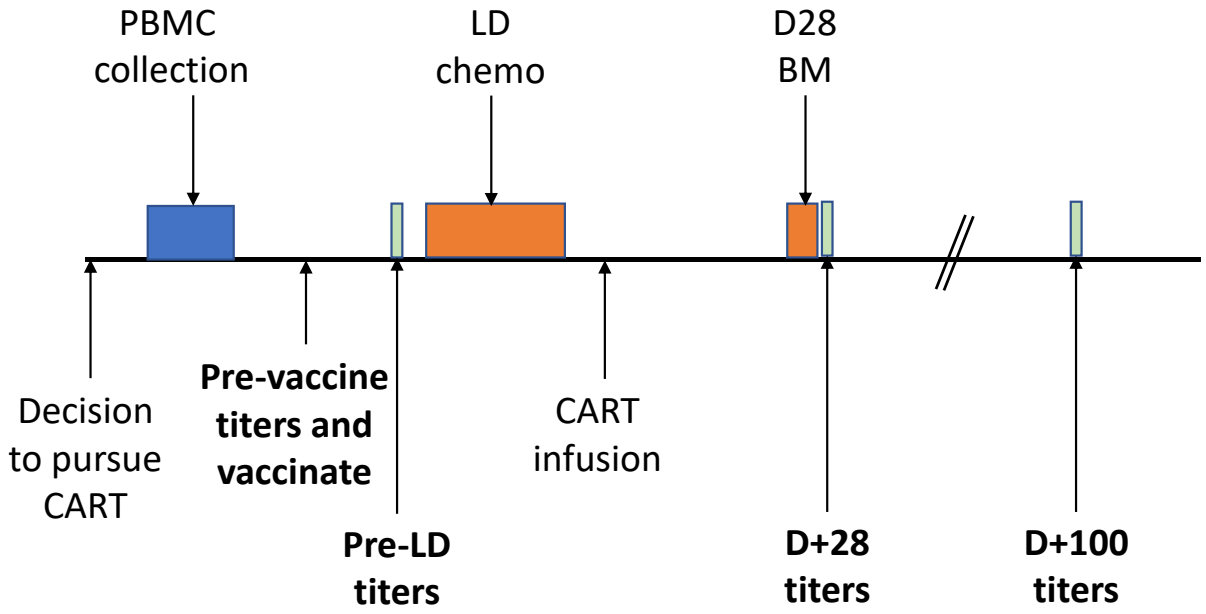
PrevCAR Protocol Details

- Eligibility: up to age 30, planned CD19 or CD22 directed T cell therapy, willing to receive Prevnar 13, willing to have blood draws
  - Excluded if receiving IV or SQ immunoglobulin replacement within past three months or unable to have Prevnar 13 due to medical contraindications



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PrevCAR Role Out

- Protocol and Consent are complete
  - SCH to submit to IRB, once approved at SCH, then all other sites could submit
  - SCH will be lead study site
- Draft CRFs completed on paper and moving to build in RedCap
- SCH will serve as data coordinating center
  - Agreements in process with all groups

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Y4 – Y5 Goals & Metrics

Deliverable	Proposed Completion Date	Comments
Disseminate Template for IB	June 2022	Incorporate as part of PV program
Safety committee to review toxicity within SCTX ClinDev group – SOP to be disseminated to CPCI sites	Jan 2022	Incorporate as part of PV program
Implement global CRFs	Jan 2023	Being developed at SCH for solid/brain/liquid oncology trials
LTFU protocol for gene therapy	Jan 2023	SCTx LTFU protocol will be implemented at some of the sites

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PV and Oversight Requirements

- Limited knowledge has been disseminated regarding academic sponsor PV programs for first in human trials
- Protocol Committee is planning to collect practice information from participating sites over next few months as part of our monthly calls
- Plan for a white paper to cover how to establish/form sponsor responsibilities of PV at academic center for first in human cell therapy trials

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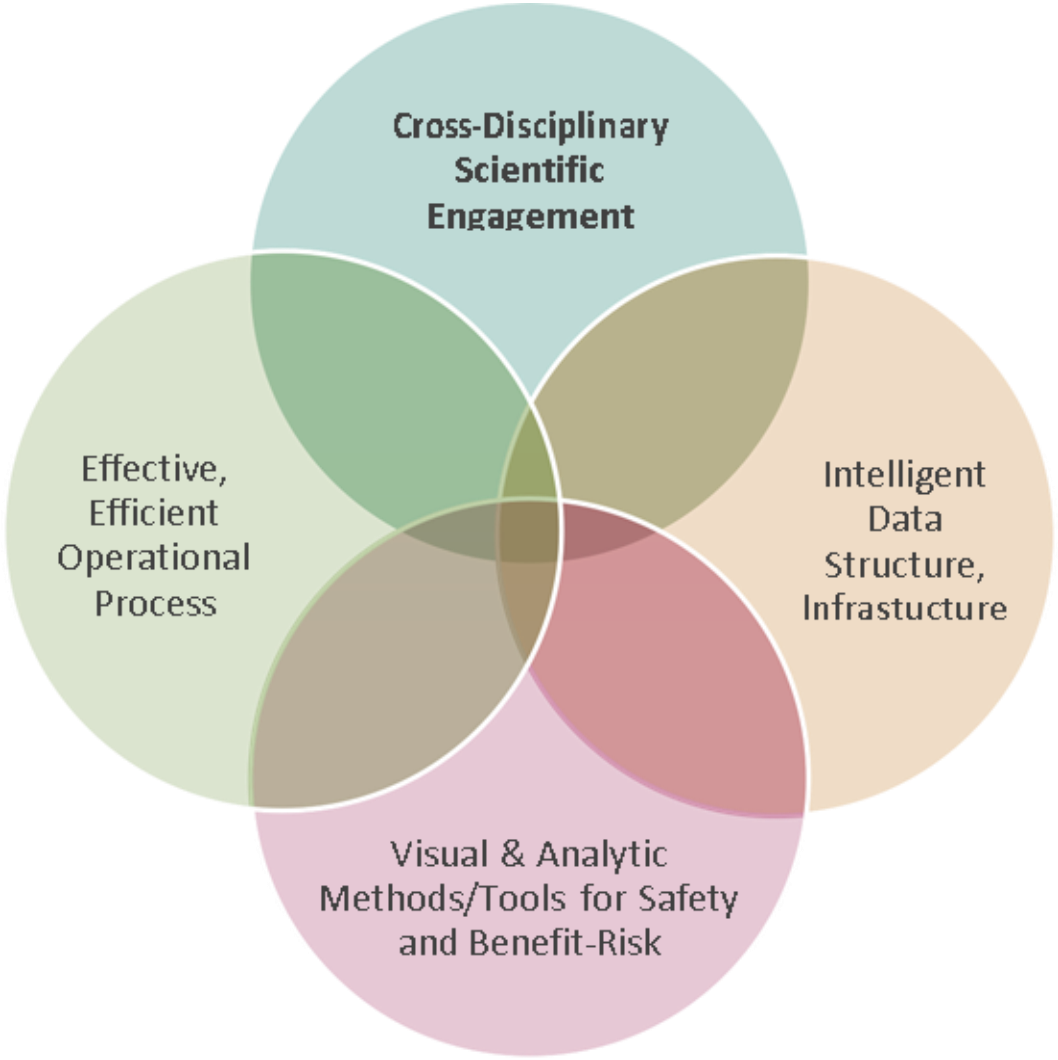
The Four Pillars of Safety Oversight

In the best interest of the patients we serve



Cell **T**herapy **O**perations **P**rogram

Trial Oversight & Remediation

Based on best practices, CPCI can assist in establishing a solid clinical oversight management structure and assess and remediate critical issues

- Data strategy definition, quality review, and remediation
- Monitoring oversight (including development of Clinical Monitoring Plan as risk mitigation strategy)
- Site education and documentation of training
- Logistics of transitioning from treatment protocol of cell and gene therapy trials (CGTs) to FDA-mandated LTFU study.
- Operational expert resources for key project milestones (Project Manager)

Pharmacovigilance

Develop and execute against a pharmacovigilance (PV) strategy to ensure compliance and patient safety

- **Strategic guidance for establishing a PV organization (templates, best practices)**
  - Medical Monitor
  - Pharmacovigilance Nurse
  - Treatment Review Committee (TRC)
  - Weekly patient oversight calls
  - Data and Safety Monitoring Committee (DSMC)

- **Assessment of safety signals and issue management**
  - AE/SAE SOPs
  - Investigator Brochure (IB)

- **Leveraging technology evaluation and selection**
  - Providing sites with rules-based AE spreadsheet
  - Customizing electronic data capture (EDC) to detect data or safety trends

Where could CPCI provide templates/best practices?

- **Strategic guidance for establishing a PV organization**
  - Medical Monitor – Job Description?
  - Pharmacovigilance Nurse - **Job Description?**
  - Treatment Review Committee (TRC) - SOP
  - Weekly patient oversight calls
  - Data and Safety Monitoring Committee (DSMC)

- **Assessment of safety signals and issue management**
  - AE/SAE SOPs, redcap database for safety
  - Investigator Brochure (IB) - template

- **Leveraging technology evaluation and selection**
  - Providing sites with rules-based AE spreadsheet
  - Customizing electronic data capture (EDC) to detect data or safety trends

Barriers to Achieving Goals

- Disseminating this information in a meaningful way
- Access to the website, information that goes on the website
- Keeping thing up to date

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Annual Meeting
Aim 2
Patient Advocacy Committee

October 11, 2021 | Anurag Agrawal

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Consortium for Pediatric Cellular Immunotherapy

Annual Meeting
Aim 2
Patient Advocacy Committee

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

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Consortium for Pediatric Cellular Immunotherapy

Membership

• Anurag Agrawal, MD	*Pediatric Hematologist-Oncologist - BCHO*
• Paibel Aguayo-Hiraldo, MD	*Pediatric Hematologist-Oncologist - CHLA*
• 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*
• Devan Duenas, MA	*Clinical Research Coordinator, Treuman Katz Center – SCRI*
• Anurekha Hall, MD	*Pediatric Hematologist-Oncologist – SCRI*
• Amy Keating, MD	*Pediatric Hematologist-Oncologist – CHC*
• Adam Lamble, MD	*Pediatric Hematologist-Oncologist – SCRI*

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Membership

• Jonathan Marron, MD, MPH	*Pediatric Hematologist-Oncologist, Clinical Ethicist – BCH/DFCI*
• Diana Merino Vega, PhD	*VP Advocacy – Childhood Cancer Survivor Canada*
• 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*
• **Anant Vatsayan, MBBS**	***Blood and Marrow Transplantation – CNH***
• Mark Walters, MD	*Director, Blood and Marrow Transplantation Program – BCHO*
• Ben Wilfond, MD	*Investigator, Treuman Katz Center for Pediatric Bioethics – SCRI*
• Lena Winestone, MD, MSHP	*Pediatric Hematologist-Oncologist - UCSF*

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Accomplishments

- Patient Advocacy Committee continues to expand
- Supplemental U01 grant
- ASH presentation re: retrospective dataset

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Overview of Works in Progress

- Retrospective review of ALL patients treated at consortium institutions (Anu H)
- Survey of patients/families that have undergone CAR-T trials at consortium sites (Anu H)
- Caregiver interviews (Devan)
- Survey of providers that have referred to consortium sites for CAR-T trials
- Referring provider interviews
- Understanding the overall landscape in accessing cellular therapies (Anant)

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Works in Progress—Retrospective Review

Access to CAR-T-Cell Therapy in Underrepresented Populations: A Multicenter Cohort Study of Pediatric and Young Adult ALL Patients

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Social determinants of health are associated with inferior outcomes

- Children with AML living in low-income areas have inferior EFS and OS
- Children with sarcoma without insurance or with public insurance had inferior OS regardless of disease stage
- Poverty independently associated with increased risk of relapse and death in NB patients
- Hispanic children with ALL have inferior EFS

Winestone LE, et al. ASH Annual Meeting 2019.
Penumarthy, et al. Cancer Med 2020.
Bona K, et al. JNCI 2020.
Kahn JM, et al. PBC 2018.

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CAR-T cells can be difficult to access

- Unique challenges in access
  - Limited number of institutions with manufacturing capabilities
  - High cost of manufacturing
  - Limited number of institutions where CAR-T cells can be safely infused

- Known disparities in enrollment on pediatric oncology trials
  - Including minority patients, children of Spanish-speaking parents, AYA patients
  - Major barriers: language discordance, travel difficulties, complex clinical trial designs

Aristizabal P, PBC 2015.
Winestone LE, Leuk Lymph 2019.
Russo C, et al. PBC 2020.

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Methods

- All patients with B-ALL diagnosed and treated at consortium site between 2012-2018
  - Including patients who enrolled on a CAR-T clinical trial for r/r B-ALL between 2012-2018

- Retrospective review
  - EMR data
  - Geospatial mapping to calculate SES scores

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Different cohorts

- **Referred CAR-T**: r/r patients referred for CAR-T from outside institutions
- **Local CAR-T**: r/r patients referred for CAR-T at their home institutions
- **Other relapse**: r/r patients not referred for CAR-T at their home institutions
- **Without relapse**: patients without r/r disease

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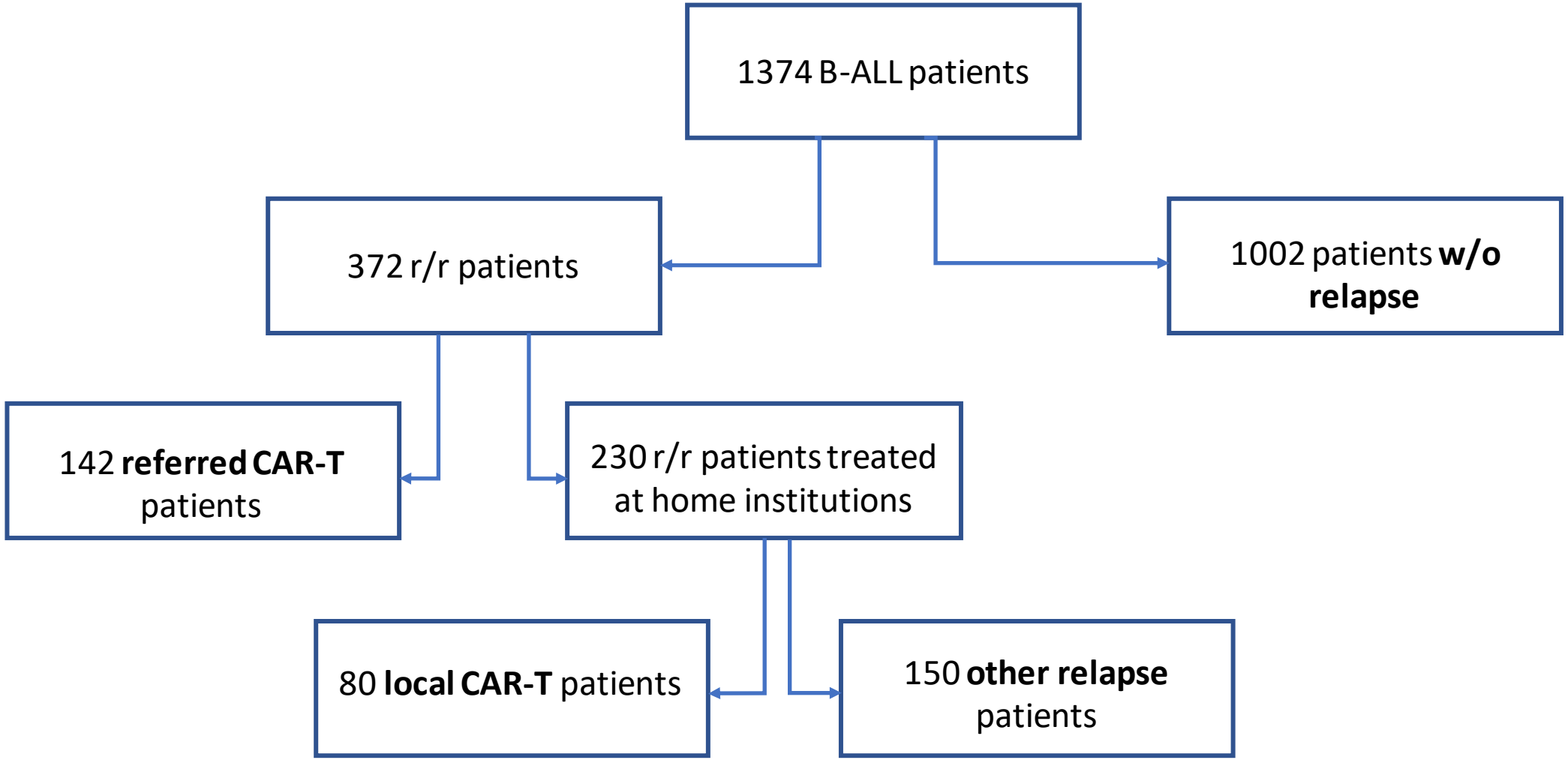
All Patients



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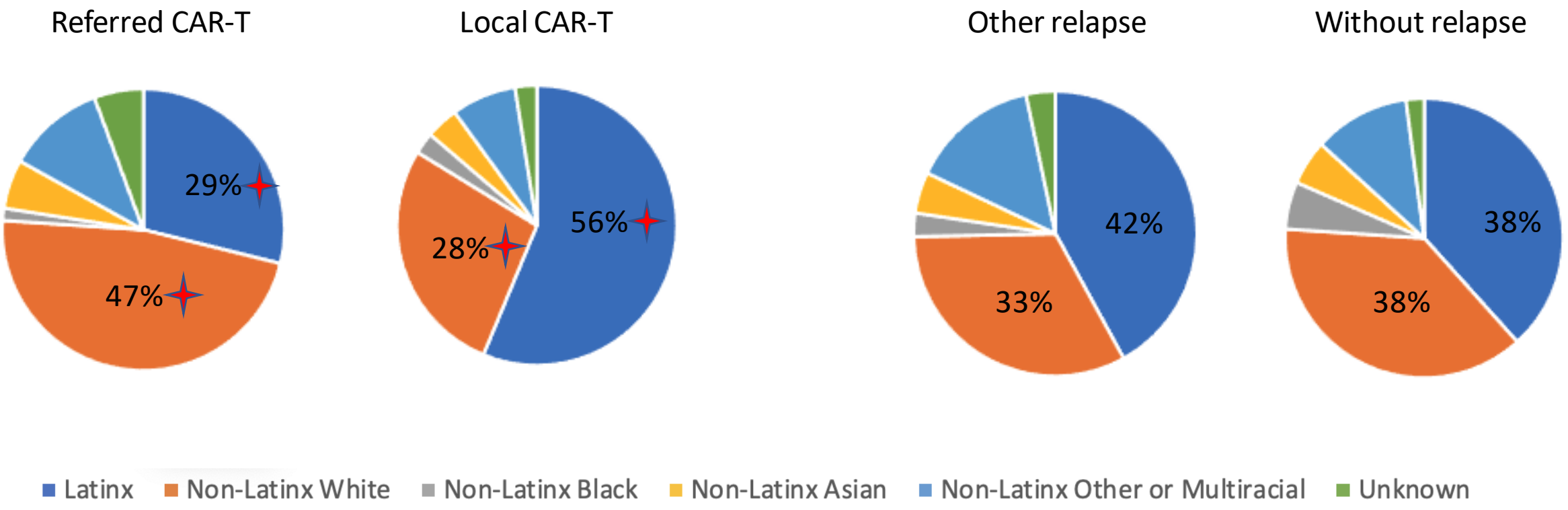
Results

	Referred CAR-T	Local CAR-T	Other relapse	Without relapse
	N=142	N=80	N=150	N=1002
Female	32%	48%	46%	45%
Age at initial Dx (yrs)	7.8	8.9	8.4	6.4
Participation in Upfront Trial	48%	41%	59%	66%
Site				
CHLA	3%	48%	15%	19%
CHO/UCSF	6%	8%	17%	19%
Colorado	18%	15%	22%	29%
Children's National	4%	3%	17%	16%
Seattle	70%	28%	29%	18%

CPCI

Race/Ethnicity



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Language and Insurance

	Referred CAR-T	Local CAR-T		Other relapse	Without relapse
Language			*		
English	85%	75%		71%	80%
Spanish	6%	24%		27%	17%
Other	9%	1%		2%	3%
Insurance			*		
Medicaid	31%	65%		55%	50%

CPCI

Conclusions

- Demographics of referred CAR-T patients notably different than local CAR-T patients
- Spanish-speaking patients and patients with public insurance underrepresented in referrals from outside institutions
- Mean SES scores similar across all groups
- Differences in part due to site-specific demographics

CPCI

Works in Progress—Surveying families who received CAR-T cells

- Including questions on barriers and access, information and knowledge
  - 32 completed at Seattle Children's Hospital

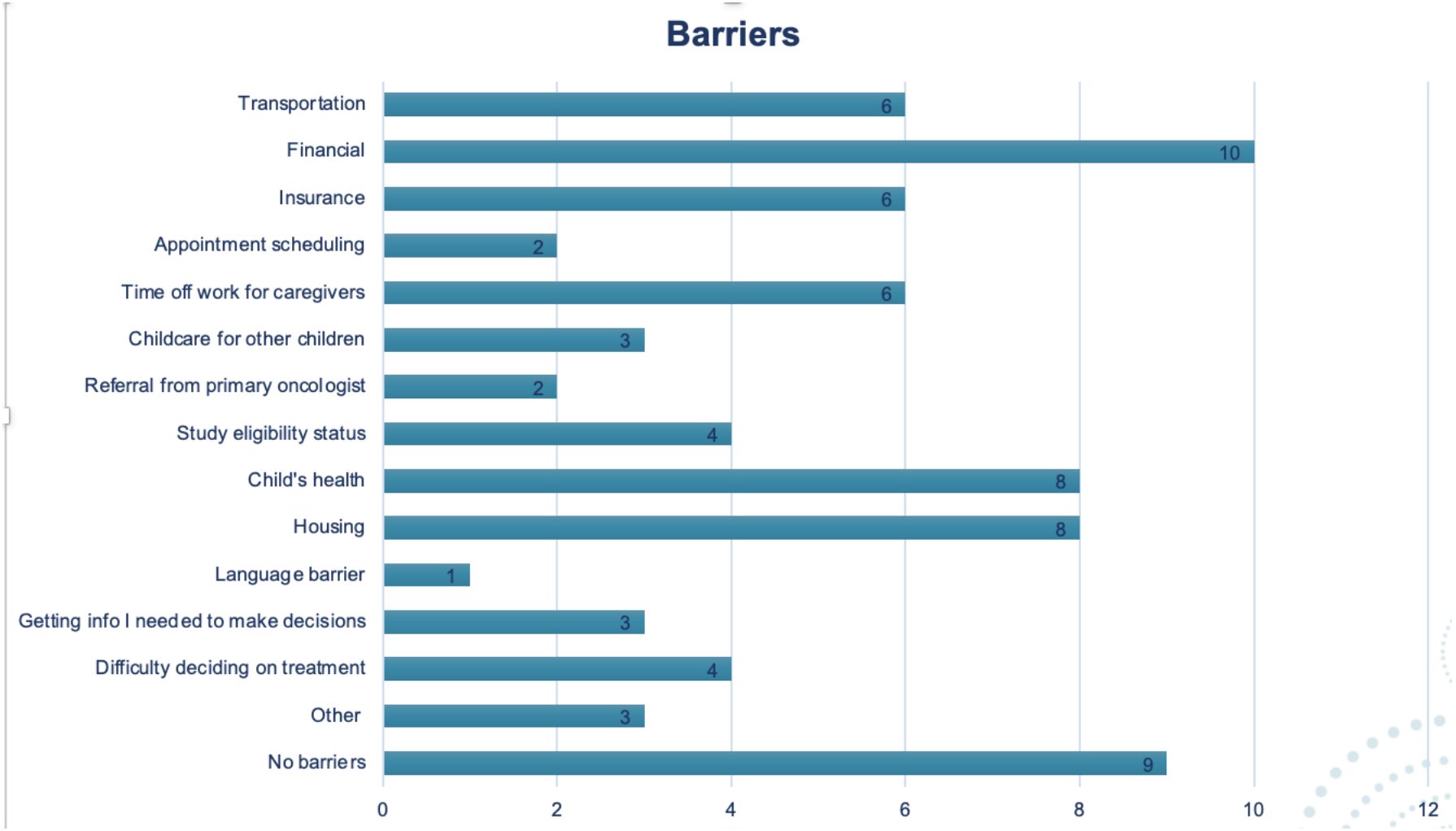
- Race/Ethnicity:
  - White: 91%
  - Latinx: 22%

- Where did you receive CAR-T cells?
  - Home institution: 15.6%
  - Within the same state: 25%

- How many hours to travel to CAR-T?
  - Mean: 7.6 hours

CPCI

What barriers did you encounter?



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How did you learn CAR-T cells may be a treatment option for your child?

- *“clinicaltrials.gov is where we found your study”*

- *“I pushed and pushed our oncologists to get our son in this study. They said there was no way he’d qualify. So I printed out the participation requirements and systematically went through each criterion, and I pushed for each test. The team continuously told me he wouldn’t qualify until they realized he only had 3 criterion left to meet. Then the oncologists started to believe us. Then our coordinator spent an entire month on the phone each day back and forth between our PPO insurance and Seattle Children’s Hospital, deciding who would cover what.”*

- *“We shouldn’t have had to push so hard, and I feel bad for other parents who lost their children to cancer because they were unaware and uninformed that these life saving experiments are out there."*

CPCI

What part of the process was the most difficult for you?

- Overwhelming gratitude for hospital, providers, nurses, social workers, RMH, all staff

- Clinical status/disease state:
  - CRS, neurotoxicity, refractory disease

- **Travel** and **time away from home** during stressful time
  - *"Being so far from home and family and our support system."*
  - *"The distance and duration traveled for treatment. We live 2,000 miles away."*
  - *"Having to travel with a low immune system"*
  - *"Traveling across country to receive them. 2.5 months away from home"*
  - *"The waiting and being separated from family."*

CPCI

Language

- 3/32 listed Spanish as their preferred language
  - 1/3 considered it a barrier in communicating with care team
  - 0/3 used interpreter services

- *“We speak both English and Spanish, but I could see how it could be very difficult for other families who don't speak English. It would also be helpful to get the CAR-T cell information in Spanish.”*

CPCI

Parent Surveys

- Helpful in identifying most prevalent barriers and identifying themes
- Free text comments insightful

- Surveys (goal N=100)
  - N=32 at Seattle Children's Hospital
  - To be sent out soon at UCSF/CHO, CHLA
  - Awaiting approval at Colorado, Children's National

- Limitations

CPCI

Works in Progress—Caregiver Interviews

- 4 interviews conducted to date
- Site(s): Seattle Children's Hospital
- Gender: (100%) Female
- Relationship to Patient: (100%) Mother
- Race/ethnicity: (75%) White, Non-Hispanic; (25%) White, Hispanic
- Language: (100%) English
- Education: (50%) College graduate; (50%) Post-graduate
- Insurance: Private

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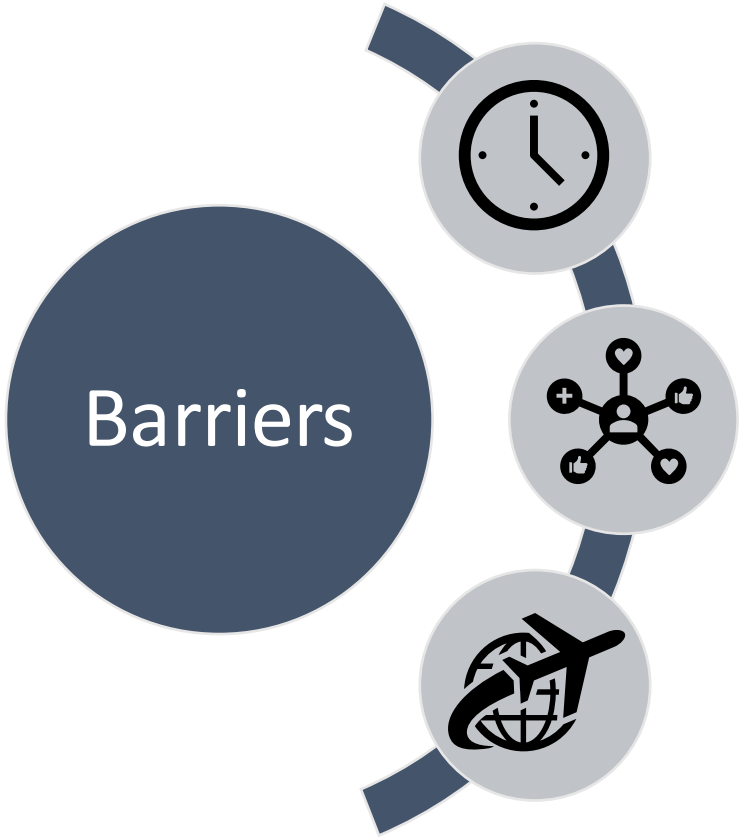
Caregiver Interviews



Social support

Patient/
family resources

Healthcare team

CPCI

Caregiver Interviews

"Ronald McDonald House, which I mentioned... You know, I should say our church connections there are so many, like our parish and the church and there was all kinds of people, praying for [our child] and supporting us. I used Caring Bridge a lot to be able to get information out to people that was pretty helpful as a resource."

"I know I keep mentioning the social workers, they were very, very, very informative.. the hospital chaplain, she would come up and bring books and resources, she was very comforting. And there were some of the greatest male nurses that were awesome to [our child]. One of them, in the middle of the night, I came in and he's playing Xbox with [our child], just being a friend."

CPCI

Works in Progress—Insurance Landscape

- Considering 4 methods to understand this:
- Proposal to CIBMTR
  - Baseline understanding of sociodemographics of pediatric and young adult patients receiving cellular therapies for pre-B ALL
- Partnering with Novartis
  - Can potentially identify Kymriah site contacts with knowledge in insurance coverage
  - Can assist with information regarding state-level Medicaid contacts

Insurance Landscape

- Considering 4 methods to understand this:
- Surveying pediatric oncologists across US
- Assessing experience of the major pediatric cellular therapy referral sites

Additional Grant Opportunities

- Submitted LOI to Leukemia & Lymphoma Society Equity in Access
  - https://www.lls.org/research/equity-access
- Prior RFA ASCO—cancer disparities in clinical trials
  - https://www.asco.org/career-development/grants-awards/funding-opportunities/gateway-discovery-grant-address-cancer
- Prior (now extended deadline) RFA NCATS R01—ethical issues in translational science research
  - https://grants.nih.gov/grants/guide/rfa-files/RFA-TR-20-001.html
  - https://grants.nih.gov/grants/guide/notice-files/NOT-TR-22-001.html
- Other opportunities

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Y4 – Y5 Goals & Metrics

Deliverable	Proposed Completion Date	Comments
Manuscript for retrospective data project	February 2022	
Completion of caregiver surveys	January 2022	Pending IRB approval from CHC, CNH
Completion of caregiver interviews	February 2022	Pending IRB approval from CHC, CNH
Completion of provider surveys	January 2022	Pending IRB approval from CHC, CNH
Completion of provider interviews	March 2022	Pending IRB approval from CHC, CNH
Abstract/manuscript for surveys/interviews	June 2022	

CPCI

Y4 – Y5 Goals & Metrics

Deliverable	Proposed Completion Date	Comments
Analysis of insurance landscape	TBD	Still determining ideal methodology CIBMTR proposal Novartis identifying potential survey group
Policy statement based on insurance landscape data	TBD	Based on landscape analysis
Additional grant applications	TBD	LLS LOI pending approval
Potential collaboration with additional consortia	TBD	

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Barriers to Achieving Goals

- Delays in IRB approval for survey/interview work
- Determining ideal approach to understand insurance landscape for CAR-T clinical trials and FDA-approved products

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Discussion

- Thoughts regarding survey and interview data to date—potential impact on future trial design
- Thoughts on how to approach the insurance landscape—potential for a policy statement
- Additional stakeholders
- Possible additional projects or grant opportunities
- Development of educational materials
- Opportunities to collaborate with other consortia

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Annual Meeting Wrap-up

October 11, 2021 | Julie Park

CPCI

Consortium for Pediatric Cellular Immunotherapy

Wrap-Up Aims 1 and 2

- Develop symposium series to better disseminate working group outputs (alternate with quarterly scientific series?)
  - Retention
  - Pharmacovigilance
  - Salesforce
- Develop consensus documents or generate discussion with FDA
  - Microbiology testing
  - Comments for FDA guidance document on multiple products in single IND
- Review PV programs in place within NCATS
- Sustainability
  - Salesforce/Benioff connections?
  - NCATS new funding mechanism – CBR2D2, for PV work?

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Annual Meeting Welcome

October 12, 2021 | Julie Park

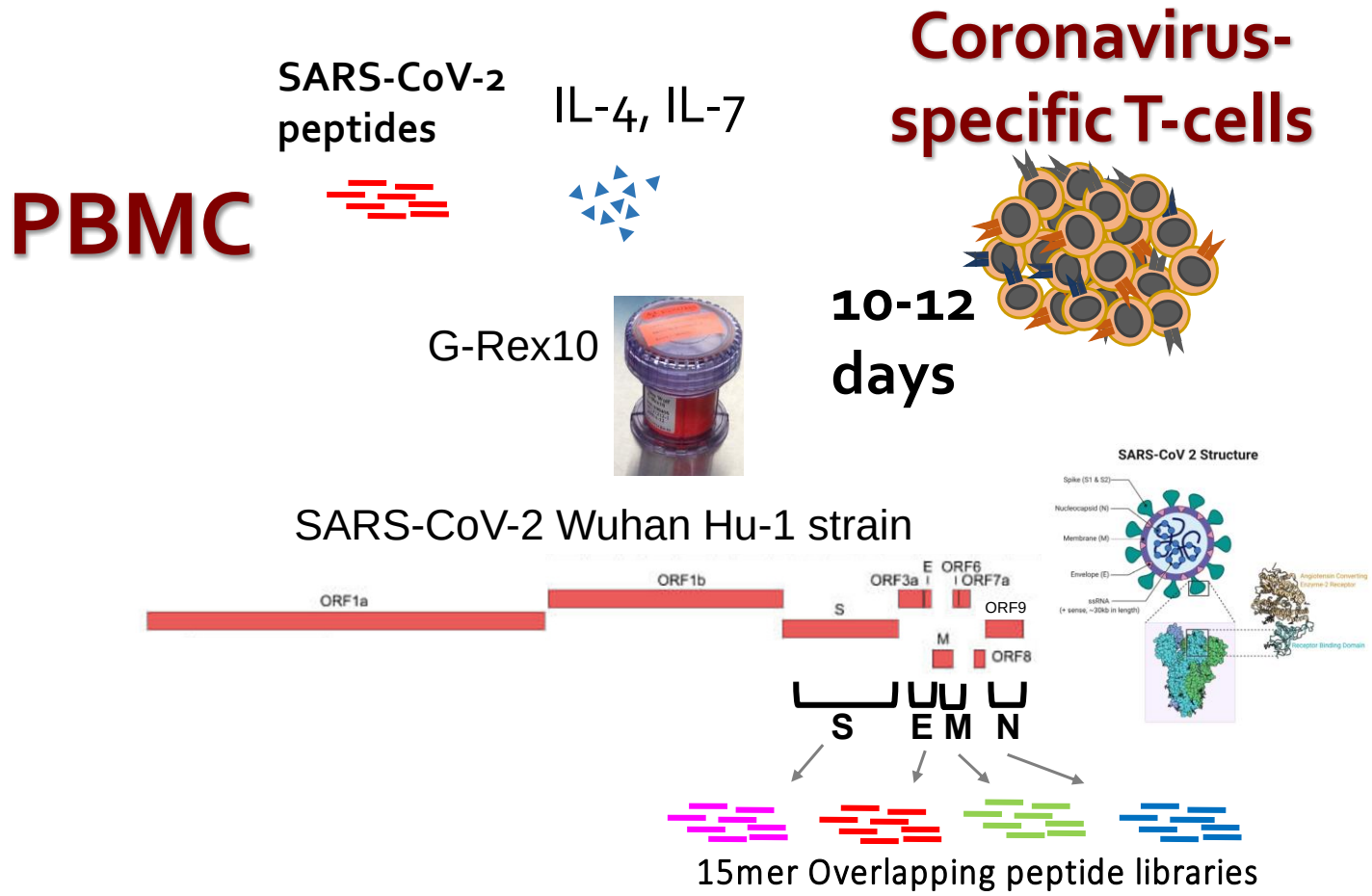
CPCI

Consortium for Pediatric Cellular Immunotherapy

Can SARS-CoV-2-specific T-cell Therapies be Developed to protect BMT patients?

Children's National Health System

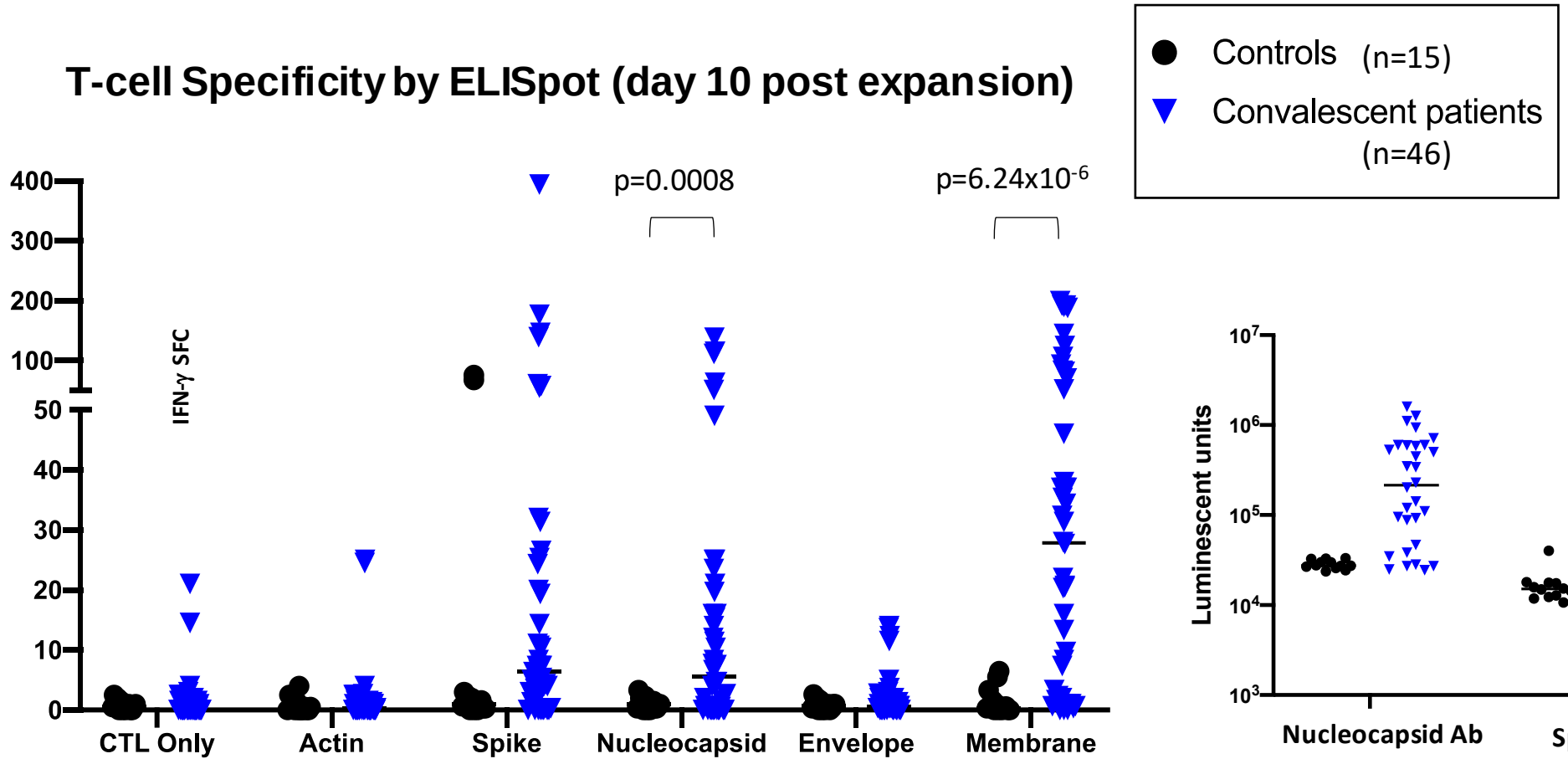
Generation of Coronavirus-Specific T-cells Using GMP Compliant Methodologies

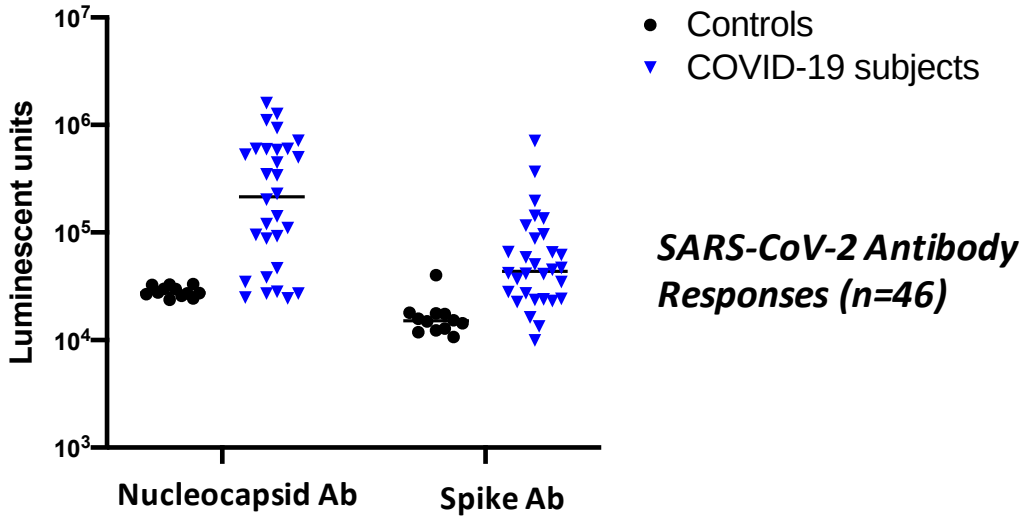


March 20, 2020
TEAM COVID

Children's National Health System

Convalescent Donor T cells Recognize Multiple SARS-CoV-2 Structural Proteins



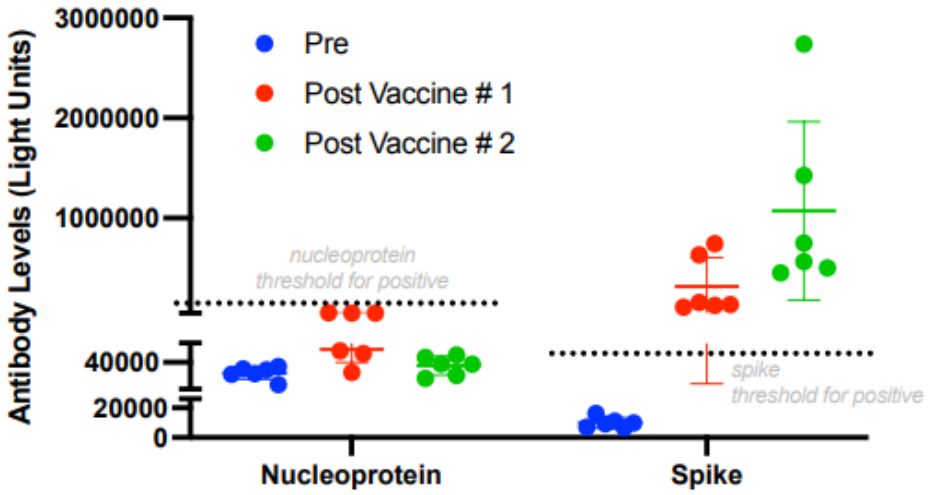


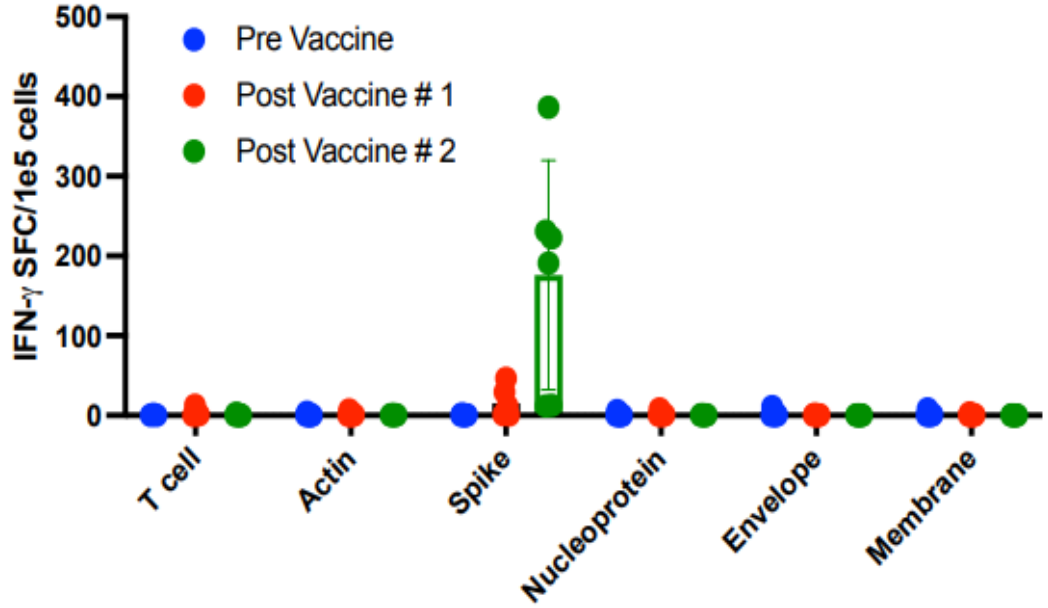
Children's National Health System

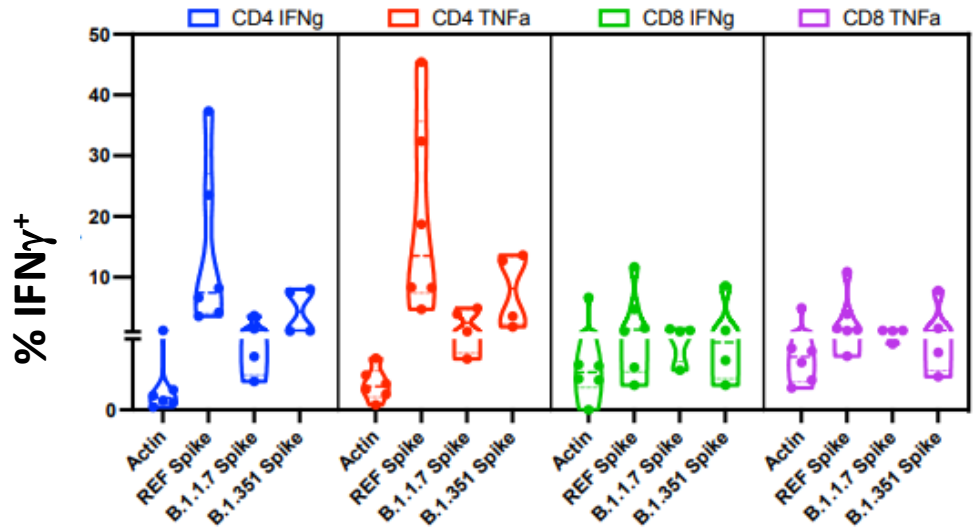
Can Vaccinated, SARS-Cov2 Unexposed Donors be used to Manufacture SARS-CoV2-specific T cells?

Children's National Health System

Vaccinated Donors Elicit Spike specific T cell responses including to variants in addition to Spike specific Ab Responses







Vaccinated Donor-Derived T cells exhibit cross-reactivity against B.1.1.7 and B.1.351 variants

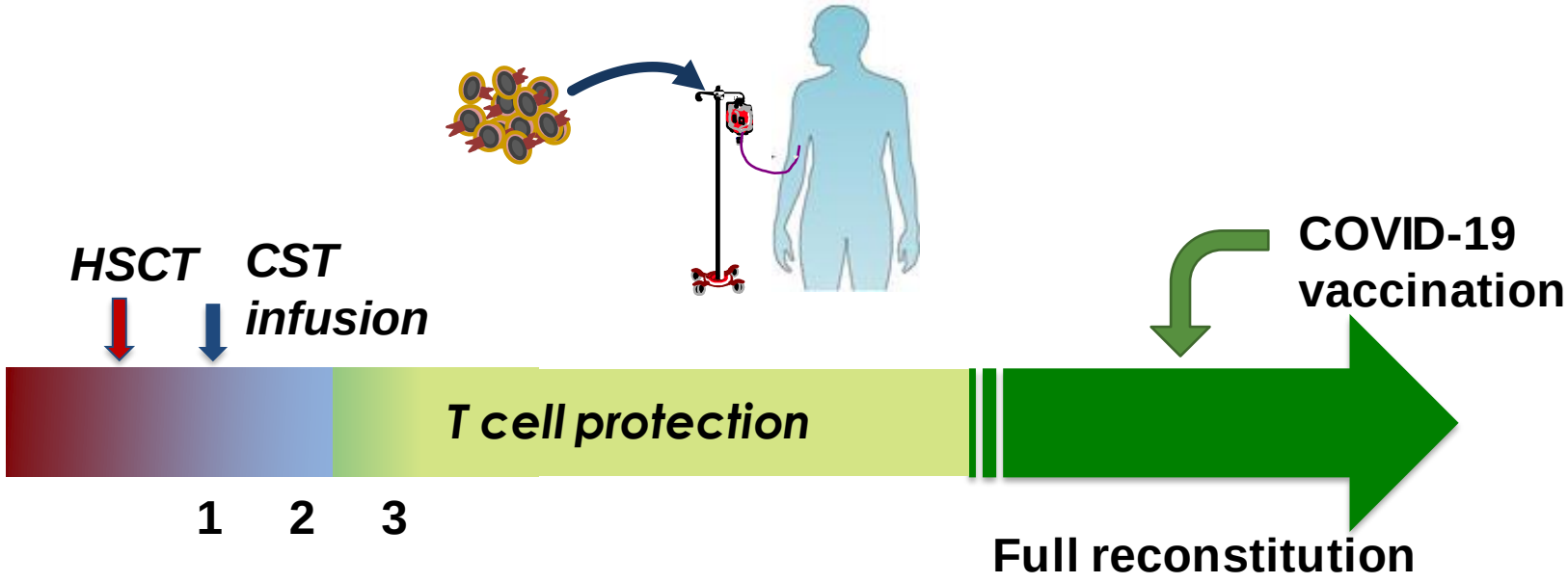
Children's National Health System

Moving SARS-CoV2 T cell Therapies to the Clinic

Children's National Health System

New Clinical Trial

- **“T-cell Therapy Opposing Novel Coronavirus Infection in Immunocompromised Patients (TONI)” IND 27588**
- Post BMT Patients only (prophylaxis)
- Potential concerns treating patients with active infection?



Children's National Health System

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Consortium for Pediatric Cellular Immunotherapy

ABOUT MAJOR INITIATIVES EDUCATIONAL RESOURCES CONSULTATIONS CONTACT US

Home › Educational Resources

EDUCATIONAL RESOURCES

PATIENT ACCESS

Test Document to Show What "Pretty Links" Look Like

Test Document Showing What Regular Links Look Like

Abstract

CLINICAL TRIAL INFRASTRUCTURE

Protocol template [confirm – is this the same thing as the clinical trial template listed in the SS?]

Standardized Adverse Event Grading/Reporting document [confirm we have a document and would want to share here]

Long Term Follow Up Protocol [in progress]

Investigator's Brochure [confirm we have a document and would want to share here]

DSC/DMC Reporting Templates [confirm we want to share here]

SOP's [table – need to create – combine with Correlative? Confirm we want to share here]

Educational Resources

CPCI

Agenda

8:15	**Aim 3 | Correlative Working Group**	*Ashley Wilson*
9:15	**Break**	
9:30	**Educational Tools Discussion**	*Russ Lackey*
10:00	**Aim 4 | Sustainability**	*Julie Park & Bonnie Ramsey*
10:30	**Break**	
10:45	**Science Talk:** Adapting B cell-directed CAR T cells for the treatment of auto- and alloimmunity	*Shaun Jackson*
11:45	**Wrap Up**	*Julie Park*
12:00	**Adjourn**	

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Annual Meeting
Aim 3
Correlative Working Group

October 12, 2021 | Ashley Wilson

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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

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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

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Membership

- Hisham Abdel-Azim, MD, MS — *Pediatric Hematologist-Oncologist – CHLA*
- **Jennifer Cotter, MD** — ***Director, Pediatric Biorepository, Neuropathologist – CHLA***
- **Anushree Datar, MS** — ***Cell Therapy Lab Lead – CNMC***
- **Amy Hont, MD** — ***Pediatric Hematologist-Oncologist – CNMC***
- Wenjun Huang, PhD — *Lead Data Scientist – SCTx*
- Kimberly Jordan, PhD — *Assistant Director, Human Immunology & Immunotherapy Initiative – CU*
- **Monica Mendez** — ***Manager, Pediatric Biorepository – CHLA***
- **Julie Saba, MD, PhD** — ***Professor of Pediatrics – UCSF***
- Ashley Wilson, PhD — *Director, Therapeutics Correlative Science – SCTx*
- Silvia Yu — *LabKey Web Developer – SCTx*

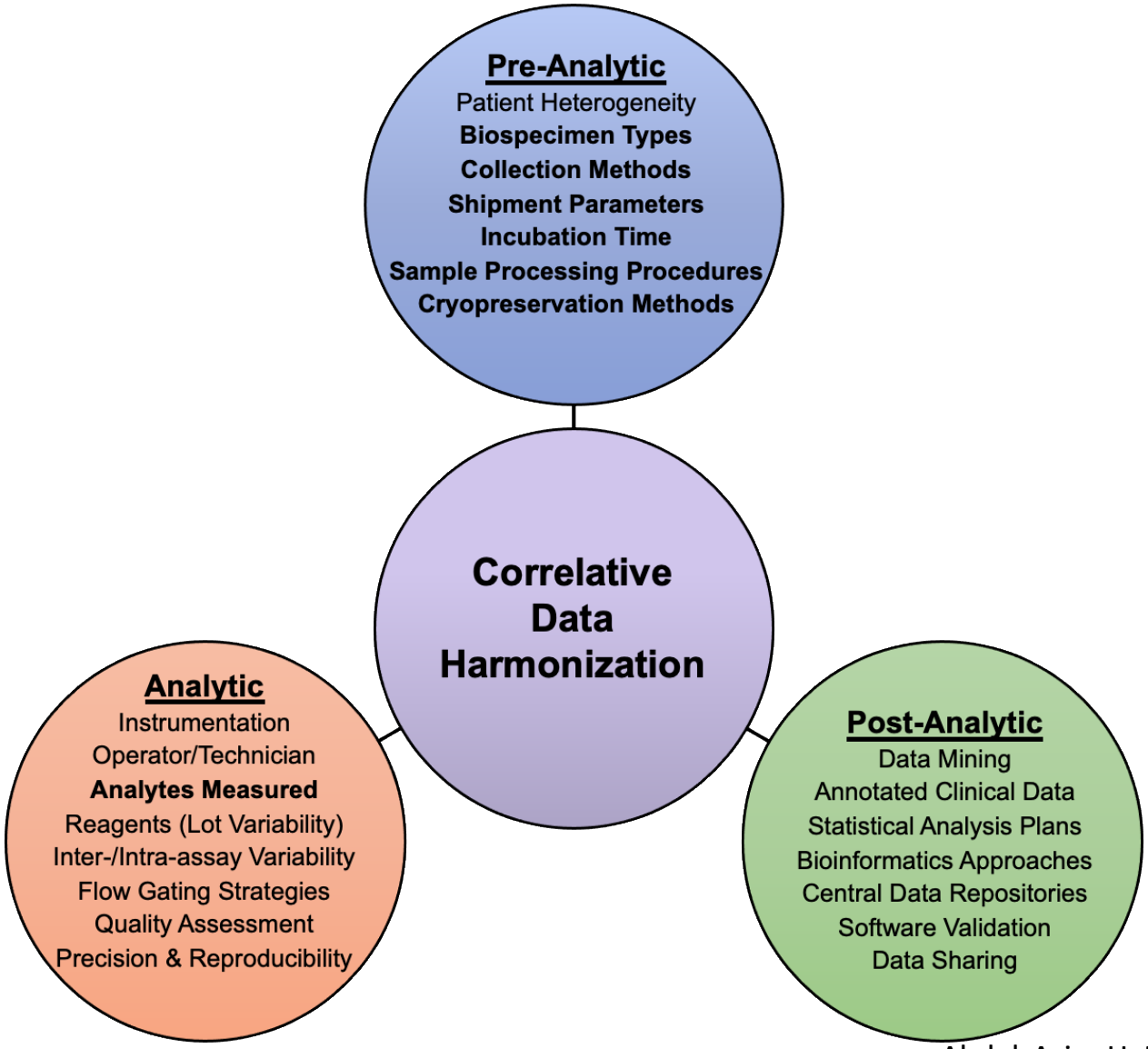
CPCI

Accomplishments

- Consensus manuscript for PB processing and analysis accepted to Cytotherapy
- LabKey implementation and access training disseminated to all CPCI sites
- Correlative data reporting to CPCI sites for 4 clinical trials (+2 external sites) and multi-directional sharing for 1 trial in LabKey
- New biorepository working group established to improve biobanking capabilities at CPCI sites
- Design of a cloud-based biobank with functionality to support correlative specimen inventory, tracking and integration with clinical data in LabKey
- Correlative analysis of cell therapy products from PLAT trials to assess biomarkers of safety and toxicity

CPCI

Alignment of practices for data harmonization across multi-center cell therapy trials



CPCI

Abdel-Azim H, Dave H, Jordan K, et al. Cytotherapy 2021

Consensus cytokine and IEC activation and exhaustion in cell therapy trials

Table 4: Recommended cytokines to measure in cell therapy trials

Cytokine	Toxicities	Roles
CSF-1		Regulates monocyte/macrophage differentiation [99]
GM-CSF	CRS, HLH and neurotoxicity	Drives CRS and neuroinflammation [63]
IFNα		MSC production [100] and cytokine delivery, induces expression of tumor suppressor proteins [101]
IFNγ*	CRS and HLH	Contributes to immunotherapy, tumor suppression and the efficacy of immune checkpoint blockade [102]
IL-1*	CRS	Innate immunity [103]
IL-2*	CRS, HLH and neurotoxicity	Promotes expansion of T and NK cells
IL-4		Promotes B cell proliferation; mediates inflammation [104]
IL-5		Promotes B cell proliferation [105]
IL-6*	CRS and HLH	Associated with CRS onset and severity
IL-8	CRS	May be predictive of resistance to ICIs [106]
IL-10	CRS	
IL-12		Activation and regulation of macrophages, T and NK cells [107]
IL-13		Promotes B cell proliferation; mediates inflammation [104]
IL-15*	CRS	Induces proliferation of CD8 memory and NK cells, cytotoxicity, and release of other cytokines (e.g. IFNγ) [108]
IL-17		Pro-inflammatory cytokine [109]
IL-21		Activates STAT3 signaling in T cell and B cell differentiation [110]
TGFβ		Promotes cancer progression [111]
TNFα*	CRS and HLH	Mediates inflammation, anti-tumor responses and infection [112]

Table 5: Recommended markers to evaluate IEC activation or exhaustion status

Marker	Role
CD3	Lineage
CD4	Lineage
CD8	Lineage
CD25	Activation
TIM-3 (CD366)	Exhaustion
CTLA-4 (CD152)	Exhaustion
LAG-3 (CD223)	Exhaustion
PD-1 (CD279)	Exhaustion
Perforin or Granzyme B*	Function
IFNγ*	Function
TNFα*	Function
IL-2*	Function

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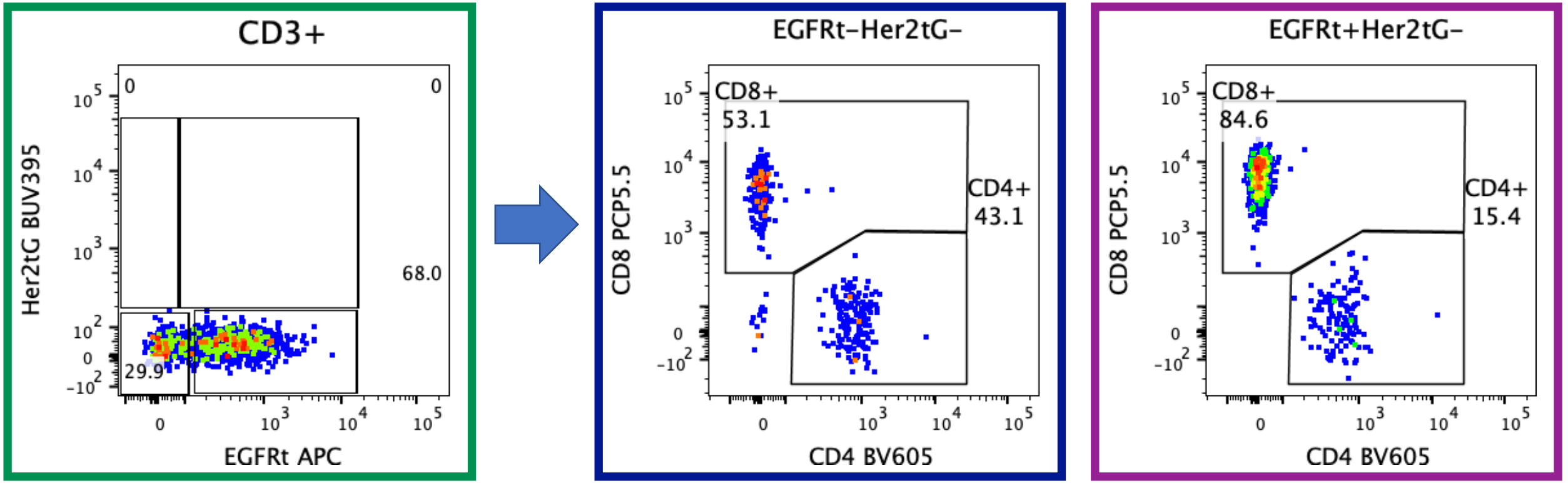
Abdel-Azim H, Dave H, Jordan K, et al. Cytotherapy 2021

Post infusion CAR detection in CSF via flow



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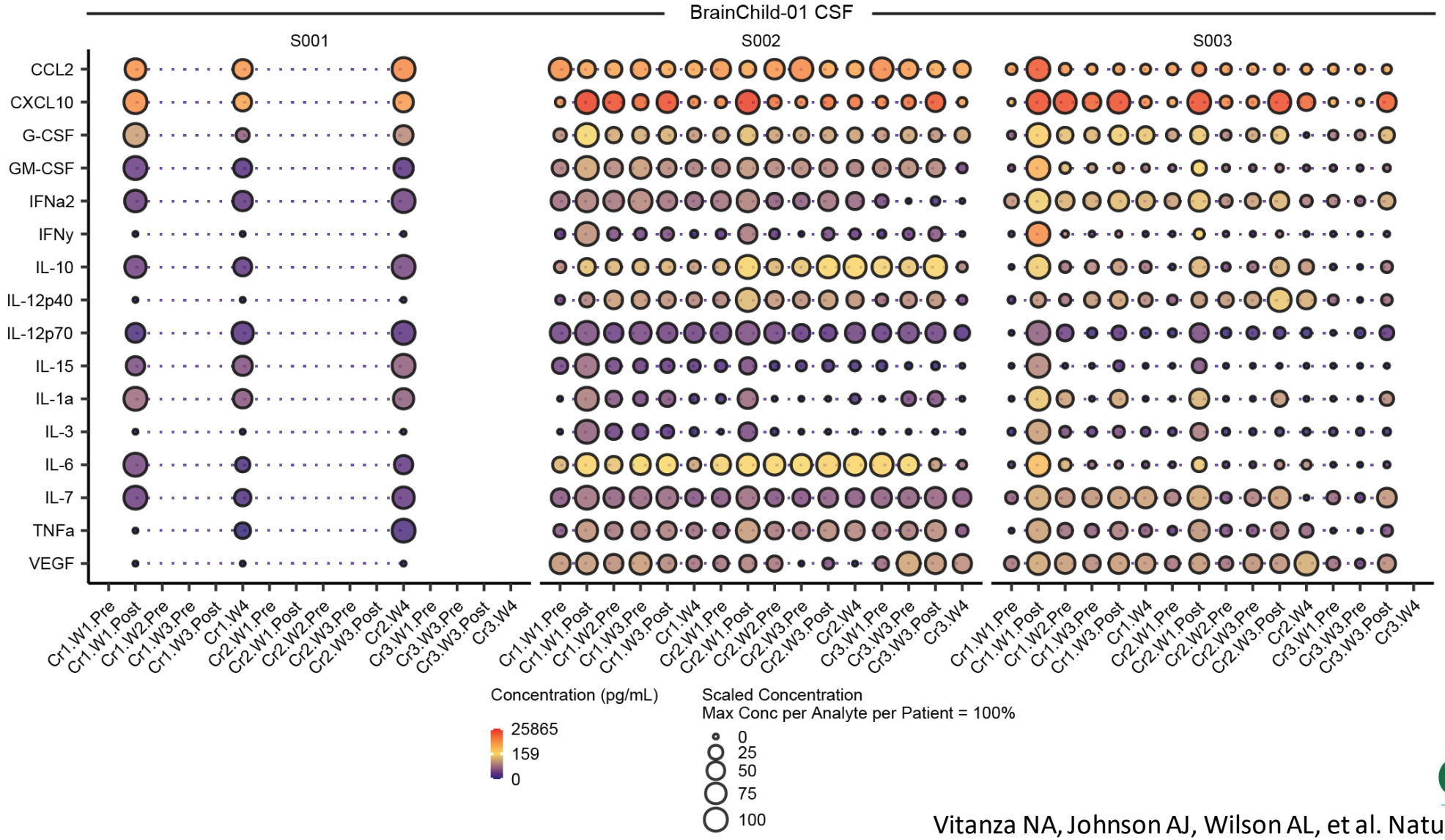
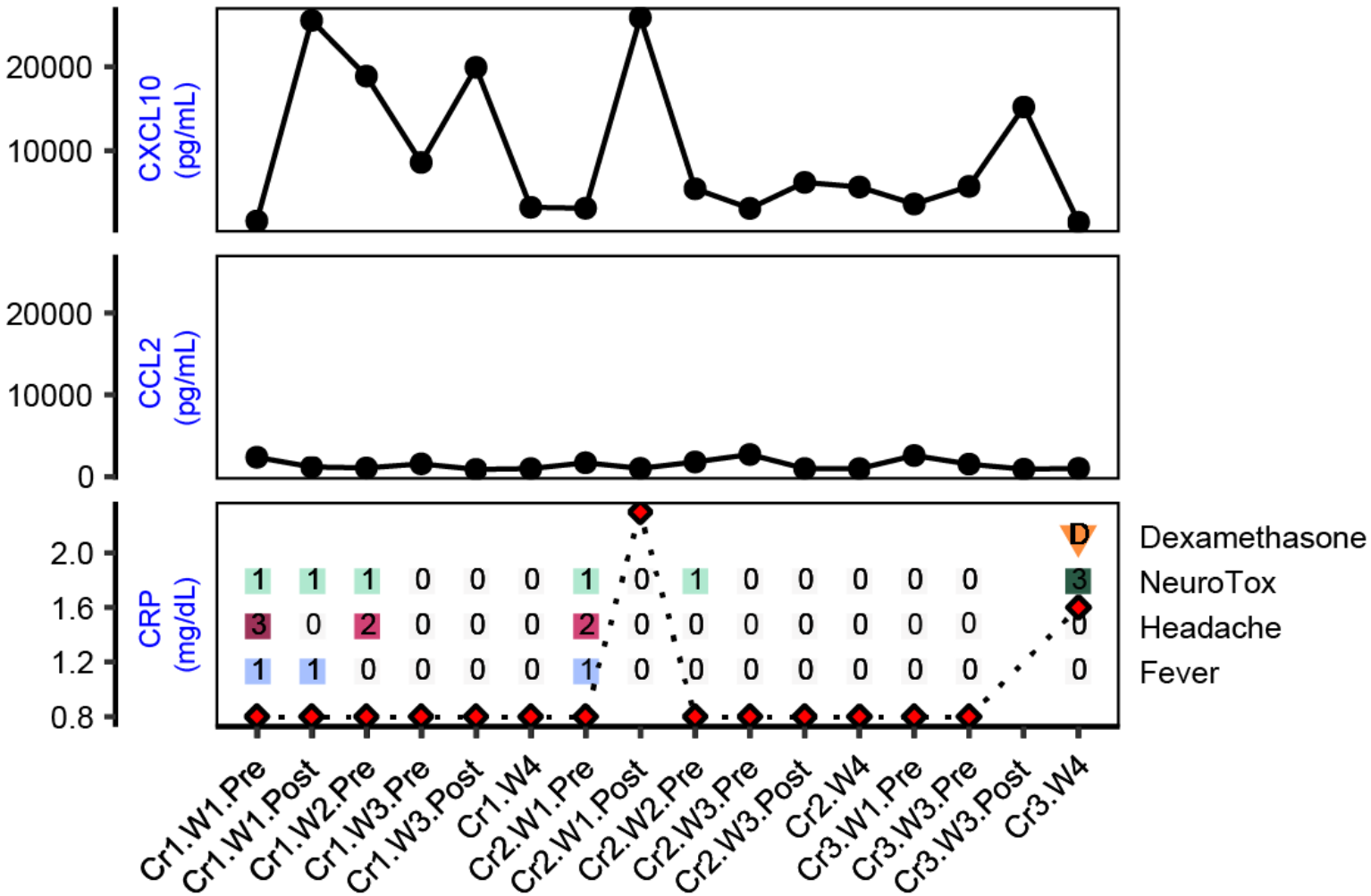
Cytokine detection in CSF

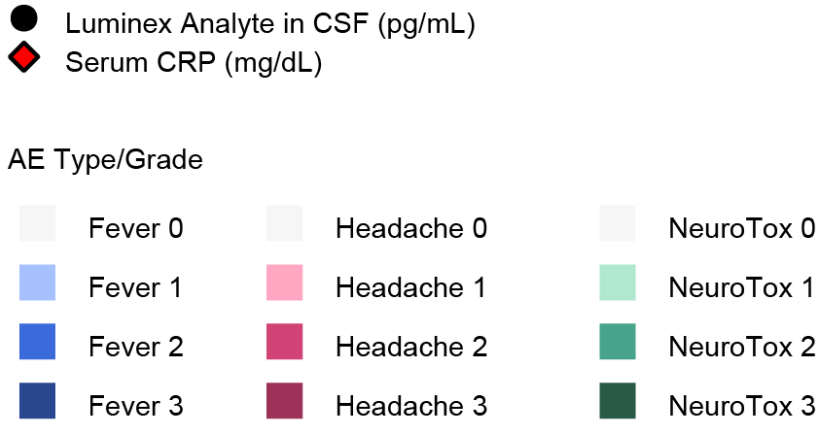


CPCI

Vitanza NA, Johnson AJ, Wilson AL, et al. Nature Medicine 2021

Correlation of CSF cytokines with inflammation and toxicity





CPCI

Vitanza NA, Johnson AJ, Wilson AL, et al. Nature Medicine 2021

Y4 – Y5 Goals & Metrics

Deliverable	Proposed Completion Date
Increase capacity to assess CSF specimen at 1 CPCI site through dissemination of analytical processes for flow and cytokine evaluation	May 2022
Maintain training and best practice utilization for LabKey across CPCI sites	May 2022
Enhance correlative biobanking capabilities across CPCI sites by aligning and sharing relevant SOPs	May 2022
Develop LabKey platform to maintain biobank specimen inventory, link specimens to clinical data, and create infrastructure to submit and track specimen or data requests	May 2022
Continue to identify potential biomarkers of neurotoxicity and CRS with CD19 CAR T cell therapy	May 2022

Central Nervous System (CNS) Working Group

- Establishment of a new CNS WG across CPCI sites to discuss CSF analytics and correlative studies related to cell therapy for CNS tumors

- CNS Symposium (initiated by CureWorks) involving CPCI sites with a focus on CSF biomarkers of safety and toxicity

• **Nick Vitanza, MD**	***Pediatric Neuro-Oncologist, CNS CAR T Lead, DIPG Lead – SCH***
• **Tom Belle Davidson, MD**	***Associate Professor of Pediatrics – CHLA***
• **Eugene Hwang, MD**	***Associate Chief, Oncology, Associate Professor of Pediatrics – CNMC***
• **Sabine Meuller, MD PhD**	***Pediatric Neuro-Oncologist, Professor of Clinical Neurology – UCSF | PNOC***
• **Ashley Wilson, PhD**	***Director, Therapeutics Correlative Science, U01 Correlative Aim Lead – SCTx***

CPCI

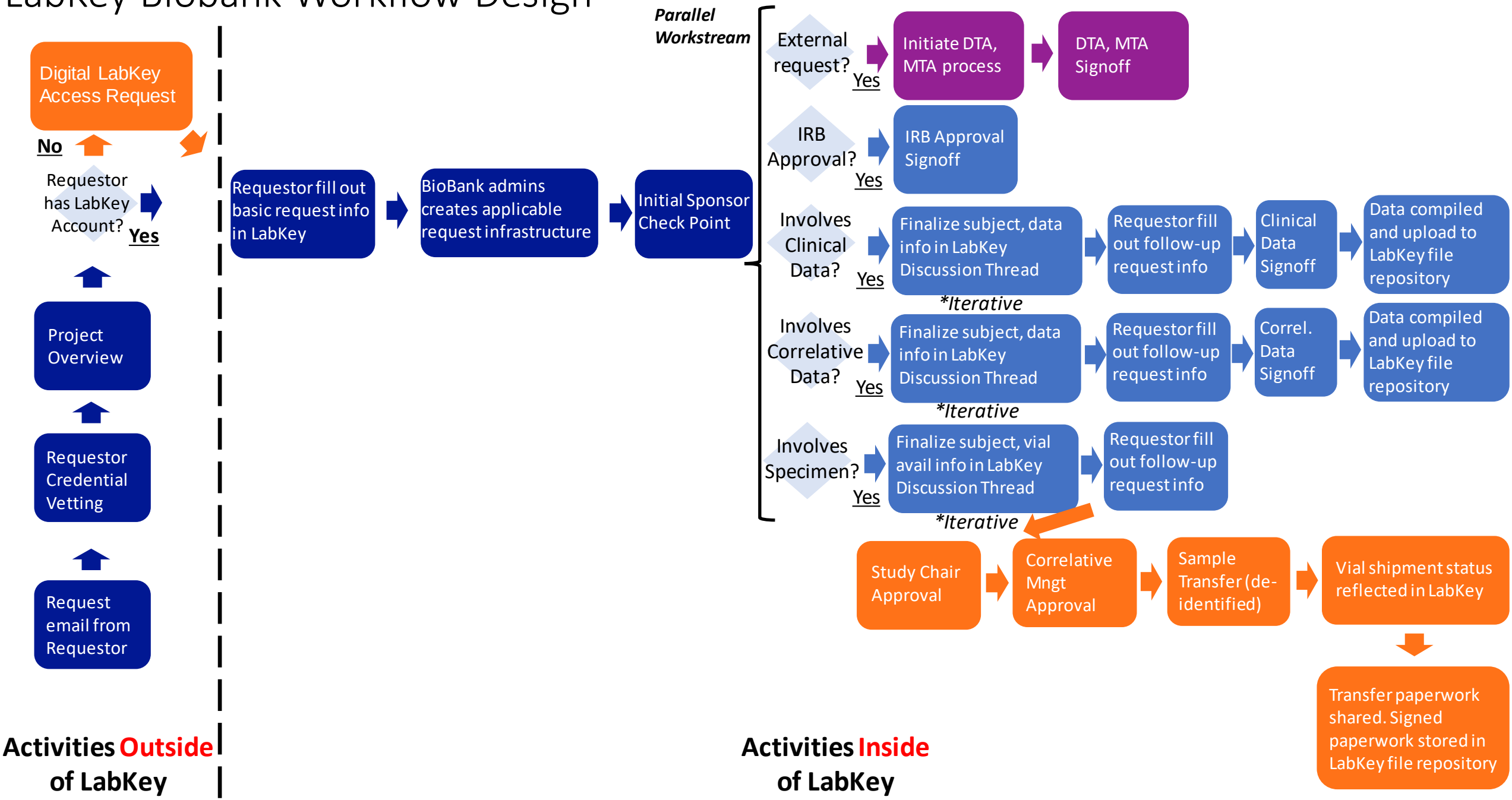
Biobank Working Group

- Established CPCI Biobank WG to discuss biorepository and specimen/data storage practices

- Gap analyses related to:
  - **Sample and Specimen Storage/Freezer Maintenance (complete)**
  - **Specimen and Sample Labeling (upcoming)**
  - Specimen and Sample Processing
  - Specimen Shipment and Sample Transfers
  - Biobank Request Workflow
  - Biobank Data Annotation/Identifiers/De-identification Practices

CPCI

LabKey Biobank Workflow Design



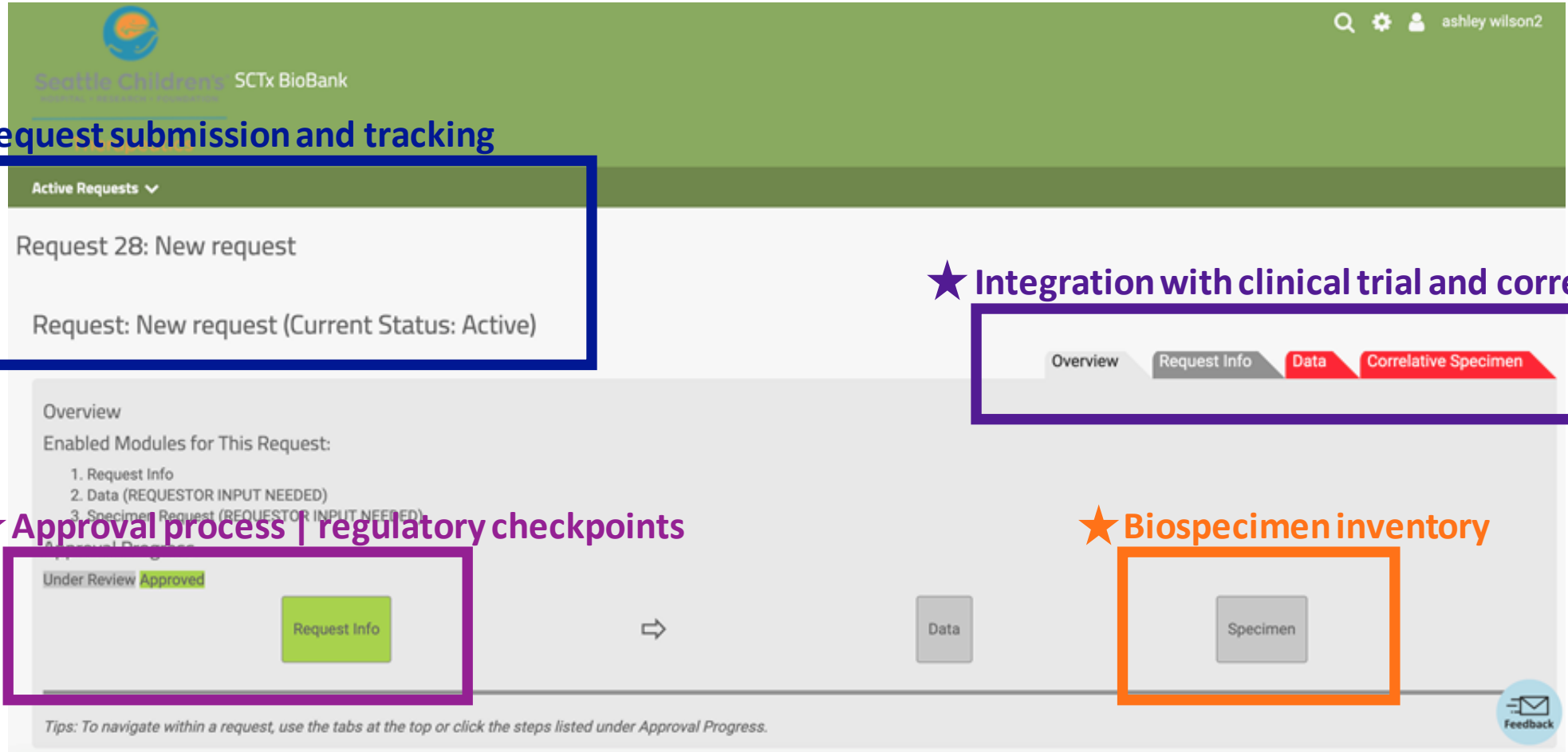
Secure, cloud-based biobanking in LabKey

★ **Request submission and tracking**

★ **Integration with clinical trial and correlative data**

★ **Approval process | regulatory checkpoints**

★ **Biospecimen inventory**



CPCI

Barriers to Achieving Goals

- Complexity of aligning biobanking processes across CPCI sites given differences in capacity and institutional guidelines

- Multi-directional data sharing in LabKey outside of SC requires buy-in from another CPCI site

Annual Meeting
Educational Tools Discussion

October 12, 2021 | Russell Lackey, MS | rlackey@uw.edu

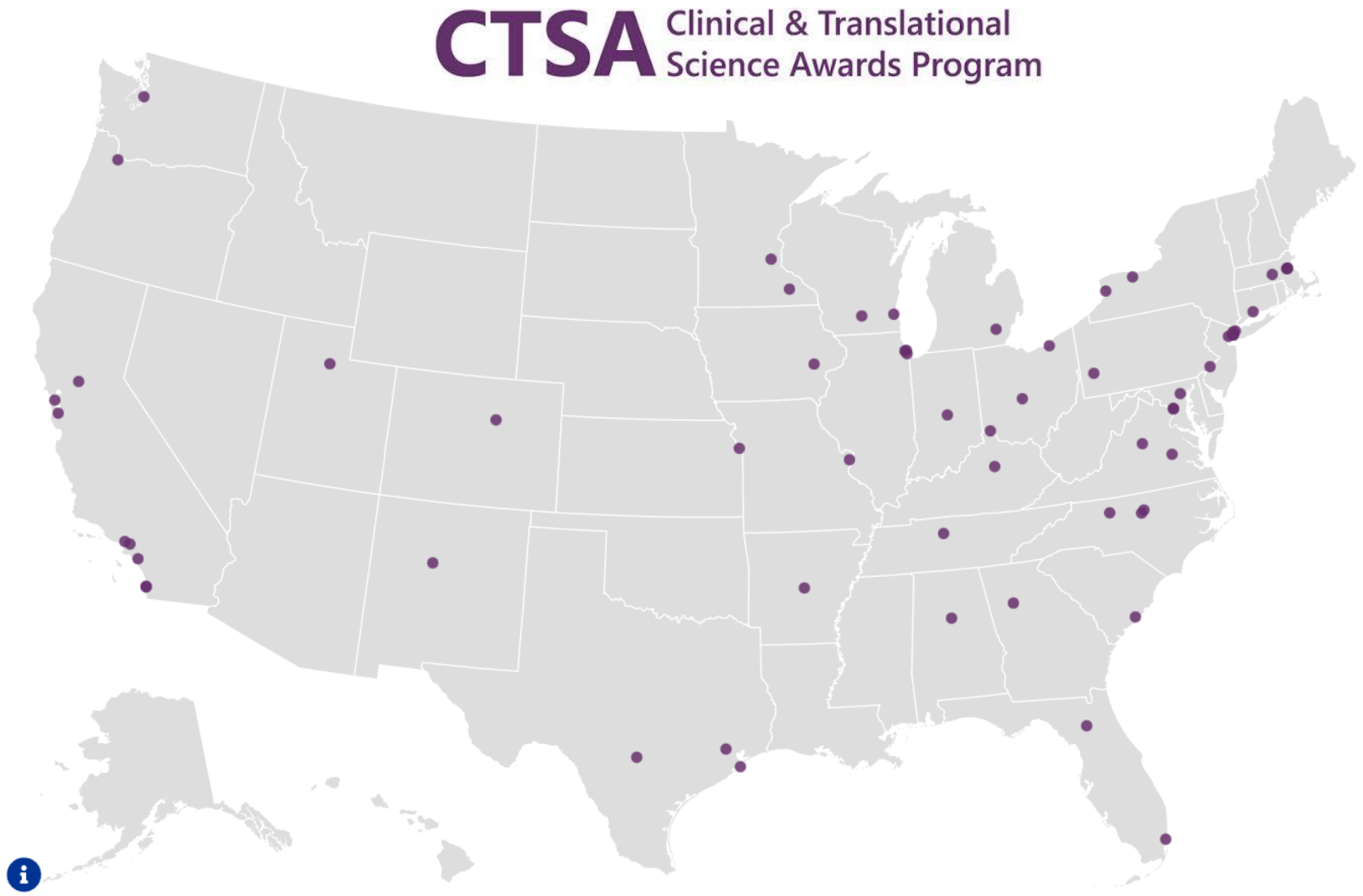
CPCI

Consortium for Pediatric Cellular Immunotherapy

Overview

- Setting the Stage
- Examples from the CTSA
- Getting the Word Out
- Open Discussion

One-Size-Fits-All?

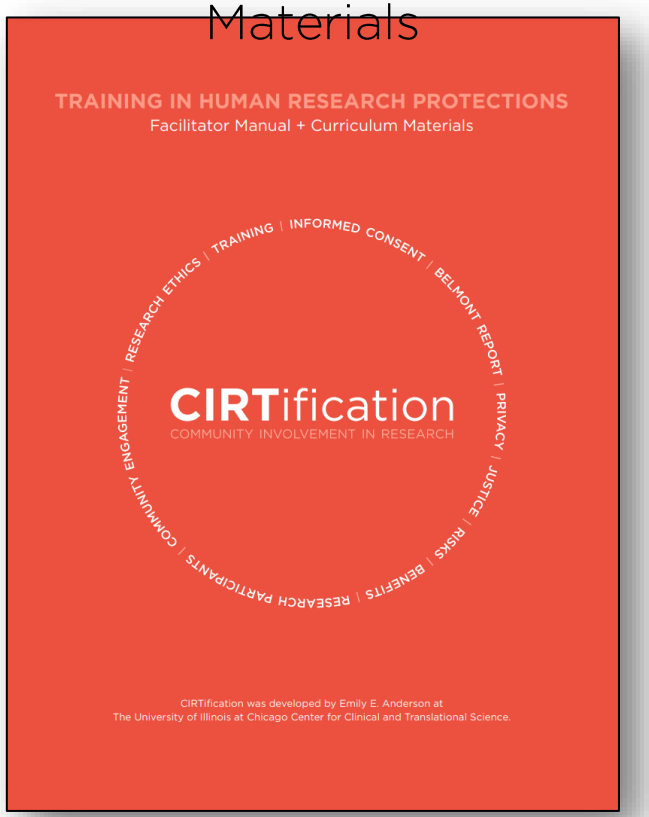


Useful Link(s): [CTSA Hub Directory]

CPCI

Guides & FAQs

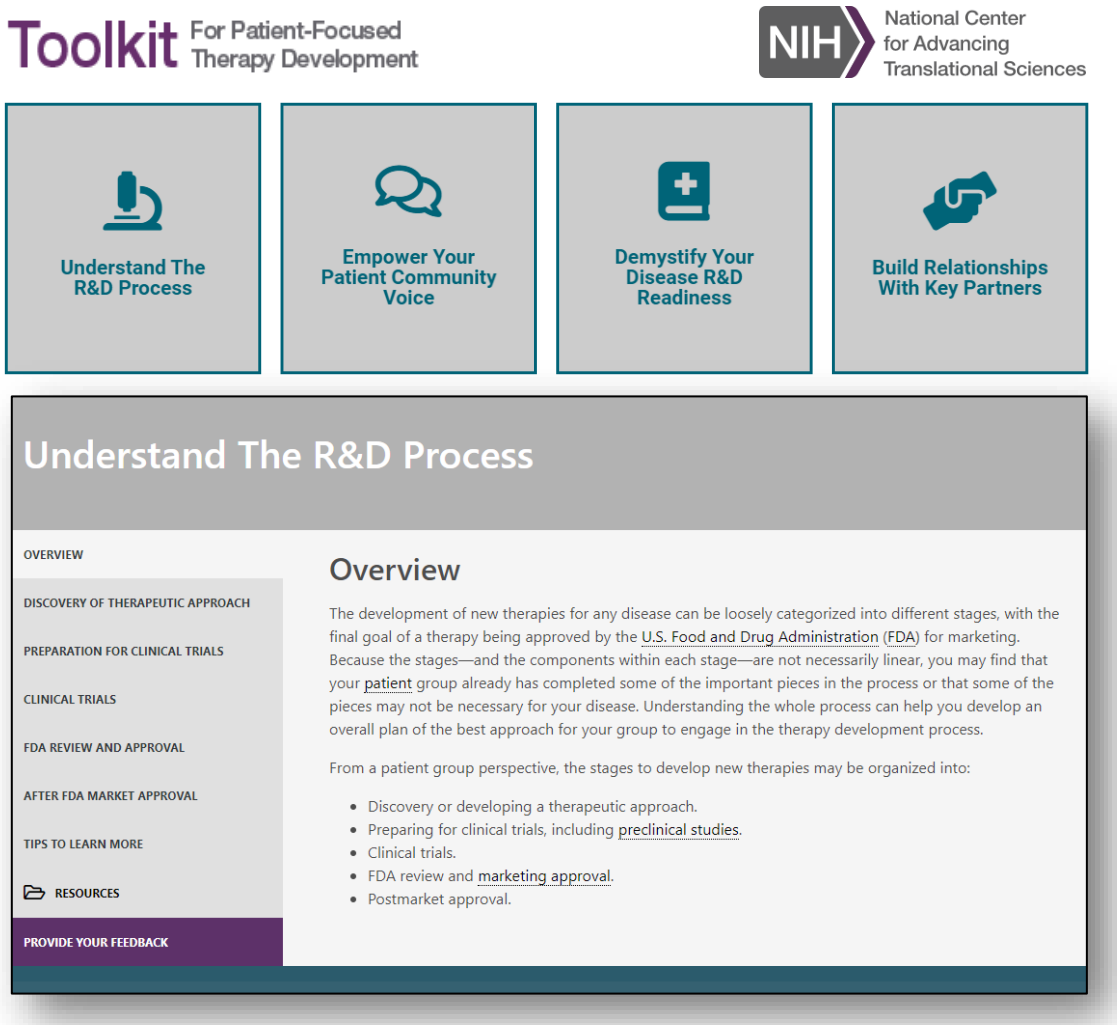
Facilitator Guides & Curriculum Materials

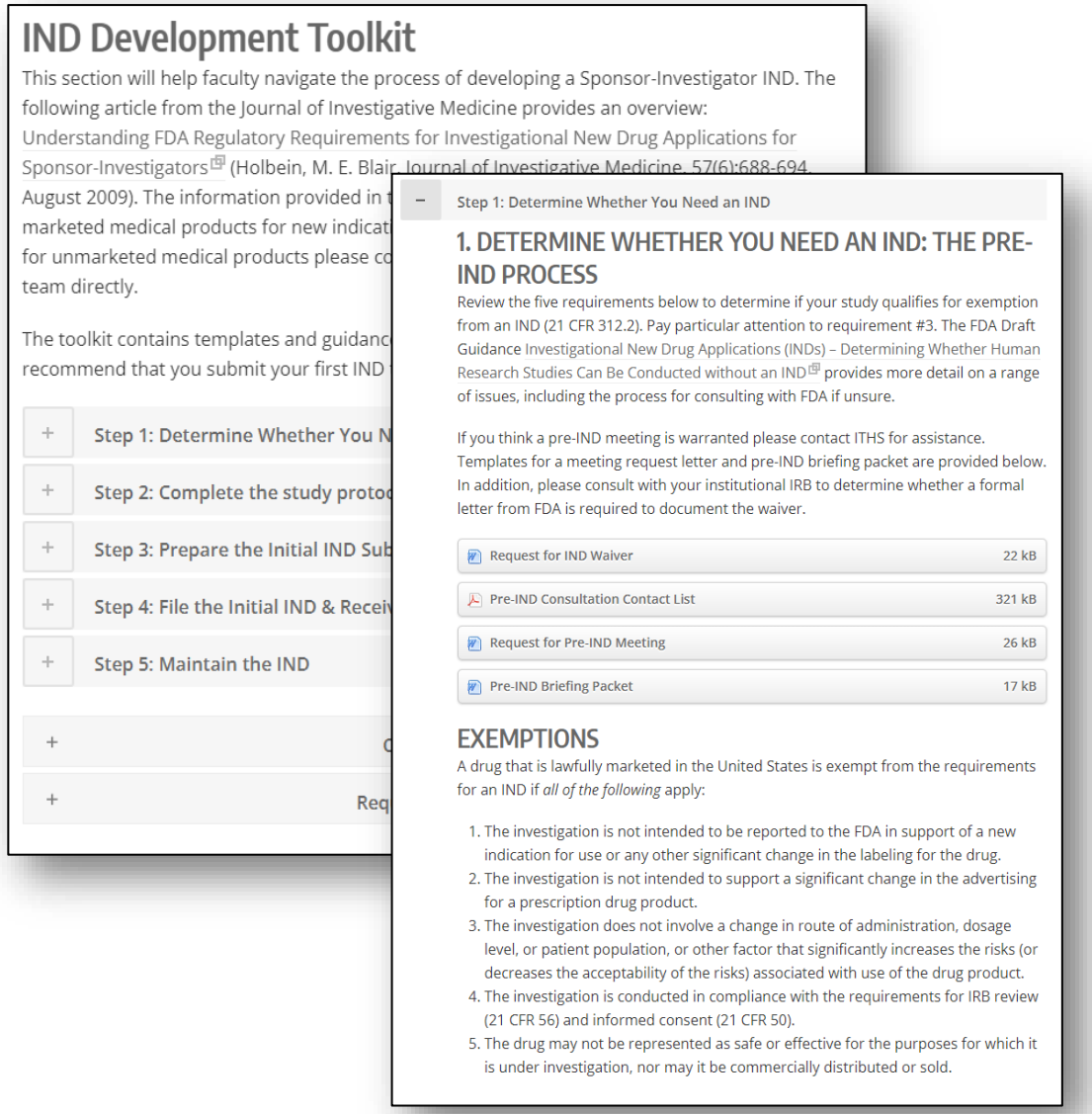


Development / Improvement Materials (Actionable Questions)

Useful Link(s): CIRTification, From Insights to Action

Toolkits



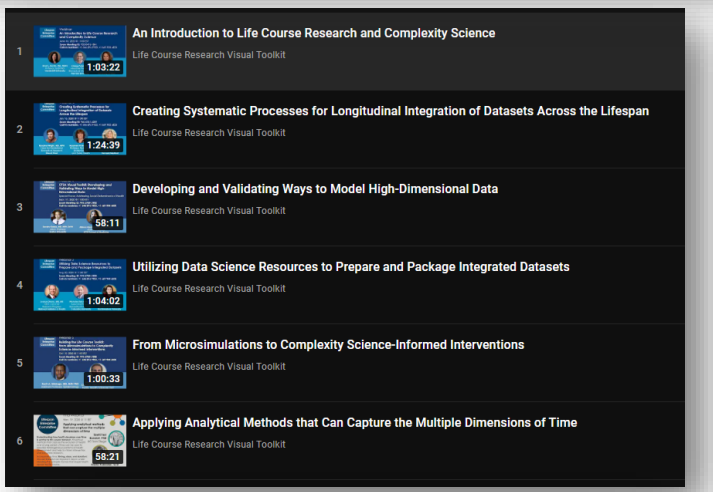


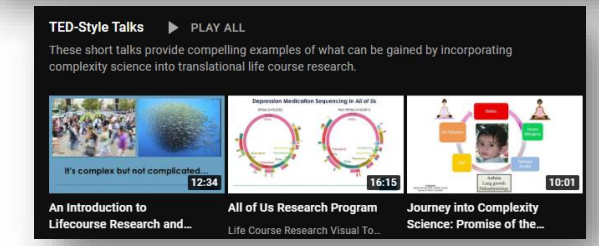
Useful Link(s): NCATS Toolkit, IND Toolkit

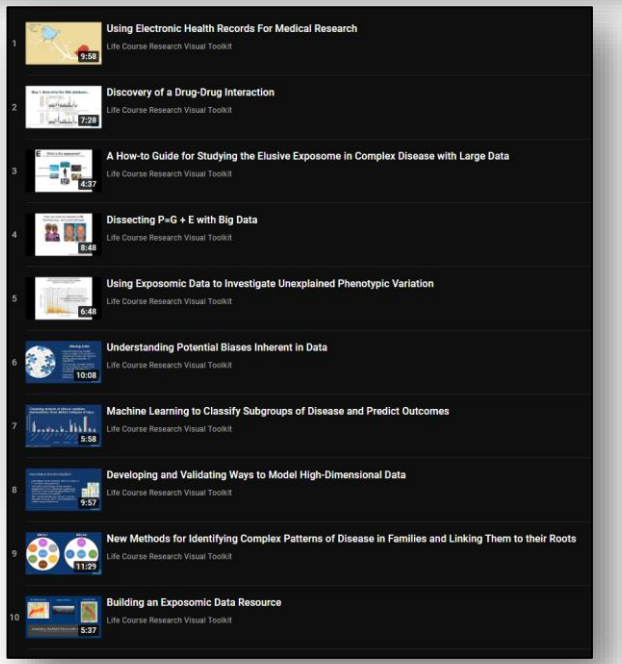
Visual Toolkits

Live Educational Webinars

Enduring Materials
TED-Style Talks
Bite-sized Video Playlists
Full Recordings





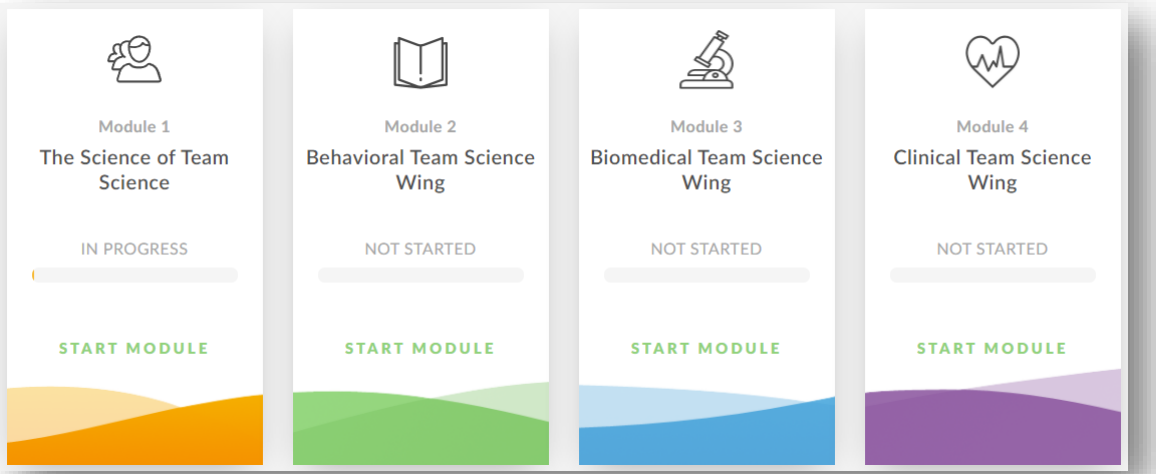


Useful Link(s): [Life Course Toolkit]

Courses

COALESCE

teamscience.net



Useful Link(s): NCATS Courses, COALESCE

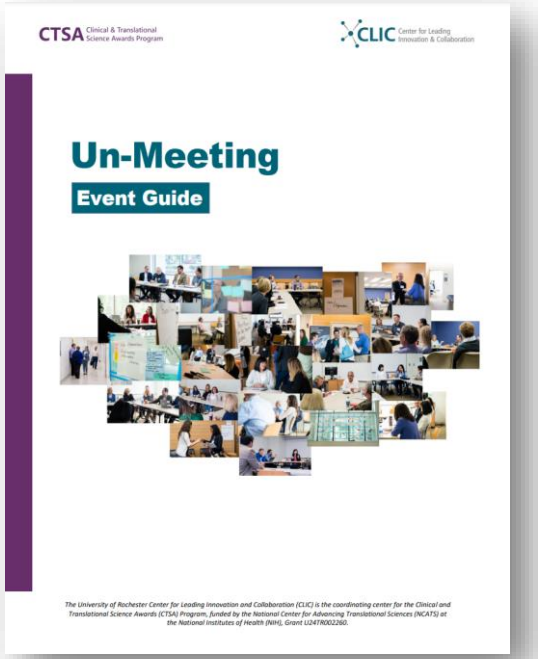
Getting the Word Out

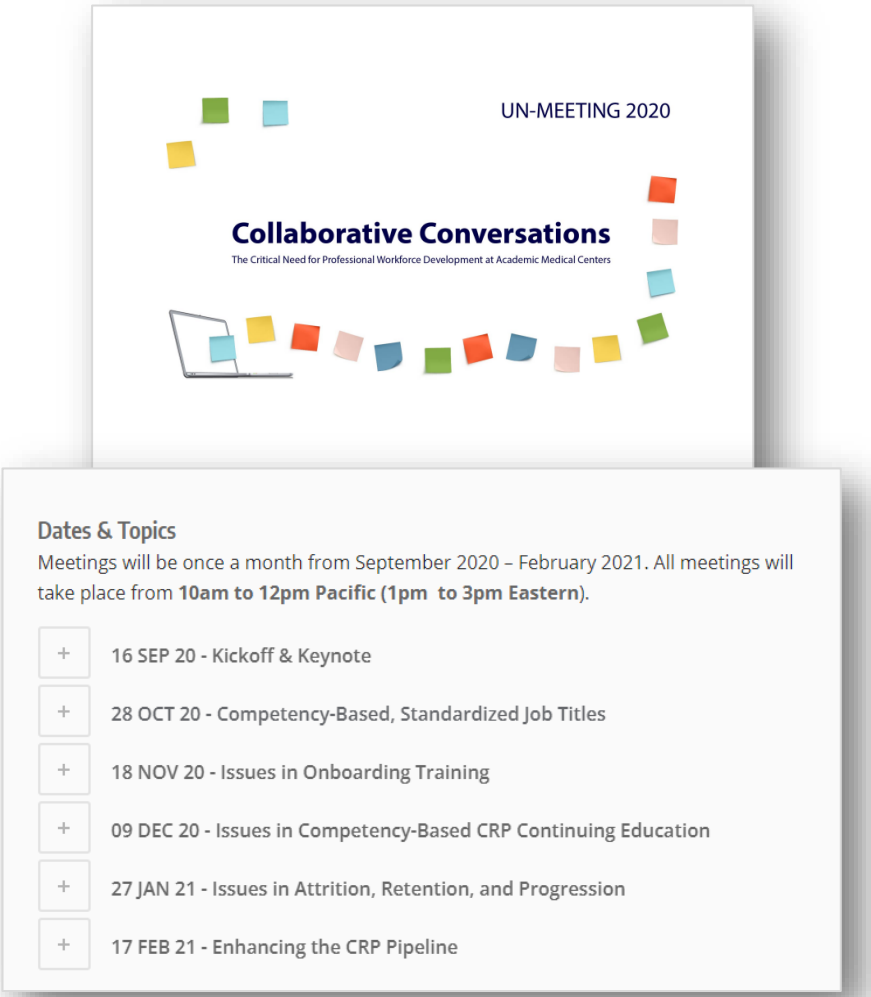
- Communication Plans
- Media Toolkits

Open Discussion

Un-Meetings

- High Engagement
- Audience Driven
- Networking & Community Building





Useful Link(s): CLIC Un-Meeting Site, ITHS Un-Meeting Example

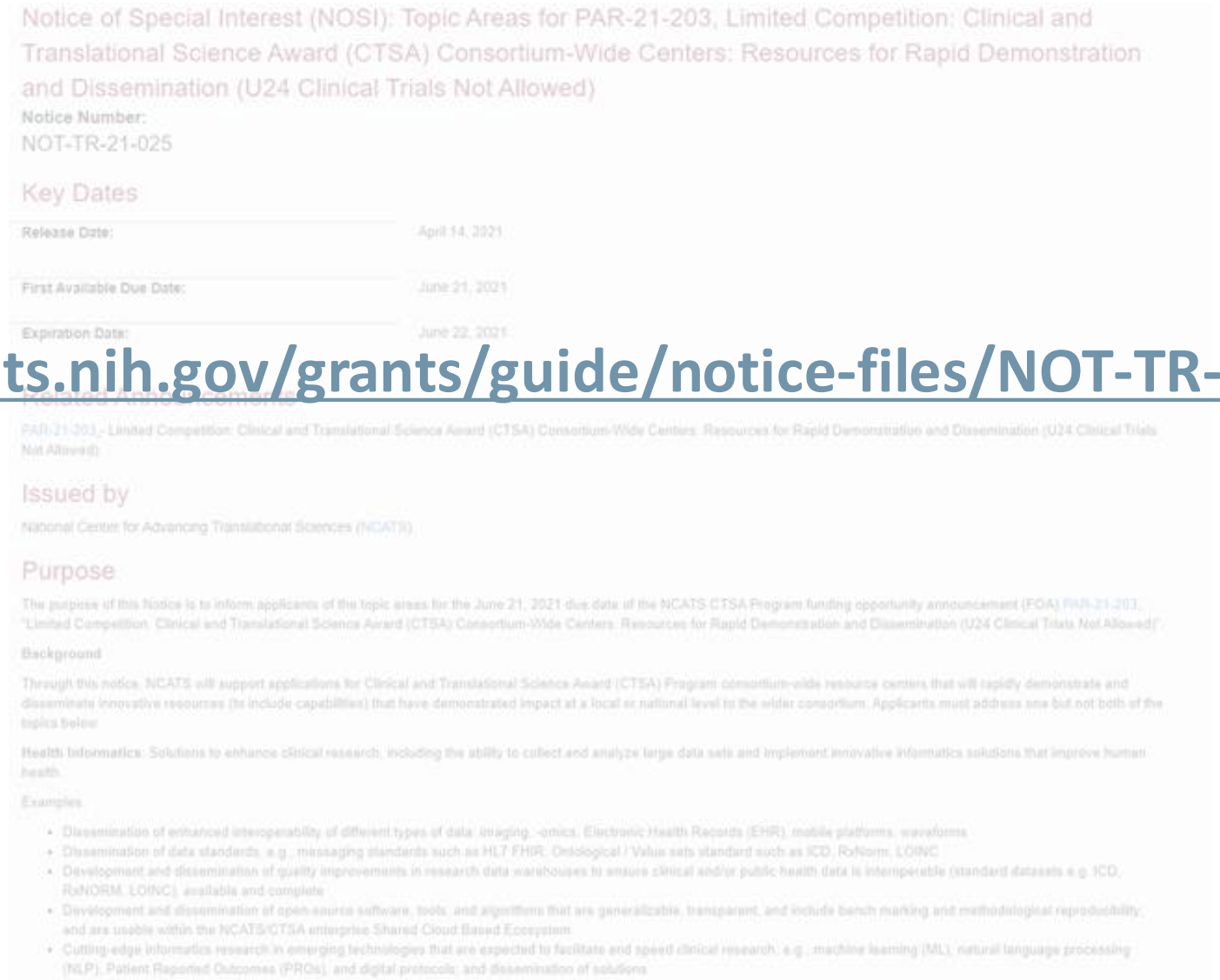
Annual Meeting Aim 4 Sustainability

October 12, 2021 | Julie Park

CPCI

Consortium for Pediatric Cellular Immunotherapy

PAR-21-203 Limited Competition- Clinical and Translational Science Award (CTSA) Consortium Wide Centers: Resources for Rapid Demonstration and Dissemination(C3R2D2)



Notice of Special Interest (NOSI): Topic Areas for PAR-21-203, Limited Competition: Clinical and Translational Science Award (CTSA) Consortium-Wide Centers: Resources for Rapid Demonstration and Dissemination (U24 Clinical Trials Not Allowed)

Notice Number:
NOT-TR-21-025

Key Dates

Release Date: April 14, 2021

First Available Due Date: June 21, 2021

Expiration Date: June 22, 2021

Related Announcements

PAR-21-203 - Limited Competition: Clinical and Translational Science Award (CTSA) Consortium-Wide Centers: Resources for Rapid Demonstration and Dissemination (U24 Clinical Trials Not Allowed)

Issued by

National Center for Advancing Translational Sciences (NCATS)

Purpose

The purpose of this Notice is to inform applicants of the topic areas for the June 21, 2021 due date of the NCATS CTSA Program funding opportunity announcement (FOA) PAR-21-203, "Limited Competition: Clinical and Translational Science Award (CTSA) Consortium-Wide Centers: Resources for Rapid Demonstration and Dissemination (U24 Clinical Trials Not Allowed)".

Background

Through this notice, NCATS will support applications for Clinical and Translational Science Award (CTSA) Program consortium-wide resource centers that will rapidly demonstrate and disseminate innovative resources (to include capabilities) that have demonstrated impact at a local or national level to the wider consortium. Applicants must address one but not both of the topics below:

Health Informatics: Solutions to enhance clinical research, including the ability to collect and analyze large data sets and implement innovative informatics solutions that improve human health.

Examples:

- Dissemination of enhanced interoperability of different types of data: imaging, -omics, Electronic Health Records (EHR), mobile platforms, waveforms
- Dissemination of data standards, e.g., messaging standards such as HL7 FHIR, Ontological / Value sets standard such as ICD, RxNorm, LOINC
- Development and dissemination of quality improvements in research data warehouses to ensure clinical and/or public health data is interoperable (standard datasets e.g. ICD, RxNORM, LOINC), available and complete
- Development and dissemination of open-source software, tools, and algorithms that are generalizable, transparent, and include bench marking and methodological reproducibility, and are usable within the NCATS/CTSA enterprise Shared Cloud Based Ecosystem
- Cutting-edge informatics research in emerging technologies that are expected to facilitate and speed clinical research, e.g., machine learning (ML), natural language processing (NLP), Patient Reported Outcomes (PROs), and digital protocols; and dissemination of solutions

https://grants.nih.gov/grants/guide/notice-files/NOT-TR-21-025.html

CPCI

Strategic Goals of the CTSA Program

- Train the CT workforce
- Engage patients, families and the community
- Promote integration of special underserved populations
- Develop innovative processes to improve quality and efficiency in CT research
- Advance informatics in CT research
- Scaling and disseminating CT resources including novel methods, technologies, interventions, processes and approaches

CPCI

Qualities of a Competitive C3R2D2 Application

- ☑ Builds on CTSA Program Hub's and five Strategic Goals
- ☑ High likelihood of creating systematic improvement in CT science
- ☑ Clearly defined outcomes and milestones
- ☑ Includes partners (patient advocates, community groups, industry)
- ☑ Can readily expand to multiple Hub's and communities
- ☑ Must relate to the NOSI topics
- ☑ 2021 NOSI foci – Health Informatics and Demonstrating Research Impact

CPCI

Additional Information

Submission Dates
June 2022, 2023

Funding
$3million/year for 5 years
2-3 per cycle

Program Officer Meetings
Several months in advance because limited submission

CPCI

CureWorks

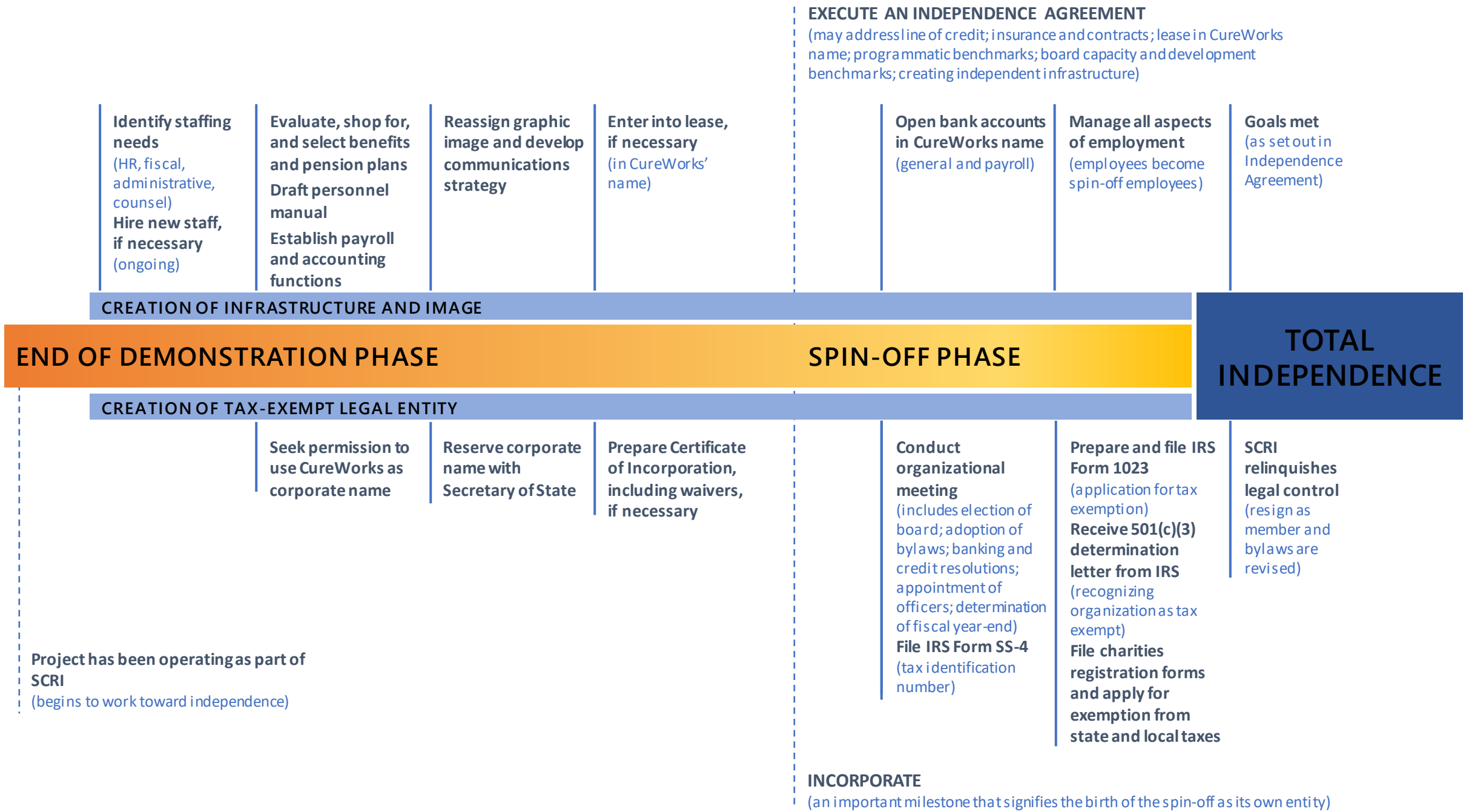
A NEW WAY TO BETTER CURES

We will accelerate the development of cures through the power of collaboration so children with cancer can grow up to realize their full potential.

CureWorks Summary/Next Steps

- Formally established in 2018
  - 5 member institutions: SCH, CNH, CHLA, Riley, BC Childrens
- Established using SCRI facilities and administration
- Ongoing discussions to determine steps necessary for autonomous 501c3 independent organization
- Consultant hired to develop a new business case for spinout
- Existing members will validate separate process and new agreements will be developed
  - Additional membership on hold until spin-out finalized
- Goal for initiation of spin-out in 2022

CPCI


EXECUTE AN INDEPENDENCE AGREEMENT
(may address line of credit; insurance and contracts; lease in CureWorks name; programmatic benchmarks; board capacity and development benchmarks; creating independent infrastructure)
Identify staffing needs
(HR, fiscal, administrative, counsel)
Hire new staff, if necessary
(ongoing)
Evaluate, shop for, and select benefits and pension plans
Draft personnel manual
Establish payroll and accounting functions
Reassign graphic image and develop communications strategy
Enter into lease, if necessary
(in CureWorks' name)
Open bank accounts in CureWorks name
(general and payroll)
Manage all aspects of employment
(employees become spin-off employees)
Goals met
(as set out in Independence Agreement)
CREATION OF INFRASTRUCTURE AND IMAGE
END OF DEMONSTRATION PHASE
SPIN-OFF PHASE
TOTAL INDEPENDENCE
CREATION OF TAX-EXEMPT LEGAL ENTITY
Seek permission to use CureWorks as corporate name
Reserve corporate name with Secretary of State
Prepare Certificate of Incorporation, including waivers, if necessary
Conduct organizational meeting
(includes election of board; adoption of bylaws; banking and credit resolutions; appointment of officers; determination of fiscal year-end)
File IRS Form SS-4
(tax identification number)
Prepare and file IRS Form 1023
(application for tax exemption)
Receive 501(c)(3) determination letter from IRS
(recognizing organization as tax exempt)
File charities registration forms and apply for exemption from state and local taxes
SCRI relinquishes legal control
(resign as member and bylaws are revised)
Project has been operating as part of SCRI
(begins to work toward independence)
INCORPORATE
(an important milestone that signifies the birth of the spin-off as its own entity)

Annual Meeting Science Talk

Adapting B cell-directed CAR T cells for the treatment of auto- and alloimmunity

October 12, 2021 | Shaun Jackson, MB ChB, PhD

CPCI

Consortium for Pediatric Cellular Immunotherapy

Annual Meeting Wrap-up

October 12, 2021 | Julie Park

CPCI

Consortium for Pediatric Cellular Immunotherapy