HDSA RESEARCH PARTNERSHIP

Research Cycle

- Patients and Families
- Description of Phenotype
- Identification of Underlying Genes
- Characterizing Mechanism from Cause to Phenotype
- Diagnostics, Management & Therapy

Rx
Pathogenesis and clinical disease

Steps in the Presymptomatic Disease Process

Factors contributing to disease susceptibility

Steps in Disease Progression

Overt Symptom

HD CAG
Trigger
POLYQ-
HUNTINGTIN

Steps in the Presymptomatic Disease Process

Steps in Disease Progression

Overt Symptom
HDSA Research Pipeline to Treatments

Discovery Research:
- Flexibility
- Variety of strategies

Applied Research:
- Identify possible treatment
- Optimize possible treatment

Preclinical research:
- Preclinical testing
- ‘model systems’

Clinical Trial Research:
- Phase 1 Clinical Trial
- Phase 2 Clinical Trial
- Phase 3 Clinical Trial

FDA approved drug

Cost scale

Target
Change due to the HD gene

HDSA Research Pipeline to Treatments
Discovery
Start with the right ore

Grants and Fellowships
Coalition
Lifeline of a brain cell with the HD mutation

Trigger mechanism
Changes that disable the brain cell
Changes that kill the brain cell

Focus of HDSA Research
Grants and Fellowships

NEW IDEAS, NEW (DEDICATED) HD RESEARCHERS

• Vital flexible funding to seed new HD research areas and to support young researchers at the start of their careers
• Grant $50,000 for one year
• Fellowship $40,000 per year (2 years)

Huntingtin protein

Model systems
Grant Recipient

Dr. Ruth Luthi-Carter, Ph.D.
Swiss Federal Institute of Technology
Lausanne Switzerland
Molecular changes in human HD brain

Fellowship Recipients

Dr. Browen Martin, Ph.D.
National Institutes of Health (Bethesda MD)
Molecules that respond to sugar

Dr. Jean Savare, Ph.D.
J. David Gladstone Institutes (San Francisco CA)
Finding all huntingtin partners in yeast

Dr. Austin Milnerwood, Ph.D. (with HSC)
University British Columbia
Brain cell function in YAC128 HD gene mice
Coalition

16 expert international laboratories committed to cooperative HD research, self-organized into teams aimed at pressing issues in HD research, closely aligned with HSC, CHDI, NIH in order to capitalize quickly on the research findings.

Gillian Bates, Ph.D.
Flint Beal, M.D.
David Borchelt, Ph.D.
Elena Cattaneo, Ph.D.
Jang-Ho Cha, M.D., Ph.D.
Marian Difiglia, Ph.D.
Robert Freedlander, M.D.
James Gusella, Ph.D.

Michael Hayden, M.D., Ph.D.
Steven Hersch, M.D., Ph.D.
Ron Kopito, Ph.D.
Marcy MacDonald, Ph.D.
Richard Morimoto, Ph.D.
Christopher Ross, M.D., Ph.D.
Leslie Thompson, Ph.D.
Erich Wanker, Ph.D.
Huntingtin - a cargo barge

Huntingtin Function
Mitochondria & Energy Metabolism
Huntingtin Proteolysis and Posttranslational Modification
Folding, Aggregation and Clearance of Mutant Huntingtin

- Full-length mutant huntingtin
- Mutant huntingtin fragment
- Aggregate being removed by cell
- Huntingtin fragment aggregate

*Folding, Aggregation and Clearance of Mutant Huntingtin*
Transcription
Mutant huntingtin

Lifeline of a brain cell with the HD mutation

Trigger mechanism

Changes that may disable the brain cell

Changes related to death of the brain cell

Death