CHDI

Accelerating therapeutic development for Huntington's disease

HDClarity: Rationale, vision and logistics

HDClarity

Beth Borowsky

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CHDI

What is HDClarity?

A multi-site cerebrospinal fluid collection initiative to facilitate therapeutic development for Huntington's disease

HDClarity

Need for a large CSF collection from well-characterized HD volunteers

CSF is an accessible body fluid that may facilitate

- Our understanding of Huntington's pathophysiology
  - Exploration of potential targets for intervention
- Identification and development of biomarkers
  - Pharmacodynamic
  - Efficacy
  - Disease State or Progression
- Such biomarkers are needed to advance and accelerate upcoming clinical trials

Need for a large CSF collection from well-characterized HD volunteers

- Existing collections limited
  - Cohort sizes are too small to power many studies
  - Need new collections to replicate findings
  - Samples are being depleted rapidly
  - Disease state coverage, matching controls
  - No repeat or longitudinal samples
- Existing collections not as carefully qualified
  - Medication use not restricted
  - Samples not evaluated for blood contamination

CHDI decided to facilitate the creation of a CSF sample repository from a large, balanced, well-characterized cohort

CHDI's vision for the collection and use of samples

- Collection:
  - Engage highly motivated Investigators to participate
  - Standardized, state of the art procedures
    - Minimize headache and other adverse events
    - Maximize likelihood of repeat customers
    - Minimize blood contamination; establish assays to quantify
    - Provide standardized collection kits
  - Be both inclusive and restrictive
    - Including full disease stage range
    - Allow most medications, but note usage and include medication-free sub-cohorts
  - Be powered! N=100 per arm

CHDI's vision for the collection and use of samples

- Sample Storage:
  - Centralized storage at a biorepository: BioRep
- Clinical Data Storage:
  - Clinical data stored in Enroll-HD database
- Analyses:
  - QC performed in batches at central labs
  - Other experimental analyses performed using rigorous protocols, on properly powered cohorts
  - CHDI will direct the transfer of samples
  - "CSF Consortium" will provide scientific oversight into the use of samples and analysis of data

Overall structure of study

- CHDI: Funding Agency
  - Science Director: B. Borowsky
  - Team of project managers
  - Manage BioRep, Enroll-HD, 2MT, Site contracts and payments

- UCL: Study Sponsor and Managing Research Organization
  - Chief Investigator: E. Wild
  - Central Coordination: G. Owen, S. Brown

- CSF Consortium: CHDI, CI and interested site PIs

- The first Enroll-HD Platform Study
  - Select Enroll-HD sites in North America and Europe
  - Fully integrated with the Enroll-HD EDC system and database
  - EDC-triggered site payments via Greenphire
  - On site monitoring by Enroll monitors
  - Site agreements and ICFs similar language

What does this structure mean to sites?

- Primary site contact is Central Coordination at UCL
- UCL will
  - Provide study documents and training materials
  - Liaise with sites on site agreements, ICFs
  - Train and approve sites
  - Remotely monitor
  - Review payment requests
- CHDI will
  - Sign and negotiate site agreements
  - Approve ICF modifications
  - Approve and authorize payments
- BioRep will
  - Send you collection kits
  - Receive your collected samples

This is a new structure for CHDI: concept of an MRO and using Enroll-HD as a platform study

So be patient….

CSF Consortium

- "CSF Consortium" will provide scientific oversight into the use of samples and analysis of data
  - CHDI, CI and PIs interested in research uses of CSF
  - First meeting with interested members later this year
  - Proposed experiments will be evaluated and strengthened along several dimensions:
    - Biologic principle being evaluated
    - Quality and suitability of assays
    - Power and statistical analysis plan
- The current prioritized analyses include:
  - Further evaluation of HTT assays, including from repeat sampling
  - Further evaluation of kynurenine pathway metabolites
  - Proteomic evaluation of previous "hot list" of proteins altered in the disease

Thanks to the entire team!

CHDI:

Amanda Klock
Cristina Sampaio
Bernhard Landwehrmeyer
Sherry Lifer
Dipinder Kaur
Eileen Neacy
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Joe Giuliano
Cheryl Knipe

UCL:

Ed Wild
Gail Owen
Stef Brown

Extended Enroll Team:

Olivia Handley
Torsten Illmann
Jürgen Nagler-Ihlein

Key Investigators:

Jan Lewerenz
Blair Leavitt

BioRep:

Stefania Michelini
Paola Casalin