Grant Development Workshop

Salt Lake City

April 3, 2014

Grant Development Workshop

- One of the suggestions at the Lund meeting was to develop and collaborate on new projects
- Steering committee considered and approved the development of the workshop and a proposal process
- Grant opportunities will be presented first
- Grant proposals will follow

Grant opportunity
AHA Genome Phenome

American Heart Association Cardiovascular Genome Phenome Study (CVGPS) Funding Announcement

The Cardiovascular Genome Phenome Study (CVGPS) is a collaborative effort, spearheaded by the American Heart Association (AHA), to accelerate the future of cardiovascular medicine. CVGPS combines the power of long-term population studies with the precision of molecular analysis to unravel key distinctions between and within subgroups of patients. The discoveries it generates will point the way toward better-targeted, safer, and more effective treatments, based on a deeper understanding of patients' characteristics, including e.g. risk profiles and therapeutic needs.

The CVGPS is a collaboration among AHA, Boston University (BU) and the University of Mississippi Medical Center (UMMC), the academic coordinating center homes, respectively, of the Framingham Heart Study (FHS) and the Jackson Heart Study (JHS). The Jackson Heart Study also involves Jackson State University (JSU) and Tougaloo College (TC) as partner institutions.

Overview of the FHS

- In 1948, researchers recruited 5,209 men and women between the ages of 30 and 62 from Framingham, MA
  - First round of extensive participant examinations and lifestyle interviews later analyzed for patterns related to CVD development.
- In 1971, the study enrolled a second-generation cohort -- 5,124 of the original participants' adult children and their spouses -- to participate in similar examinations.
- In 1994 and 2003 recruitment of two multi-ethnic cohorts (approximately 400-500 participants each) began (OMNI).
- In April 2002, the enrollment of a third generation of participants, the grandchildren of the original cohort. It involved 4,095 participants.
- A joint project of the National Heart, Lung and Blood Institute and Boston University.

Table 1. Number and percent[1] of Framingham participants overall and within each generation with genetic/OMICs resource listed

RESOURCE	GROUP			
	ALL IDTYPES	IDTYPE 0	IDTYPE 1	IDTYPE 3
	ALL GEN	GEN1[§]	GEN2	GEN3
TOTAL PARTICIPANTS(%total)	14169 (100)	5079(36)	5012(35)	4078(29)
	N(%)	N(%)	N(%)	N(%)
Genotypes				
CARE GENOTYPES (candidate genes chip)	7546 (53)	647 (12.7)	3022 (60.3)	3877 (95.1)
CARE IMPUTED GENOTYPES	7544 (53)	647 (12.7)	3021 (60.3)	3876 (95.0)
CHARGE-S EXOME SEQ	621 (4)	13 (0.3)	487 (9.7)	121 (3.0)
CHARGE-S TARGETED SEQ	1095 (8)	36 (0.7)	957 (19.1)	102 (2.5)
CHARGE-S WHOLE GENOME SEQ*	846 (6)	12 (0.2)	713 (14.2)	121 (3.0)
ESP Whole EXOME SEQ**	464 (3)		291 (5.8)	173 (4.2)
ADSP Whole exome SEQ**	1927 (1.4)	475 (9.4)	1452 (29.0)	
EXOME CHIP (Illumina v 1.0)	8051 (57)	655 (12.9)	3377 (67.4)	4019 (98.6)
MICROSATELLITE MARKERS	4112 (29)	454 (8.9)	1400 (27.9)	2258 (55.4)
NHGRI MEDSEQ***	1703 (12)		1703 (34.0)	
OMNI 5 CHIP (Illumina)	2472 (17)		2472 (49.3)	
100K GENOTYPES	1341 (9)	258 (5.1)	1083 (21.6)	
PERLEGEN GENOTYPES	1649 (12)		1649 (32.9)	
PGA GENOTYPES	1748 (12)		1748 (34.9)	
SHARE (550K GENOTYPES)	9163 (65)	1529 (30.1)	3746 (74.7)	3888 (95.3)
SHARE IMPUTED GENOTYPES	8372 (59)	954 (18.8)	3558 (71.0)	3860 (94.7)
SHARE FOLLOWUP GENOTYPES	7974 (56)	659 (13)	3295 (65.7)	4020 (98.6)
OMICS				
Whole blood gene expression (Affymetrix GeneChip Human Exon 1.0 ST Array)			2446 (48.8)	3180 (80)
Whole blood microRNA			3500 (69.8)	3500 (85.8)
Metabolome (350 metabolites)			2500 (49.9)	

[1]the percentage in the TOTAL PARTICIPANTS is across all cohorts, not within cohort

- **CVGPS Pathway Grants** – funded at $250K/year for 2 years for a total of $500K
- **CVGPS Grand Challenge Awards** – funded at $500K for 4 years for a total of $2MM
- Letter of intent due in June
- Selection committee will then invite formal applications

The broad objectives of the new collaboration are to:

- conduct novel 'dense' phenotyping that will substantially add to extant genotypic, OMICs, and phenotypic data collected from an expanded sample set that extends beyond the existing FHS and JHS funded cohorts. The integrative data-exchange across the datasets using varying depths of phenotyping should provide important insights into the pathways to CVD.

- build a state-of-the-art phenotypic and genotypic repository that will integrate previously collected data from FHS/JHS in their current repositories with new phenotypes collected on these cohorts and other new samples (in the new CVGPS biorepository) This repository will be open to qualified investigators.

- build a national network biorepository resource by building upon the foundational population science resources of the AHA-FHS-JHS partnership. Leverage the collective talent and experience of AHA, FHS, and JHS in population science to establish best practice data-sharing standards and harmonize the dense phenotyping across datasets so that the knowledge harnessed will have wider generalizability and facilitate detailed analyses of the determinants of CVD risk and ethnic and socioeconomic differences therein;

Potential Specific Programs

Deep Phenotyping:
- Phenorepository
- Repeated Monitoring
- Orthogonal Phenotyping

Genomics:
- WGS/WES
- Gene Expression
- Secular Monitoring

"CV-GPS" Collaboration

American Heart Association / Boston University (Framingham Heart Study+) / University of Mississippi (Jackson Heart Study+)

Analytics:
- Network Analysis
- Systems Analysis
- The Health eHeart Study

Education:
- Genomics
- Bioethics

Some specific opportunities

- Dense phenotyping – CCS?
- Phenotypic extremes – affected at a very young age, with minor risk factors compared to elderly with greater risk factors?
- Longevity studies
- Health disparities between Framingham and Jackson

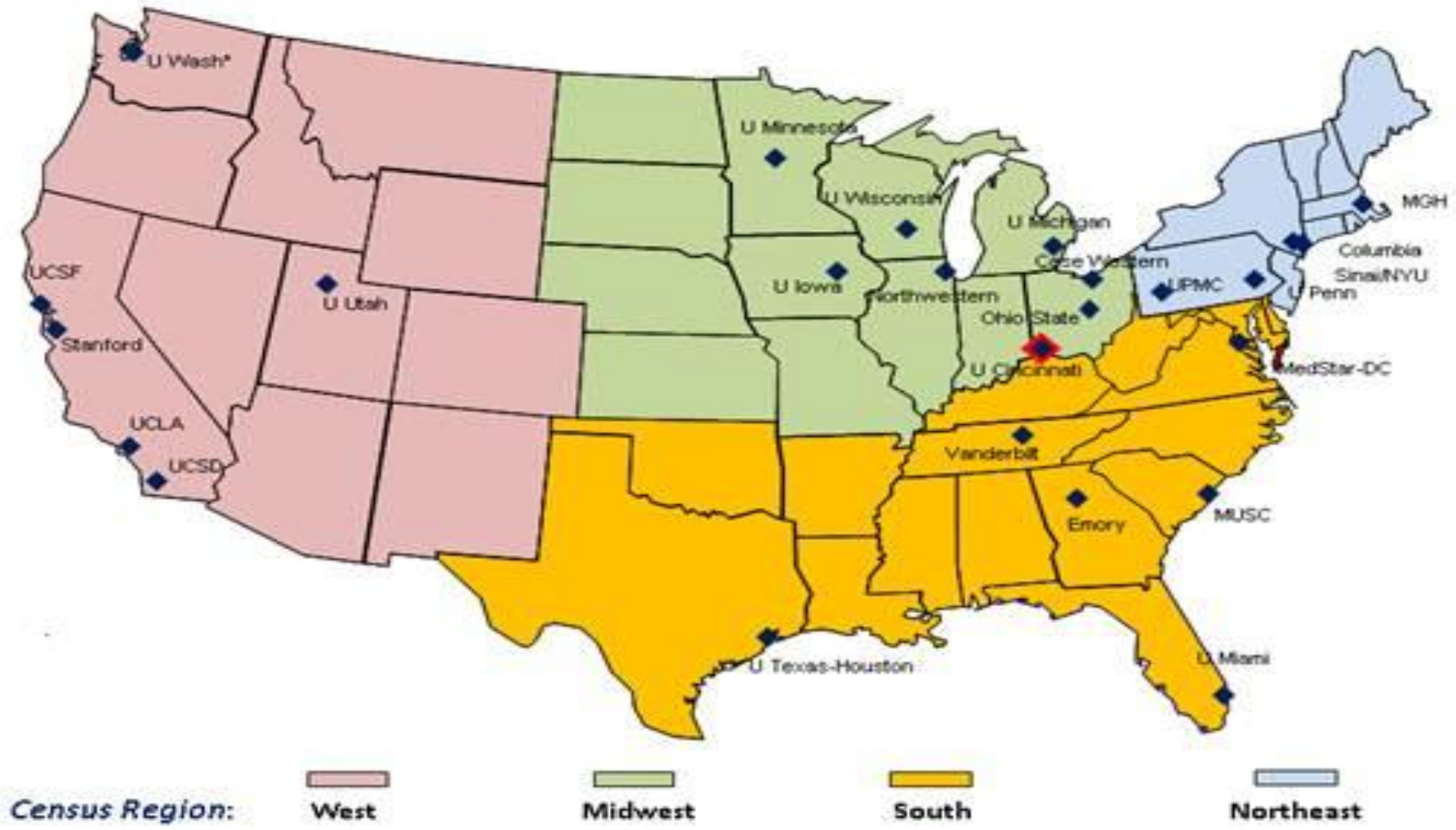
- **NIH funded stroke trials network – began October 2013**

- **Regional Coordinating Centers**
  - 25 in the US, >200 hospitals
  - Serve as both infrastructure and pipeline for new trials

- **1 National Coordinating Center** (Univ of Cincinnati)
- **1 National Data Management Center** (Medical University of S. Carolina)

- **Objective-** ***Reduce burden of stroke***
  - Increasing the efficiency of developing, promoting, and conducting high-quality, multi-site clinical trials focused on key interventions in stroke ***prevention, treatment and recovery***

National and Regional Coordinating Centers



NIH StrokeNet

Prevention Treatment Recovery

Objectives of NIH StrokeNet

- Increase trial efficiency
  - Central IRB, Master Trial Agreement
  - Facilitate patient recruitment and retention
- Balanced, prioritized set of early phase 2 and 3 trials in prevention, treatment and recovery
- Stable infrastructure to enable improved team research among different subspecialties
- Improved ability to work in public-private partnerships with non-profits and industry

NIH StrokeNet
Prevention Treatment Recovery

Grant Proposals to NIH StrokeNet

- Primary focus is clinical trials
- Biomarker and clinical validation studies:
  - Possible …
  - But must be the type of study that would produce a validated maker that could be immediately used in a phase 2 trial
  - Investigational or discovery type studies of biomarkers will not be allowed at this time.
- Biomarkers that measure clinical effects in trials and therapeutic studies are welcome (could include genetic markers)
- Purely observational epidemiologic / genetic studies do not fit into the current, expected portfolio

NIH StrokeNet
Prevention Treatment Recovery

Proposal Discussion Format

- Every proposal is available as a paper copy
- Each presenter will have 10 minutes to present succinctly the overall grant idea
  - 7 minutes
  - 3 minutes for questions
- Following the four proposals, 20 to 25 minutes of break out sessions to develop the idea and **action items**
- Last part of the session will summarize progress and action items by each presenter.