

CCSS Investigator Meeting

June 14, 2023

CCSS
Childhood Cancer
Survivor Study



An NCI-funded Resource

Meeting Agenda Overview

CCSS

Time (Central Time)	Presentation
2:00 pm – 3:00 pm	Principal Investigator Report, Support Facility Reports
3:40 pm – 4:00 pm	Break
4:00 pm – 6:30 pm	Plenary Session
6:30 pm – 7:30 pm	Founders Reception (Garden Courtyard)
6:30 pm – 9:00 pm	6:30 pm – 7:30 pm
Thursday, June 15	
7:00 am – 7:45 am	CCSS 101: Led by Eric Chow!
8:00 am – 10:30 pm	Plenary Session: Working Group Chair Reports
10:30 am – 11:30 am	Working Group Breakout Sessions

CCSS 101 is back!

An introduction to CCSS how to maximally leverage the resource for survivorship research

Thursday, June 15, 7:00- 7:45 AM

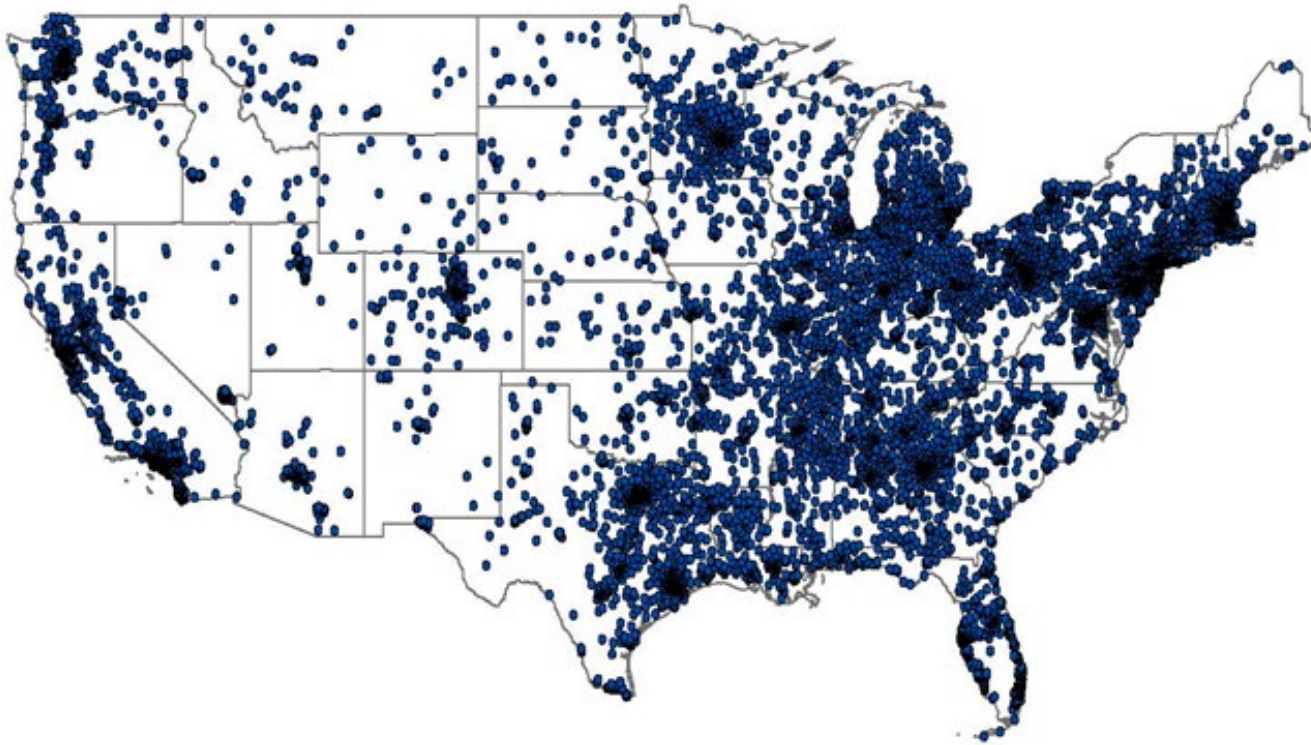
Eric Chow, MD
Co-Chair, Chronic Conditions Working Group



Childhood Cancer Survivor Study (U24 CA 55727)

Study Participants

CCSS



Resource for Survivorship Research

- Multi-institutional (n=31)
- 38,036 eligible survivors
- Open resource

- Cited >26,500 times
- >1,225 Investigators
- 91 Early career trainees

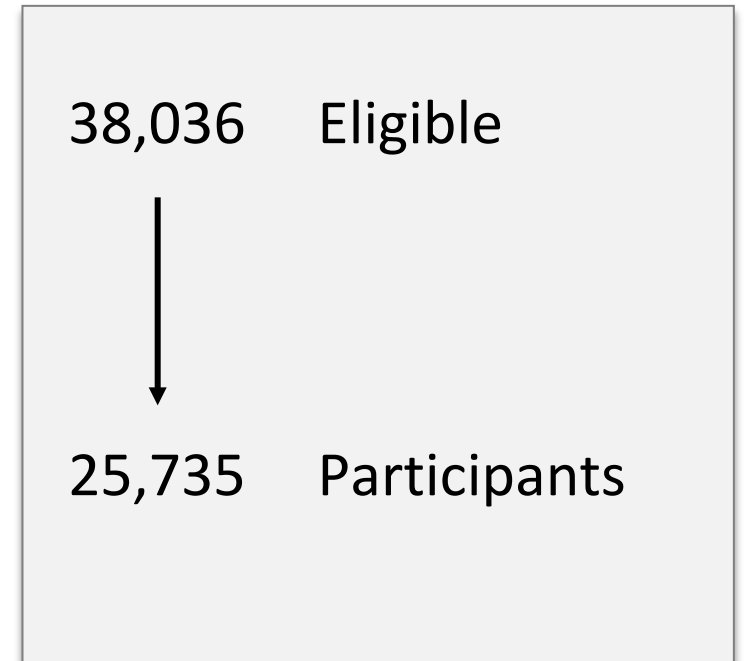
- 66 Investigator-initiated studies
- >\$80 million investigator-initiated grant support

Childhood Cancer Survivor Study

(U24 CA55727)

CCSS

- Funded in 1994
- Retrospective cohort, recent expansion includes survivors diagnosed 1970-1999
- 5-year survival
- Leukemia, lymphoma, CNS, bone, Wilms, NBL, soft-tissue and bone sarcoma
- Detailed treatment data
- Wide range of outcomes



* indicates expansion cohort population

CCSS Principal Investigator Report

June 14, 2023

CCSS
Childhood Cancer
Survivor Study



An NCI-funded Resource

Maintain and Promote the Resource

- Ongoing Follow-up of the active participants in the cohort (1970-1999)
- Support for Coordinating Center (St. Jude) and four support facilities for tracking/tracing, data cleaning/freeze, blood/tissue collection, SMN pathology confirmation, biorepository, and analysis/publication of results

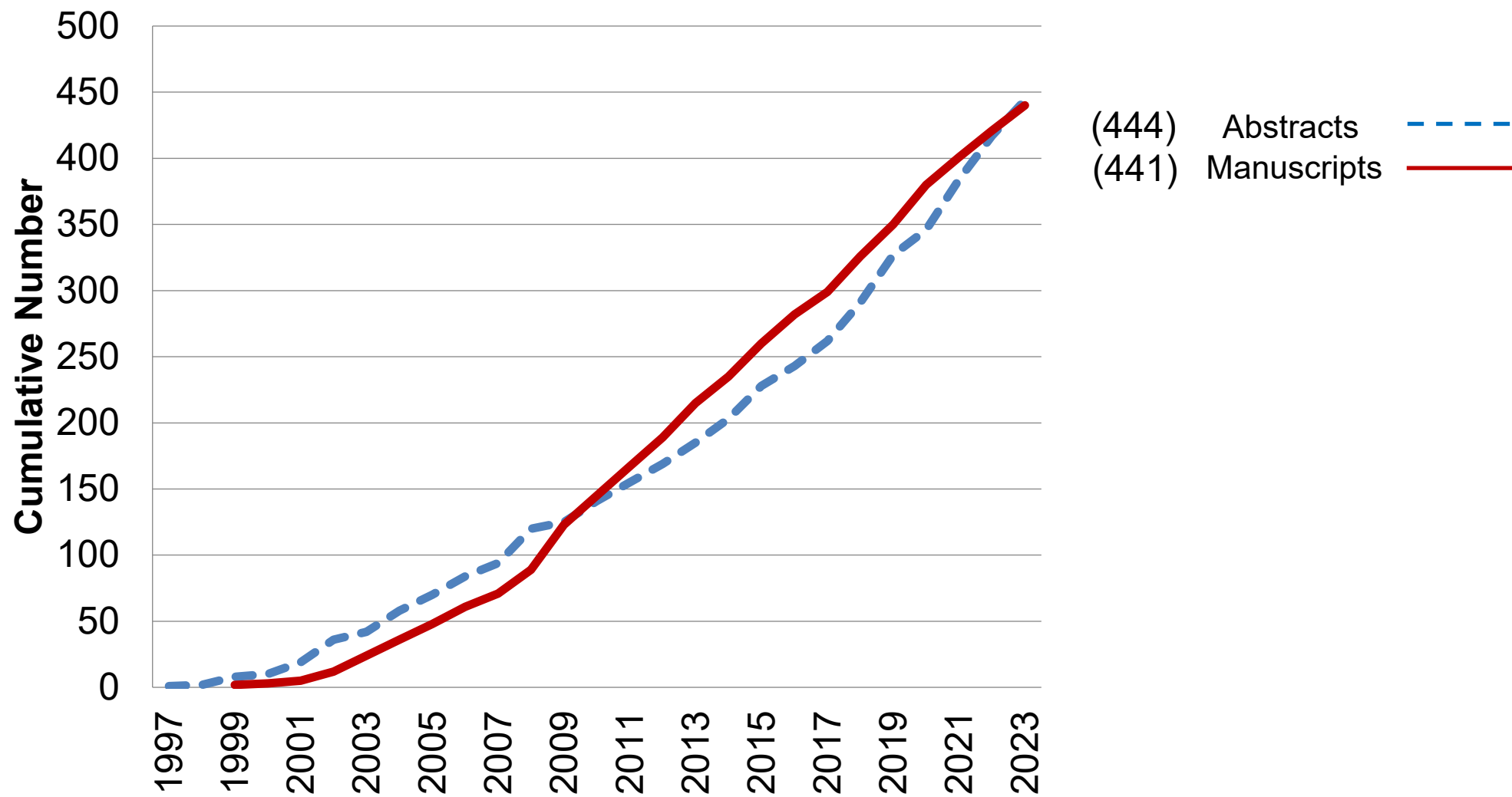
Enhance the Resource

Major New Objectives:

1. Aging and Accelerated Aging
2. Health Services Research
3. Cloud-based Data Sharing / Data Analysis Ecosystem
4. Strategic Plan for Future Cohort Expansion

CCSS Abstracts and Publications

CCSS



2022-2023 CCSS Publications (n=39)

CCSS

Impact Factor >10 (N=22)

Am J Hum Genet
Blood
J Clin Oncol
JAMA Netw Open
JAMA Oncol
JNCI
Lancet
Lancet Oncol
Nature Medicine

-54% in journals with impact factor >10 (vs. 26%, 2021)

Impact Factor 5-10 (N=7)

Cancer
JACC CardioOncol
J Am Heart Assoc
JCO Precis Oncol
Transl Psychiatry

Impact Factor <5 (N=10)

Biomed Phys Eng Express
BMC Health Services Research
BMC Open
Cancer Epidemiol Biomarkers Prev
Clin Orthop Relat Res
J Cancer Surv
PloS One

2023 to date:

29 unique abstracts submitted for presentation

ASCO (15 submitted: 1 oral, 2 poster discussion, 8 poster, 4 online only/withdrawn)

- Oral: Medicaid Enrollment Changes After Medicaid Expansion, Xu Ji, Emory University
- Poster Discussion:
 - Genetic Study of Type 2 Diabetes in Diverse Populations (SJLIFE/CCSS), Cindy Im/Yadav Sapkota
 - Predicting Therapy Induced Cardiomyopathy (SJLIFE/CCSS), Katyrina Petrykey/Yadav Sapkota

Title

First Author

Oral Presentation

Genetic study of diabetes in diverse populations (SJLIFE)

Yadav Sapkota (SJCRH)

Treatment and toxicity after subsequent breast cancer

Cindy Im (U. Minn.)

Predicting breast cancer after HL (Dutch HL Surv. Study)

Roberti Sander (Netherlands Ca. Inst.)

Subsequent meningiomas

Lucie Turcotte (U. Minn.)

Cumulative burden of major surgical intervention

Andrew Murphy (SJCRH)

GWAS of doxorubicin induced cardiomyopathy (SJLIFE)

Kateryna Petrykey (SJCRH)

Polygenic risk of anthracycline cardiomyopathy (COG)

Noha Sharafeldin (UAB)

Cancer predisposition variants and late mortality (SJLIFE)

Cheng Chen (SJCRH)

Mortality and SMNs beyond age 50

Rusha Bhandari (City of Hope)

Title

First Author

Rapid Oral Presentation

Updated colorectal RT dosimetry

Constance Owens (MDA)

Subsequent CNS malignancies

Robert Galvin (U. Minn.)

Role of BAG3 and TTN in cardiomyopathy (SJLIFE)

Achal Neupane (SJCRH)

Injury-related late mortality

Margaret Lubas (Radford)

7 Ongoing Intervention Trials (Ancillary Studies)

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Communication
Health
Coordination with
Primary Care

Recruitment Complete,
Follow-up Ongoing

ASPIRES



health
insurance
navigation
tools

EMPOWER

Recruitment & Follow-up
Complete



SLEEPWELL



ENGAGE



salsa

Study of Active
LifeStyle Activation

Follow-Up 7 Survey: Completed!

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Goal: Comprehensive Outcome Assessment of the Cohort (32 pages)

Status: Complete!

Data Freeze:

- Survey data freeze **complete**
- SMN, CTCAE graded health conditions, NDI data pending freeze
 - Final freeze anticipated by end of summer

Aging and Accelerated Aging

We will expand the collection of data to evaluate physiologic and neurocognitive function with aging, characterize accelerated aging, and investigate the underlying physiology of aging as survivors enter their 4th - 6th decades of life.

1. PRO-based data collection, focused on functional outcomes

Follow-up 8: New Measures for Aging

- 20 pages in length, Development Team: Ness, Krull, Snyder, Nathan, Leisenring, Alston, McDonald
- Field tested with minor concerns addressed
- Includes all new scales as we proposed in the competitive renewal

Attachment 4, Table 2: Proposed Patient Reported Outcomes for Assessment of Aging and Accelerated Aging in the Next Funding Period	
Name of Scale	Main Constructs Included
PHYSICAL PERFORMANCE ASSESSMENT	
Katz Activities of Daily Living	Self-reported functional status including bathing, transferring, dressing, self-care tasks for independent living.
Lawton Instrumental Activities of Daily Living	Self-reported functional status including using the telephone, transportation, housekeeping, ability to manage finances and prepare meals and other tasks required to live independently.
Fried Frailty Criteria (Self-reported)	Identifies survivors with physiologic frailty
Cumulative Illness Rating Scale	Summarizes disease burden across 14 organ-systems, with items scored 0-4 (none to extremely severe problem).
NEUROCOGNITIVE ASSESSMENT	
CCSS Neurocognitive Questionnaire (NCQ)	Task efficiency (attention + processing speed), memory, executive function.
PROMIS Cognitive Function SF	General cognitive function.
PROMIS Social Roles and Activities SF	Social roles and community activities.
Alzheimer's Disease Caregiver Questionnaire	Memory, language, executive function, behavior.

Follow-Up 8 Survey: CURRENT STATUS

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Goal: Assessment of aging functional outcomes (20 pages)

Status:


- First e-only push, and first paper mail-out complete
- Anticipate completion of FU8 in 2024

Current Funding Period: Major Objectives

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Aging and Accelerated Aging

We will expand the collection of data to evaluate physiologic and neurocognitive function with aging, characterize accelerated aging, and investigate the underlying physiology of aging as survivors enter their 4th - 6th decades of life.

1. PRO-based data collection, focused on functional outcomes
 2. **Web-based neurocognitive assessment (CNS Vital Signs)**
 3. Develop a population resource for intervention trials through **remote** functional assessment of 1000 sub-cohort of survivors (frail, pre-frail, not frail)
- 
1. Entire CCSS population
 2. Twice in funding period

Health Services Research

Given the unique healthcare needs of survivors we will enhance the resource to facilitate the conduct of health services research through collection of data to evaluate **patient**, **provider** and **health care system** factors and their associations with **access**, **quality**, and **cost** of care. Ultimately, we aim to provide a resource to identify how survivors' healthcare influences outcomes.

- FU8 Survey will assess survivors' perspectives of their **unmet needs**
(**CCSS Needs Assessment Questionnaire & Health Care Needs Study**)
- Expand expertise: Claire Snyder, Ph.D.
 - Co-Chair, Cancer Control and Intervention Working Group with Paul Nathan
 - Solicit proposals for Ancillary studies



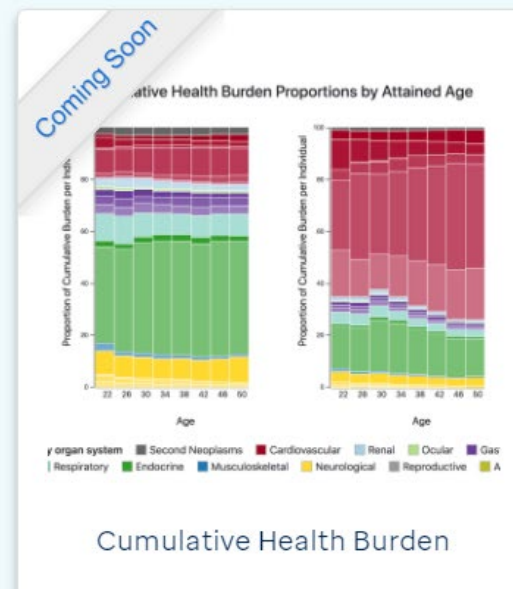
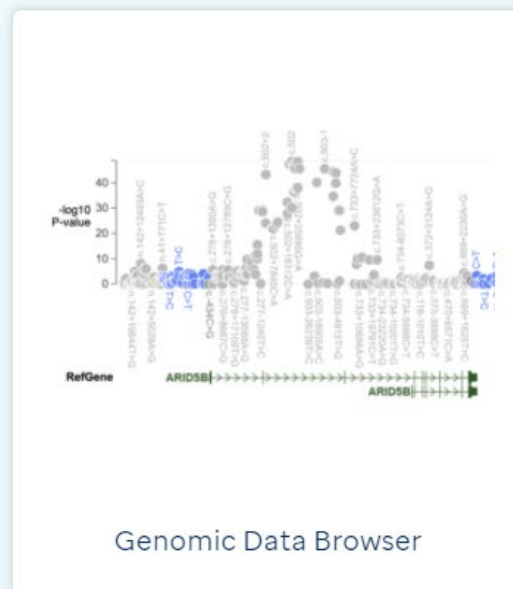
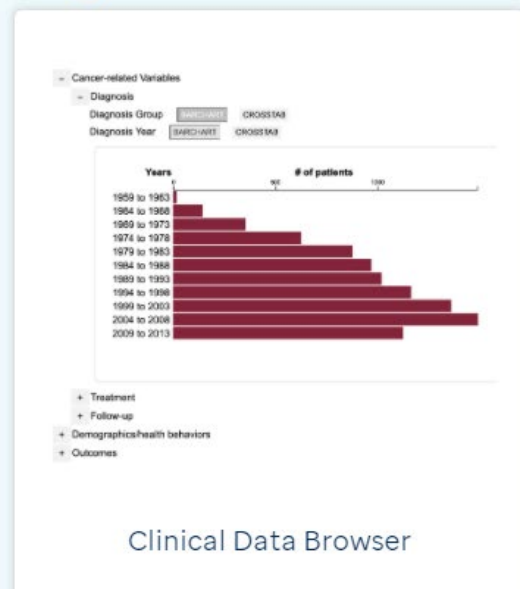
Current Funding Period: Major Objectives

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Enhance Data Sharing

To maximize access to the CCSS resource we will leverage a cloud-based sharing platform (**SJ Cloud Survivorship Portal**) to develop a data analysis ecosystem with tools for data access, visualization and analysis of genetic, treatment exposure and outcome data. (<http://survivorship.stjude.cloud/>)

Projects



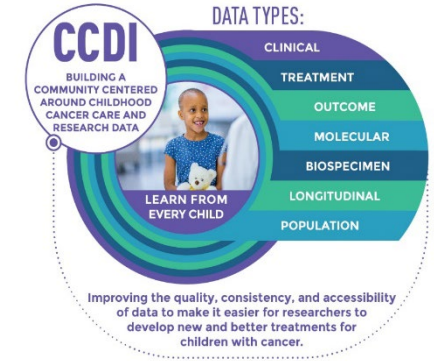
Status:

- All 25,665 participant data to be incorporated by **end this year**
- Genotype imputation on the existing SNP array data so that they can be harmonized with the WGS samples for integrative analysis **by end of this year**

Demo of SJ Cloud: ISLCCC, Thursday at 5:30pm !!!

Expanding the Genomic and Biospecimen Resource: Supplemental Funding 2021

CCSS



- **SMN somatic tissues with matched germline specimens**
 - 218 breast cancer, 116 thyroid, 111 meningioma
 - WGS, WES (Hudson Alpha), and RNAseq (St. Jude)
 - Approved concept to examine the effects of prior therapy on the genomic landscape, timing of mutation acquisition and immune infiltration signatures (Zhang)

Expanding the Genomic and Biospecimen Resource: Supplemental Funding

CCSS

	Breast Cancer		Thyroid Cancer		Meningioma		Melanoma	
Initial Cases with Tissue in CCSS BioPathology Center	218		116		111		12	
Cases Meeting Criteria and Submitted to HudsonAlpha	127 (58%)		85 (73%)		109 (98%)		12 (%)	
	WGS	WES	WGS	WES	WGS	WES	WGS	WES
Cases Processed and had adequate nucleic acid quantity/quality from tumor tissue	90 (42%)	83 (36%)	66 (56%)	71 (63%)	71 (70%)	71 (69%)	11 (%)	3 (%)
Current Status								
In Library prep	0	0	0	0	0	0	0	0
In Sequencing	0	0	0	0	0	0	0	0
Sequencing Complete	90	82	66	71	71	71	11	3
Matched Pairs with Germline	78	76	51	65	54	57		
RNA Seq	42		49		34			

Expanding the Genomic and Biospecimen Resource: Supplemental Funding 2021

CCSS

- 1,350 Survivors with **CTCAE grade 3 and 4** chronic health conditions
 - At high risk for mortality
 - Banking 40ml specimen** as a resource for investigators, including Paxgene tube for gene expression studied
 - COMPLETED!**

New resource for studies of: biomarkers, gene expression, multi-omics

1. Additional support to increase (maximize) **blood banking participation** from 36% to >50%
 - Acknowledges that in-home blood draw was performed during a pandemic
 - Re-invite participants to in-home blood draw
 - Increase incentive to \$100
2. **Additional WGS/WES** of CCSS participants
 - 1,750 survivors have provided a new, first-time specimen
 - saliva (2,098)
 - blood (292)
 - Sequencing by Hudson Alpha
 - **Goal:** 1,500 additional survivors with WGS/WES



Resource for Genetic Investigation

CCSS

Characteristic	Genotype Data Diagnosed 1970-1986 (N=5912)	Whole Exome Diagnosed 1970-1986 (N=5451)	WGS and WES Data Diagnosed 1987-1999 (N=2641)
Sex	N	N	N
Male	2781	2630	1240
Female	2958	2821	1401
Ancestry (based on genotype)			
European	5324	5105	2114
Non-European	415	346	527
Data Access	Available in dbGap	Available in dbGap	WGS Available in the St. Jude Cloud

Now Available: Phenotype data on all 25,665 CCSS participants in dbGap, including diagnosis, treatment and long-term outcome data

dbGaP Study Accession: phs001327.v2.p1

STAR ACT 2023: Supplemental Funding Application Submitted

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Leverage the newly banked blood specimens to perform **methylation profiling** on 2,285 survivors with blood specimens

- **Rationale:**
 - Mechanistic insights into the increased risk of adverse outcomes among survivors of childhood cancer
 - Enables the quantification of biological aging among survivors who experience accelerated aging and increased burden of aging-related morbidity and mortality
 - Move us a step closer to future multi-omics integrative approach for precision survivorship research and care
- **Supplement submitted, NOA pending**

Strategic Plan for Future Millennium Cohort Expansion

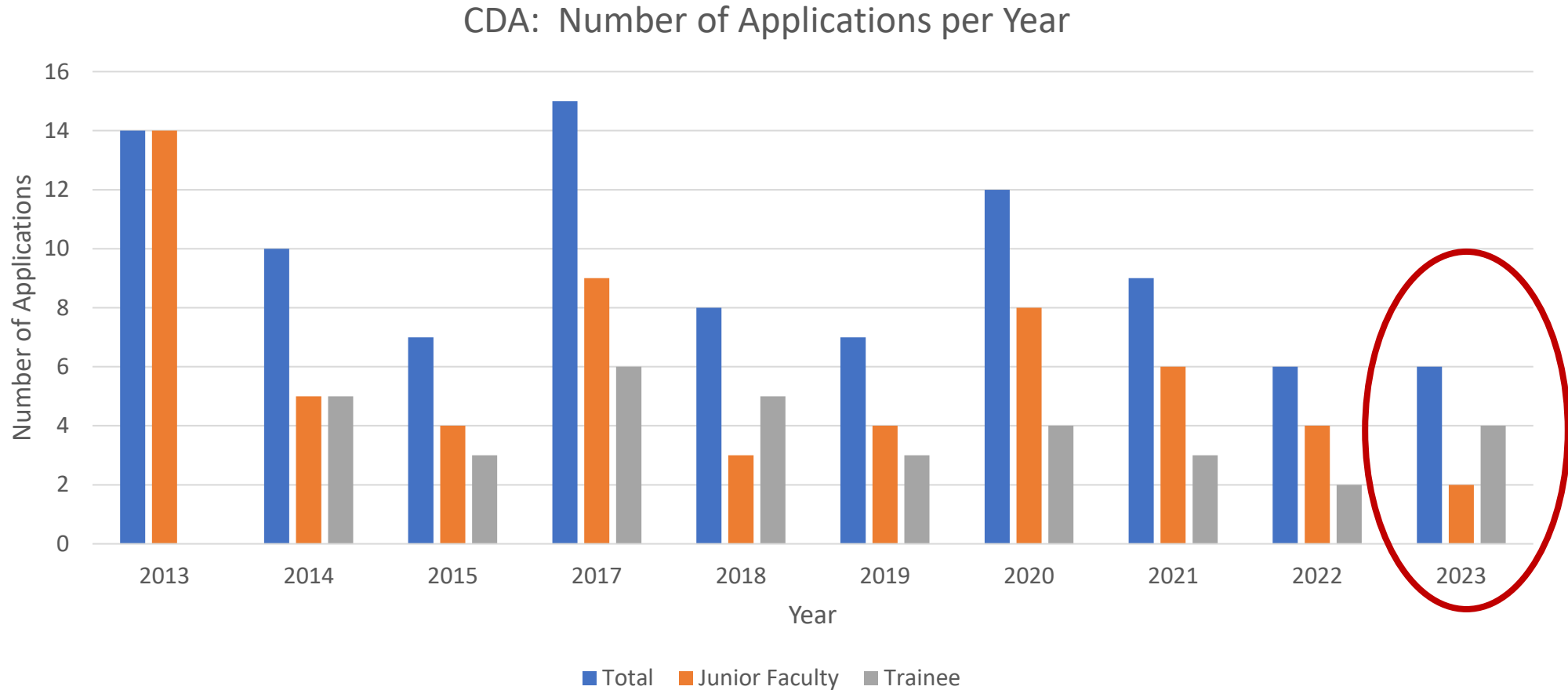
In the future, assessment of late outcomes of novel therapies (immunotherapy, targeted/biologic, proton beam) will be essential. Thus, with NCI oversight, CCSS will formulate a strategic plan for cohort expansion.

Begin in Funding Year 29 (Year 2 of the next award).

- Establish leadership / governance
- Convene stakeholders
- Enumerate objectives and priorities of an expansion
- Establish expertise
- **Determine feasibility:** define eligible population, recruitment, MRAF, identify and collect preliminary data
- Summarize assessment: infrastructure needs, feasibility, timeline, cost
- Delivery of final strategic plan report to NCI (Year 4)

Career Development Award

2023: 6 applications (2 Junior faculty, 4 trainee)



Career Development Award 2023

CCSS

CCSS Career Development Award Winners						
Category	Awardee	Application Title	Direct Costs Awarded	CCSS Working Group	Primary Mentor	Status
2023						
Junior Faculty	Rebecca Ronsley	Prevalence of gonadal failure and infertility in survivors of childhood brain tumors	\$20,000	Chronic Disease	Eric Chow	Concept Pending Approval
Trainee	Perri Tutelman, PhD University of Calgary	Longitudinal Patterns and Predictors of Cancer Fears in Survivors of Childhood Cancer	\$3,000	Psychology	Fiona Schulte	Concept Pending Approval
Trainee	Chiara Papini, PhD St. Jude Children's Research Hospital	The impact of sleep trajectories on neurocognitive functioning in adult survivors of childhood cancer	\$3,000	Psychology	Tara Brinkman	Concept Pending Approval

Career Development Award

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Announcing the 2024 CCSS Career Development Award
Application due date: October 2, 2022

See call for applications at:
<http://ccss.stjude.org>

Designed to create an opportunity for early career investigators and trainees with an interest and aptitude in childhood cancer survivorship research to develop and complete an initial research study within the CCSS.

Leadership Transitions: CCSS Data and Statistics Center

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May 1, 2023: Transition from Fred Hutch to St. Jude

Principles of the Transition:



- Kumar Srivastava leads the Center
 - Developing a statistical team in Memphis to assume data management
 - Mingjuan Wang, Senior Biostatistician + 2 new FTEs
- Wendy Leisenring has transitioned to Co-Chair Epi/Biostats Working Group
 - Pam and Kayla (Fred Hutch) will continue with same level of support from CCSS

Leadership Transitions: CCSS Coordinating Center

CCSS

February, 2023: Aaron McDonald, PhD



- Promoted to Director of Research, Department of Epidemiology and Cancer Control, St. Jude Children's Research Hospital

New CCSS Project Director (July 17, 2023): Vikki Nolan, PhD



- PhD in Epidemiology, Boston University
 - MPH, Yale
- Assoc. Dean for Academic Affairs, University of Memphis
- 2008: CCSS/SJLIFE data analyst

You are formally invited to attend the
CCSS Founders Reception

Tonight!

6:30 - 7:30 pm
Garden Courtyard

Steering Committee: Initial Members

CCSS

Les Robison
John D. Boice
Norman E. Breslow
Sarah S. Donaldson
Dan Green
Frederic P. Li
Anna T. Meadows
Ann Mertens
John Mulvihill
Joe Neglia



Mark E. Nesbit
Roger J. Packer
John D. Potter
Charles A. Sklar
Malcolm A. Smith
Marilyn Stovall
Louise C. Strong
Yutaka Yasui
Lonnie K. Zeltzer

Initial Institutional Principal Investigators

CCSS

Arthur Ablin

Roger Berkow

George Buchanan

Zoann Dreyer

Daniel Green

Mark Greenberg

Holcombe Grier

Melissa Hudson

Raymond Hutchinson

Michael Link

Anna Meadows

Joe Neglia

Lorie Odom

Maura O'Leary

Thomas Pendergrass

Gregory Reaman

Kim Ritchey

Kathy Ruccione

Frederick Ruymann

Charles Sklar

Anthony Smithson

Louise Strong

Robert Weetman

Teresa Vietti

Lonnie Zeltzer

Team Science: Thank You!

CCSS

Working Group Chairs

Smita Bhatia, University of Alabama at Birmingham
Eric Chow, Fred Hutchinson Cancer Center
Kevin Krull, St. Jude Children's Research Hospital
Paul Nathan, Toronto Hospital for Sick Children
Joe Neglia, University of Minnesota
Kevin Oeffinger, Duke University
Claire Snyder, Johns Hopkins University
Lucie Turcotte, University of Minnesota
Yutaka Yasui, St. Jude Children's Research Hospital

Support Facility Leaders

Aaron McDonald, St. Jude Children's Research Hospital
Michael Arnold, Children's Hospital Colorado
Stella Davies, Cincinnati Children's Hospital
Rebecca Howell, MD Anderson Cancer Center
Wendy Leisenring, Fred Hutchinson Cancer Center

Executive Committee

Saro Armenian, City of Hope
Smita Bhatia, University of Alabama at Birmingham
Eric Chow, Fred Hutchinson Cancer Center
Dan Green, St. Jude Children's Research Hospital
Rebecca Howell, MD Anderson Cancer Center
Melissa Hudson, St. Jude Children's Research Hospital
Kevin Krull, St. Jude Children's Research Hospital
Wendy Leisenring, Fred Hutchinson Cancer Center
Paul Nathan, Toronto Hospital for Sick Children
Joseph Neglia, University of Minnesota
Kiri Ness, St. Jude Children's Research Hospital
Kevin Oeffinger, Duke University
Les Robison, St. Jude Children's Research Hospital
Nita Seibel, National Cancer Institute
Charles Sklar, Memorial Sloan Kettering Cancer Center
Claire Snyder, Johns Hopkins University
Lucie Turcotte, University of Minnesota
Yutaka Yasui, St. Jude Children's Research Hospital

Publications Committee

Saro Armenian, City of Hope
James Bates, Emory University
Kim Edelstein, Princess Margaret Cancer Center
Monica Gramatges, Texas Children's Hospital
Rebecca Howell, MD Anderson Cancer Center
Anne Kirchhoff, University of Utah
Wendy Leisenring, Fred Hutchinson Cancer Center
Aaron McDonald, St. Jude Children's Research Hospital
Chaya Moskowitz, Memorial Sloan Kettering Cancer Center
Goli Mostoufi-Moab, Children's Hospital of Philadelphia
Kiri Ness, St. Jude Children's Research Hospital
Yadav Sapkota, St. Jude Children's Research Hospital
Noha Sharafeldin, University of Alabama at Birmingham
Lucie Turcotte, University of Minnesota
Ellen van der Plas, University of Arkansas Medical School
Lynda Vrooman, Dana-Farber Cancer Institute
Zhaoming Wang, St. Jude Children's Research Hospital
Suzanne Wolden, Memorial Sloan Kettering Cancer Center

Steering Committee

John Boice, Vanderbilt University
Sandy Constine, University of Rochester
Lisa Diller, Dana-Farber Cancer Institute
Sarah Donaldson, Stanford University
Lori Henderson, National Cancer Institute
Ann Mertens, Emory University
Lindsay Morton, National Cancer Institute
Louise Strong, MD Anderson Cancer Center
Chris Weldon, Boston Children's Hospital
Lonnie Zeltzer, UCLA

St Jude Faculty and Staff

Shani Alston	Harmony Farner	Zhenghong Li	Kumar Srivastava
Nita Anderson	Jessica Flynn	Janna Lipford	Rachel Tillery
Abbe Anderson	Tracie Gatewood	John Lucas	Ramona Vejandla
Jessica Baedke	Tolly Gillenwaters	Telisa McKinney	Chris Vukadinovich
Theresa Bailey	Haley Harlan	Aimee Montgomery	Mingjuan Wang
Netha Banks	Geehong Hyun	Wonjong Moon	Sharon Walker
Ollie Battle	Lisa Jacola	Daniel Mulrooney	Stacy Wallace
Yaniz Booth	Elizabeth Johnson	Brent Orr	Lauren Williams
Tara Brinkman	Patricia Key	Robyn Partin	Nicole Wilson
Andrew Cobble	Margie King	Casey Mastio-Partridge	Carmen Wilson
Christie Cooper	Komal Kochar	Avnisha Patel	Porsceh Wright
Tabitha Cross	Jennifer Lanctot	Nick Phillips	Jinghui Zhang
Sheila Crutcher	Kathy Laub	Sean Phipps	
Shannon Dodds	Michael LaVoice	Suyena Poudel	
Ricardo Duran	Trinity LaVoice	Dayton Rinehart	
John Easton	Carol Lee	Sedigheh Mirzai Salehabadi	
Matthew Ehrhardt	Kisten Lenoir	Tishana Sharp	
Lacy Ellis	Barbara Lewis	Jin-ah Sim	

Education Committee

Catherine Coleman, Harvard University
Kayla Foster, Texas Children's Hospital
Melissa Hudson, St. Jude Children's Research Hospital
Carol Lowenstein, Harvard University
Aaron McDonald, St. Jude Children's Research Hospital
Diana Merino, All Stripes
Kathy Ruccione, Azusa Pacific University
Julia Stepenske, Advocate Children's Hospital

Institutional Principal Investigators

Saro Armenian	Jennifer Dean	Jill Ginsberg	Ray Hutchinson	Denise Rokitka	Kimberly Whelan
Carola Arndt	Lisa Diller	Rob Goldsby	Katherine Rae Lange	Karim Sadek	
Scott Baker	ZoAnn Dreyer	Tanja Gruber	Paul Nathan	Jenna Sopfe	
Donald Beam	Karen Effinger	Robert Hayashi	Lilibeth Torno	Louise Strong	
Dan Bowers	David Freyer	Tara Henderson	Randy Olshefski	Jean Tersak	
Jackie Casillas	Danielle Friedman	Melissa Hudson	Jennifer Reicheck	Terry Vik	

External Advisors

Garnet Anderson, Fred Hutchinson Cancer Center
Melissa Bondy, Baylor College of Medicine
Susan Cohn, University of Chicago
David Hodgson, University of Toronto
Timothy Rebbeck, Harvard University
Flora Van Leeuwen, Netherlands Cancer Institute
Susan Weiner, Children's Cause for Cancer Advocacy