

CHS Biorepository Research Project RFA/Solicitation

Version 11052021

Summary: Funds are available for assays (no salaries or other operational expenses) using CHS Biorepository samples. This is the first of two solicitations, with a total of ~\$150,000 Direct Cost available at this time. Emphasis on early career investigators; all projects need a CHS Sponsor. Project minimum is \$50,000 for one year. Proposals due January 15, 2022.

Details:

1. **Overview:** In the latest renewal of CHS, the NHLBI has agreed to provide funds for soliciting, identifying and funding CHS biorepository-based research projects. These funds are for assays only, not salary, travel, or other operational expenses, so no subcontracts are needed. A broad overview of CHS Biosample types and collection years is attached at the end of this solicitation.
2. **Opportunity description:** The goal is to expand the research use of the CHS Repository for the betterment of the health of older Americans, with special emphases on a) enabling access to sustainable research careers for early career investigators; and b) projects focused on heart, lung, blood and sleep disorders. The total funds available are \$300,000, to be distributed over two separate solicitations, with ~\$150,000 available for each solicitation.

To assist Early Career Investigators, CHS will make available expertise to mentor and assist investigators before, during, and after the assays are run, including help with biosample availability, assay appropriateness and selection, funding for outside labs if appropriate, advice on statistical approach, etc.

We anticipate two solicitations, with the goal of awarding ~half the total funds at each solicitation. The distribution of funds will depend on the number of submitted and highly ranked projects. While a single, two-year project utilizing all available funds is conceivable, smaller two-year or even one-year projects may have great merit for developing pilot data for future grant applications. The minimum funded project will be one year for \$50,000-worth of assays.

3. **Dates for this first solicitation:**
 - a. **November 1, 2021:** RFA/Solicitation published;
 - b. **January 15, 2022:** deadline for proposals to be submitted as CHS Ancillary Study Proposals (click [here](#));
 - c. **February 15, 2022:** awardees notified;
 - d. **August 15, 2022** (approximately, depending on assays): Data submitted from lab to investigators (six months post award);
 - e. **September 15, 2022:** (or 1 month post receipt): Cleaned data submitted by investigators to CHS Coordinating Center;
 - f. **October 15, 2022** (or 1 month post receipt at the CC): CHS analysis dataset transmitted to investigators;

4. **Award mechanism and submission information:** Proposals should be in the format of a CHS Ancillary Study Proposal (click [here](#)) and adhere to the CHS Ancillary Study policies. A cover note should indicate that the investigator is responding to this RFA, and identify a CHS Sponsor (a CHS investigator (see website for list¹) who accepts responsibility for monitoring the project for progress, compliance with CHS policies, etc; CHS investigators may act as their own sponsor). Funds will be used solely for assay work, and not for other items such as investigator salary or travel; therefore, subcontracts will not be used. While we anticipate that the CHS Central Blood Lab will be the site for much proposed assay work, outside laboratories may also be proposed. As part of the award, CHS will provide an analytic dataset to the investigator for data analyses. Once funds are allocated to an investigator's project, the research project can begin.
5. **Eligibility:** This solicitation is open to all qualified researchers. Preference will be given to early career investigators (students, postdocs, and assistant professors). Investigators must identify a CHS Sponsor.
6. **Review information:** After being received, proposals will be administratively reviewed by the CHS CBL investigators for adherence to the RFA. Compliant proposals will be scored by a review committee comprised of CHS investigators from the CHS Lab Committee, CHS Publications Committee, and other experts (as needed). In cases where appropriate expertise isn't available from these sources, CHS investigators or collaborators who are not currently on the Publications or Laboratory Committees may be recruited to the committee. CHS has hundreds of expert investigators to call upon, but in rare cases non-CHS investigators may be called upon for topics where novel expertise may be needed. Review Committee members will be proposed by the Chair of the CHS Lab Committee, and approved by the CHS Executive Committee. The overall application will be judged on a 5-point scale (1=best), with reviewers providing comments explaining their score. Completed reviews will send to the CHS Steering Committee and NHLBI for final selection.
Review criteria will include:
 - a. In general, being consistent with the mission and purpose of CHS;
 - b. Specifically, priority will be given to studies which focus on:
 - i. Heart, lung, blood and/or sleep disorders;
 - ii. Disorders of aging and older age;
 - iii. Longitudinal trajectories (given the unique availability of biosamples in CHS covering > 25 years of followup);
 - iv. Already strong CHS areas such as cognitive decline, atherosclerosis/heart failure, renal disease, frailty, etc;
 - v. Integrating CHS into the growing body of multiomic data and data analysis;

¹ select the Directory on the top menu bar, once in the Directory select CHS Investigators Group to list CHS members eligible to serve as sponsors

- c. Reviewers should comment on the traditional review areas such as Significance, Innovation, Approach, Investigator team, and Environment;
- d. Preference will be given to early career investigators (students, postdocs, and assistant professors);
- e. Preference will be given to proposals that indicate how this work both builds on prior work, and provides data for future work via a grant submission.

7. Metrics for success:

- a. Monitoring progress: The CHS sponsor will have primary responsibility for monitoring the project. Progress reports from the awardees to CHS are due annually, and final report due at the end of the project. The project must be compliant with all relevant CHS policies, as well as Human Studies policies, data sharing policies, etc.
- b. Progress Reports from CHS to the NHLBI should include demographics on the awardee PIs and affiliations, and range of scientific topics should also be provided
- c. All manuscript proposals and manuscript submissions associated with the funded research projects will undergo review by Publications Committee, Steering Committee, and NHLBI. Data generated by these projects will be incorporated into the CHS database and deposited in dbGaP, BioLINCC or other appropriate repositories such as BioDataCatalyst as directed by NHLBI. Data deposit in any other repository must be approved by CHS and NHLBI at the time of application.
- d. Other metrics associated with a successful project:
 - i. Samples were identified and requested;
 - ii. Assays were performed;
 - iii. Data were collected and integrated into a more extensive database;
 - iv. Data were analyzed;
 - v. Data were reported in a manuscript;
 - vi. An Annual Progress report was submitted on time (on the award date if a two-year award);
 - vii. Final report was submitted on time (within 1 month of award ending date);
 - viii. Aspirational: publication in a high-profile journal;
 - ix. Aspirational: data provides inspiration/preliminary data for a successful grant submission;

8. **Overview of CHS Biosample Types and Availability:** The following table offers a broad overview of the Biosamples collected at major CHS exam years. The actual amount available and freeze/thaw status of each sample type will vary by exam year; contact the Repository for more details.

Visit Year	# of PARTICIPANTS Main Cohort / Minority Cohort	EDTA Plasma orig. #vials (ml/vial)	EDTA BUFFY COAT	for DNA prep.	Room Temp.	4C	Serine Protease Inhibitors	OGTT	platelet inhibitors	Cryo-preserved Cells #vials @ ~20x10E6 cells/vial	Year
2 main cohort baseline	5178 / 0	3 (1.0)	X		1 (1.0)	1 (0.5)	4 (0.5)	3 (1.0)			89-90
3	2 sites only	X						X			90-91
4	2 sites only	X						X			92-93
5 Minority cohort baseline	4168 / 661	6 (0.5)	X		2 (0.5)	2 (0.5)	8 (0.25)	6 (0.5)			93-94
6	3787 / 529	6 (0.5)	X								94-95
7	3573 / 495	6 (0.5)	X					3 (1.0)		2 (0.4)	95-96
8	one site only	6 (0.5)	X								96-97
9	3064 / 459	7 (0.5)	X			4 (0.5)	8 (0.25)	7 (0.5)	7 (0.5)		97-98
10	2675 / 394	7 (0.5)	X								98-99
11	2569 / 363	1 (2.0)	X							2	99-00
18	919/142	8 (1.0)						8 (1.0)			00-01

9. **Overview of previously measured biomarkers:** A summary of the CHS data collection timeline, types of data available, and previously measured laboratory measures follows. Additional details regarding data collection and CHS data access may be found on the CHS website under “Researchers”.

10. **Contact for questions:** please contact the CHS Central Blood Lab for more information:

- a. For sample availability: Elaine Cornell at elaine.cornell@uvm.edu
- b. For design or assay issues: Russell Tracy, CBAL Director, at Russell.tracy@uvm.edu
- c. For Proposal submission issues: Erika Enright at eenright@uw.edu

1. Calendar of Exams and Events Surveillance Phone Calls

	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999
Exams		Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10	Y11
Phone calls		Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10	Y11

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	
Exams	Y11						Y18 (All-Stars)					
Phone calls	Y11	Y12p	Y13p	Y14p	Y15p	Y16p	Y17p	Y18p	Y18p	Y20p	Y21p	
		Y12a	Y13a	Y14a	Y15a	Y16a	Y17a	Y18a	Y19a	Y20a	Y21a	

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	
Exams											Y31	
Phone calls	Y21p	Y22p	Y23p	Y24p	Y25p	Y26p	Y27p		Y28p	Y29p	Y30p	Y31p
		Y22a	Y23a	Y24a	Y25a	Y26a	Y27a	Y28a		Y29a	Y30a	Y31a

2. Summary of Key Data Collection Components

Clinic/In-Person Visits														Phone Calls
	BASE	YR 3	YR 4	YR 5	YR 6	YR 7	YR 8	YR 9	YR 10	YR 11	YR 18	YR 31	Y12-17; 19-33	
Questionnaires														
Access to Care							X	X	X	X				
Caregiver Screening				X										
Comorbidity index				A										
Depression Scale (CES-D)	X	X	X	X	X	X	X	X	X	X	X	X	X	
Food Frequency (Diet)	X						X							
Medical History	X	X	X	X	X	X	X	X	X	X	X	X		
Medications - Prescription	X	X	X	X	X	X	X	X	X	X	X	AD ¹	X ²	
Medications - OTC					X	X	X	X	X	X				
Occupation	X				X	X	X	X	X	X	X			
Parental Longevity			X								X			
Personal History	X	X	X	X	X	X	X	X	X	X	X			
Physical Activity	X			X				X			X	X		
Physical Function: ADL/IADL	X	X	X	X	X	X	X	X	X	X	X	X	X	
Quality of Life	X	X	X	X	X	X	X	X	X	X		X		
Respiratory Symptoms	X	X	X	X	X			X						
Rose Angina	X	X	X	X	X	X			X		X			
Rose Claudication	X	X	X	X	X	X			X		X			
Self-Perceived Health	X	X	X	X	X	X	X	X	X	X	X	X		
Sibling CVD History	X										X			

Clinic/In-Person Visits													Phone Calls
	BASE	YR 3	YR 4	YR 5	YR 6	YR 7	YR 8	YR 9	YR 10	YR 11	YR 18	YR 31	Y12-17; 19-33
Physical Function: Finger Tapping			X	X	X	X	X	X	X	X			
Resting 12-Lead ECG	X	X	X	X	X	X	X	X	X	X			
Retinal Photography									X				
Saliva specimen collection												X	
Six-Minute Walk/Oximetry								X					
Sleep study							A			A			
Spirometry	X				X			X			X		
Spot Urine Collection								X					
Ultrasound - Carotid	X			X						X			
Ultrasound - Aortic				X									
Visual/Hearing Acuity	X	X	X	X	X	X		X		X			

X : collected as part of CHS main study

A: collected by ancillary study

¹AD= Alzheimer medications

²Medication collection ended after Year 29

CHS YEAR	2	3	4	5 Orig.	5 New	6	7	8	9	10	11	18
Plasminogen	S											
Plasmin/Antiplasmin Complex	S			S	S							
D-dimer Fragment	S			S	S							
Inflammation Factors												
Albumin	X			X	X				X			
C-Reactive Protein	X			X	X				X			X
α_1 -Acid glycoprotein	S			S								
White Cells	X			X	X							X
IGF-1	S			S	S	X	S		X	S		X
IL-6	X			X	X				X			X
sCD14	X				X							
sCD163	X				X							
sIL-2R α	X				X							
ICAM-1	S				S							
Serum amyloid P (SAP)	S											
Pentraxin 3	S											
Lp-PLA2	X				X							
TGF-Beta 1				S	S				S			
antiphospholipid antibodies	S				S		S					
IGF-BP1									X			X
IGF-BP3						X			X			X
Galectin-3	X			X	X		S					
AGEs				S	S							
IL-1RA	X				X							
IL-18	X				X							
sTNFR1	X				X							
YKL40				S	S				S	S		
Oxidation Factors												
Homocysteine/B ₆	S											
Myeloperoxidase				S	S							
Hormonal Factors												
Fasting Glucose	X			X	X		X		X		X	X
Fasting Insulin	X			X	X				X			
2-Hour OGTT	X								X			
2-Hour insulin	X								X			
Proinsulin, specific insulin, anti-insulin	S				S							
HbA1c	S											
TSH	S			X	X		X		X			X
FT4	S			X	X		S		S			X
T3				X	X		S		S			X
C-Peptide									X			
DHEA	S			X	S	S	S		X	S		X
Androstenedione							S		X			X

CHS YEAR	2	3	4	5 Orig.	5 New	6	7	8	9	10	11	18
Testosterone				S	S		S					
Free testosterone				S			S					
SHBG				S			S					
Dihydrotestosterone							S					
PTH				S	S							
CML									X			
Platelet Count	X			X	X							X
Other												
Uric Acid	X			X	X							
Potassium	X			X	X							
Hgb/Hct				X	X							X
Klotho				X	X							
PIIINP									X			
Medications												
Salicylate				S								
Digoxin				S								
Propranolol				S								
Hydrochlorothiazide				S								
Renal												
Cystatin C	X			X	X				X			X
Urinary albumin									X			
Urinary creatinine									X			
Urinary uromodulin									S			
Serum uromodulin									S			
Creatinine	X			X	X				X			X
Serum Calcium				S	S							
Serum Phosphorus				S	S							
C-terminal FGF-23									X			
Intact FGF-23									S			
Ferritin									S			
Iron									S			
Iron binding capacity									S			
Alkaline Phosphatase				X	X							
Vitamins												
Vitamin D				S	S				S			X
Vitamin E	S											
β-carotene	S											
Homocysteine/B6	S											
Bone												
Bone alkaline phosphatase				S	S							
Osteocalcin				S	S							
SDF-1a							S					
DPPIV Activity							S					
CTX				S	S							

CHS YEAR	2	3	4	5 Orig.	5 New	6	7	8	9	10	11	18
Obesity-related												
Adiponectin total				X	X				X			X
Adiponectin HMW				X	X							
Total fasting NEFA				X	X				S			
Total 2-hr NEFA									S			
Individual fasting NEFA									S			
FABP4				X	X							
Fetuin A				X	X				X			
Leptin				S								
Cardiac markers:												
BNP	X			X	X		S		X			
ANP	S											
Procollagen peptides	S											
Troponin	X			X	X		S					
ST2	X			X	X		S					
Gas6				S	S							
Brain-related												
Neurofilament light (Nfl)				S	S	S			S			
Tau				S	S	S			S			
UCH-L1				S	S	S			S			
GFAP				S	S	S			S			
Microbiome-related												
TMAO	X				X				X			
Choline	X				X				X			
Betaine	X				X				X			
Carnitine	X				X				X			
Butyrobetaine	X				X				X			
Crotonobetaine	X				X				X			
Serology & autoimmunity												
anti-Twar antibodies	S											
anti-CMV antibodies	S											
anti-HSV-1 antibodies	S											
TPO antibodies	S			X	X							X
Muscle-related												
Follistatin							S					
FSTL3							S					
GDF8/myostatin							S					
GDF11							S					
Oxytocin							S					
GDF15							S					