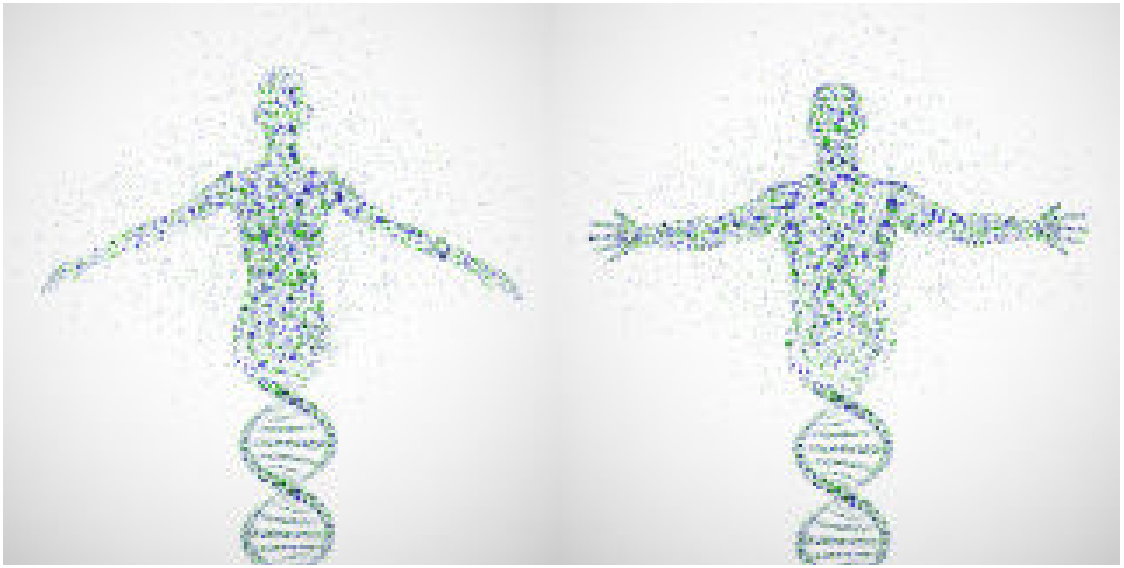
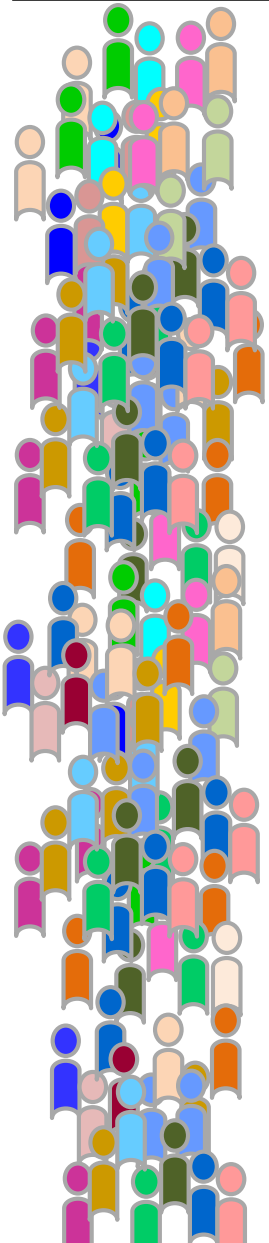
Towards precision medicine for people with intellectual and developmental disabilities (IDD)

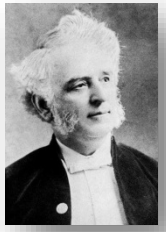


1. People with IDD and their families have led the way toward precision medicine.
2. Now, continued help is needed to reach this goal.

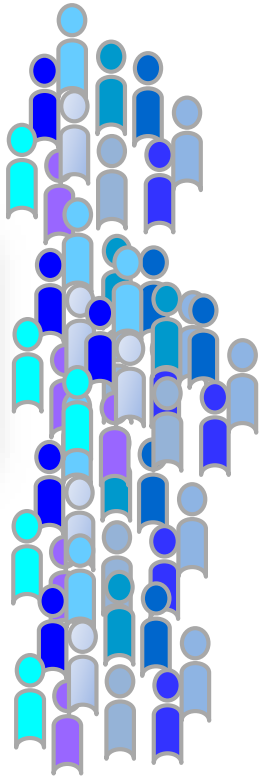
People with IDD

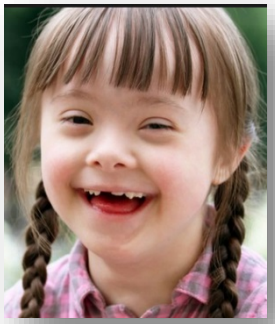


…with short stature and specific facial traits

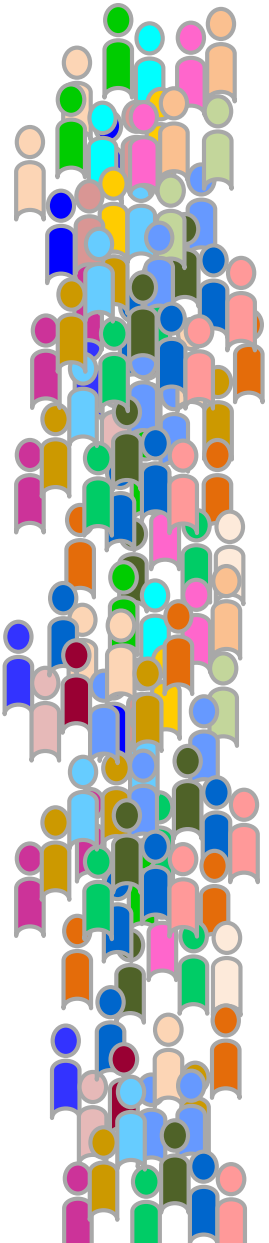


1866





People with IDD



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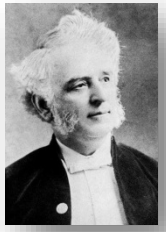

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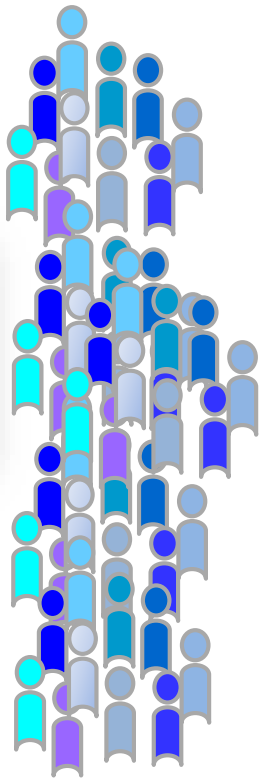
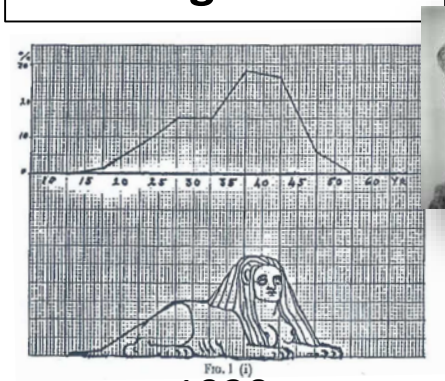
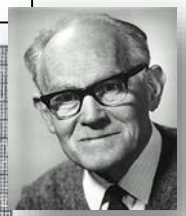
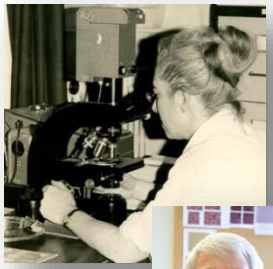


Etiologic–based diagnosis

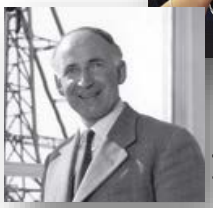




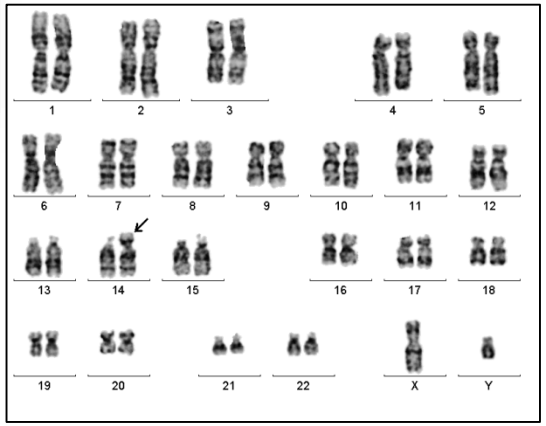
1930s



1959



1960



People with IDD

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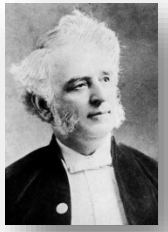


1866

Etiologic–based diagnosis

Full trisomy 21: 95%

Mosaic trisomy 21: 1%

Translocation : 4%

Mechanistic–based diagnosis

Error in egg

Error in sperm

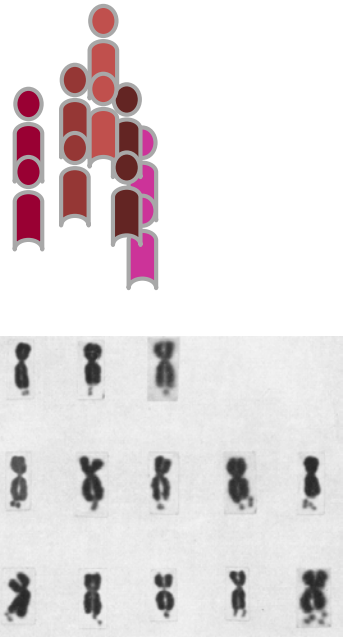
People with IDD

…with X-linked inheritance pattern and no obvious clinical traits

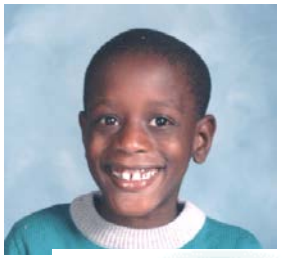
Lerke 1969

Turner 1970s

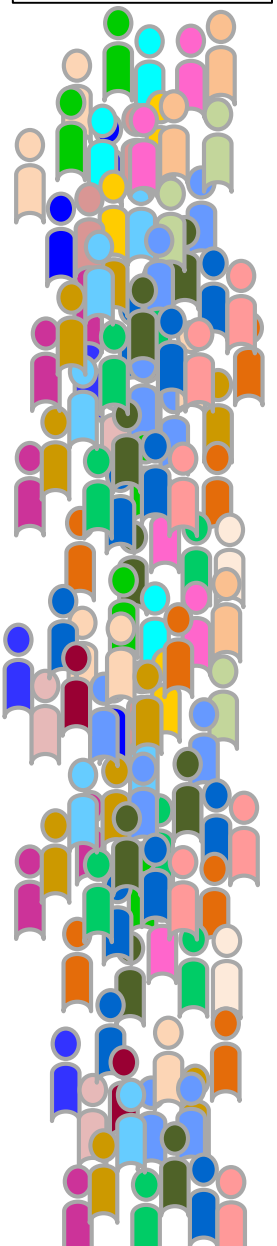
…with X-linked inheritance pattern, macro-orchidism, cytogenetic marker X



Lubs 1969;
Sutherland 1977



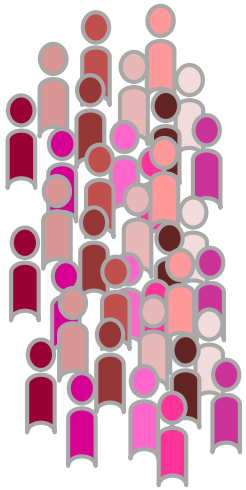
People with IDD



…with X-linked inheritance pattern and no obvious clinical traits

Lerke 1969

Turner 1970s



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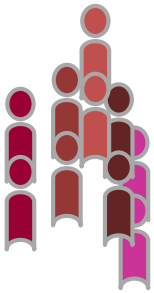
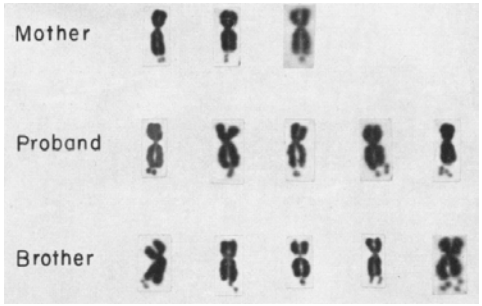
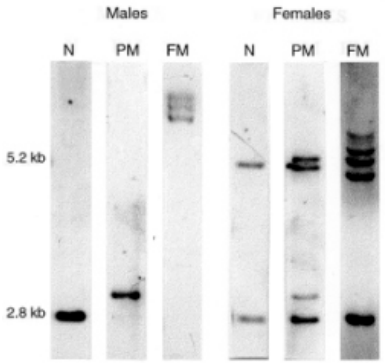




Lubs 1969;
Sutherland 1977

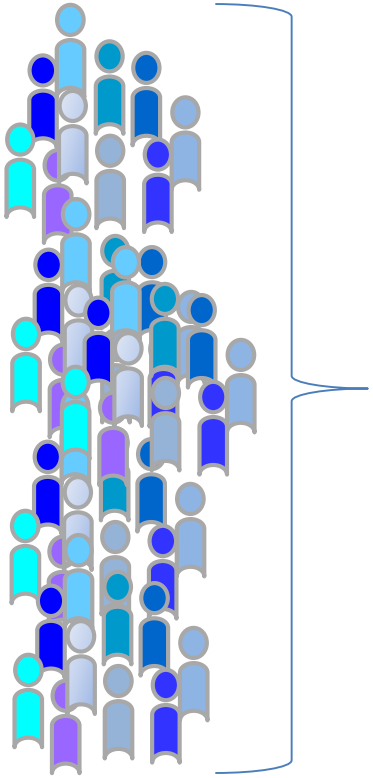
Etiologic-based: CGG expanded repeat disorder—fragile X syndrome



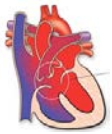
Ostra, Warren, Nelson 1991

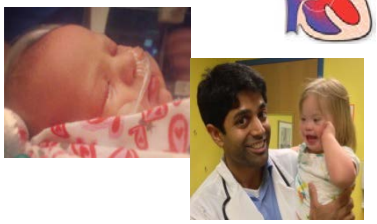
But what now? Are we done?
Have we reached the goal of precision medicine?

Down syndrome



Birth defects



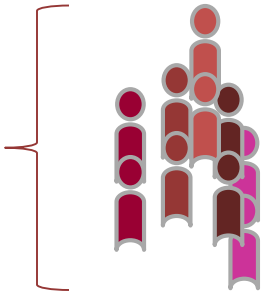


Cognition and behavior

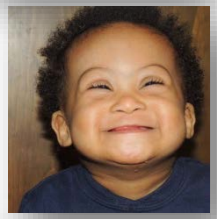
Seizures
Language
Autism

Drug response

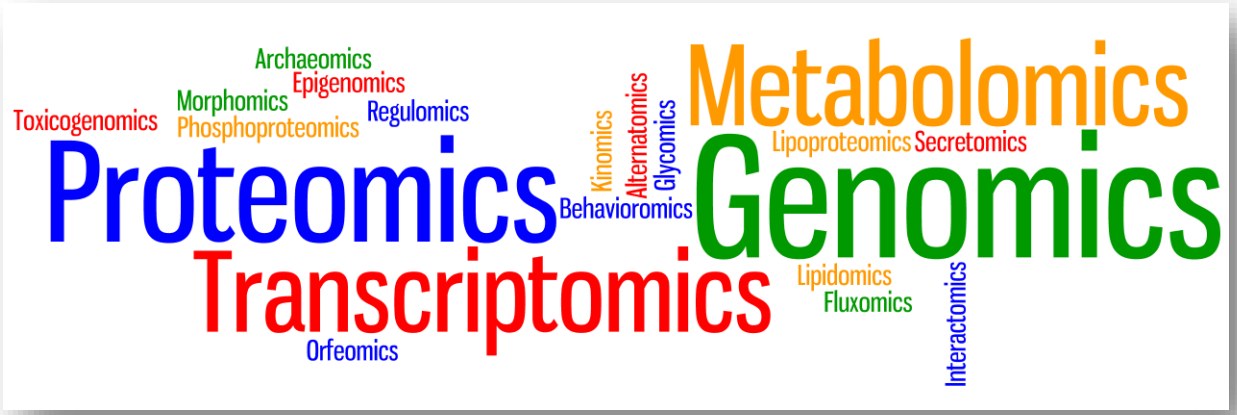
Fragile X syndrome

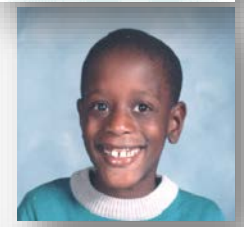


Alzheimer disease and aging



What contributes the variation in clinical outcomes?



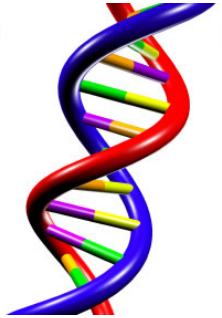


One Strategy:

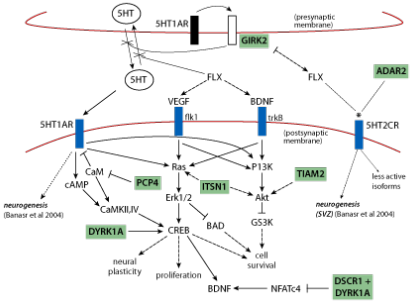
Compare the “extremes” of a specific clinical outcome among those with the same genetic disorder

Environmental factors

Genetic factors



Identify affected biological pathways



Develop interventions that target imbalance

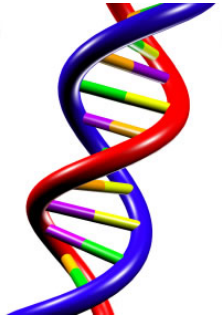
Baltimore
Portland
Tucson
Atlanta
Davis
DC

DS cognition project

Exploring cognitive variation in people with Down syndrome

Environmental factors

Genetic factors



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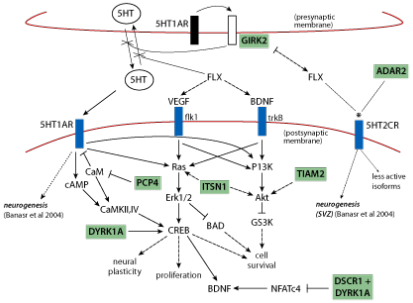
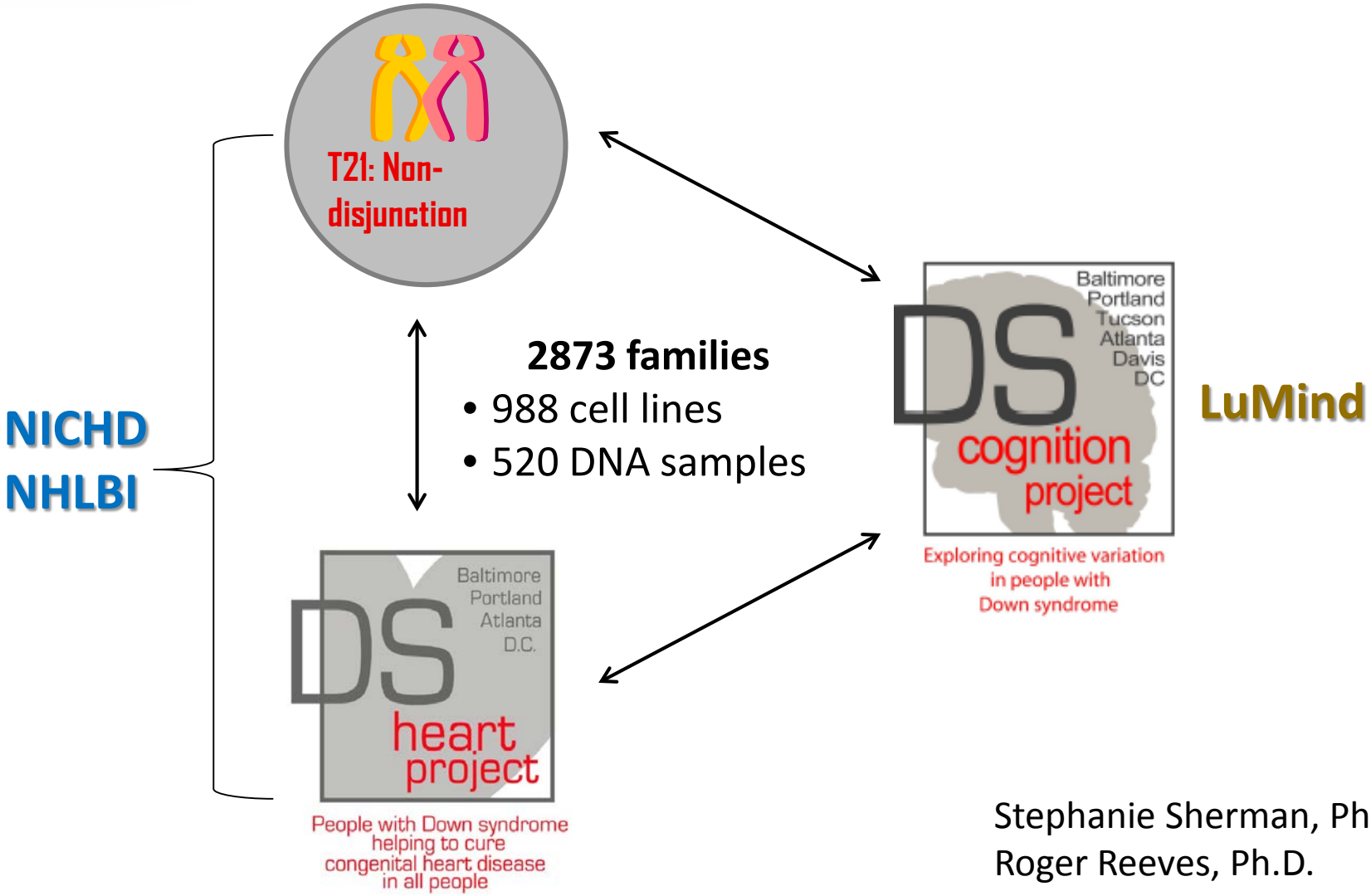


Develop interventions that target imbalance

Setting the foundation for DS360:

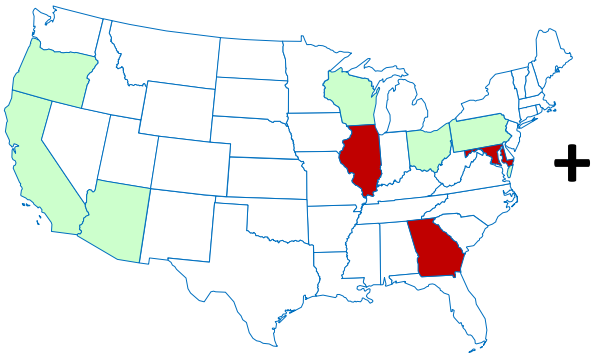
A Genotype/Phenotype project to move towards precision medicine for people with Down syndrome



Stephanie Sherman, Ph.D.
Roger Reeves, Ph.D.

Examples of contributions from DS360 to the research community

Clinical research ready sites



\+ National Down Syndrome Society

Outcome measures for clinical trials

- Test-retest studies (Edgin et al. 2017)
- T21RS Clinical and Developmental Committee:
  - Creation of a core battery
  - Data harmonization

Resource for other studies

- Genomic data to DS-cancer studies
- Cognitive data to examine adverse effects of cancer treatment
- Cell lines to examine genomic stability

Potential avenues of expansion of DS360

- **Merging with existing cohorts—examples:**
  - LonDownS (Strydom)
  - Univ of Geneva (Antanorakis)
  - Human Trisome Project (Espinosa)
  - LeJeune Foundation
  - …
- **Using existing infrastructures and services:**
  - NIH DS-Connect®
  - NHLBI Pediatric Cardiac Genomics Consortium (PCGC)
  - NIH-supported Clinical and Translational Science Institutes
- **Working with T21RS to create an international consortium**

Launched Sept. 6, 2013

DS-Connect® is a powerful resource where people with Down syndrome and their families can:

- Connect with researchers and health care providers.
- Express interest in participating in certain clinical studies on Down Syndrome, including studies of new medications and other treatments.
- Take confidential health-related surveys. These surveys are aimed at better understanding of the health of people with Down Syndrome across their lifespans.

Información en español

How do I turn on subtitles/captions and specify their language?

Registration Goal

Goal: 10000
Current: 3734

Download the Flyer

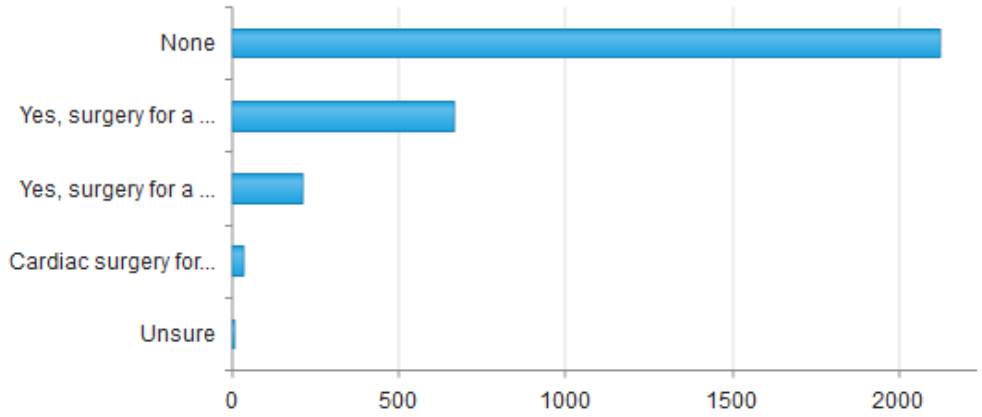
DS-Connect®: Facilitate Clinical Research

Explore and analyze de-identified natural history data

- Initial Health Questionnaire
- Sleep Questionnaire
- Heart Questionnaire
- Prenatal and Birth History
- Skeletal Questionnaire
- Gastrointestinal Questionnaire
- Development Questionnaire
- Adulthood Questionnaire
- Diabetes Questionnaire
- Celiac Disease Questionnaire
- Thyroid Questionnaire
- Men's Health Questionnaire
- Women's Health Questionnaire
- Leukemia Questionnaire

Has the participant ever had any cardiac or heart surgery? (Select all that apply.)

Answer	Number of Responses
None	2121
Yes, surgery for a congenital heart defect in the first year of life	667
Yes, surgery for a congenital heart defect after the first year of life	213
Cardiac surgery for other reason later in life	36
Unsure	8



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- Thyroid Questionnaire
- Men's Health Questionnaire
- Women's Health Questionnaire
- Leukemia Questionnaire

Sujata Bardhan, PhD

Melissa Parisi, MD, PhD

Advise and help recruit for approved studies

Sleep issues
Feeding issues
Thyroid screening
Alzheimer dx and aging (ABC-DS)
Obesity and diabetes
Motor and balance
Gynecological issues
Language
Autism spectrum disorder
Transition to adult care service
Wayfinding
Use of nutritional supplements
Opinions of medical research
…

Potential avenues of expansion of DS360

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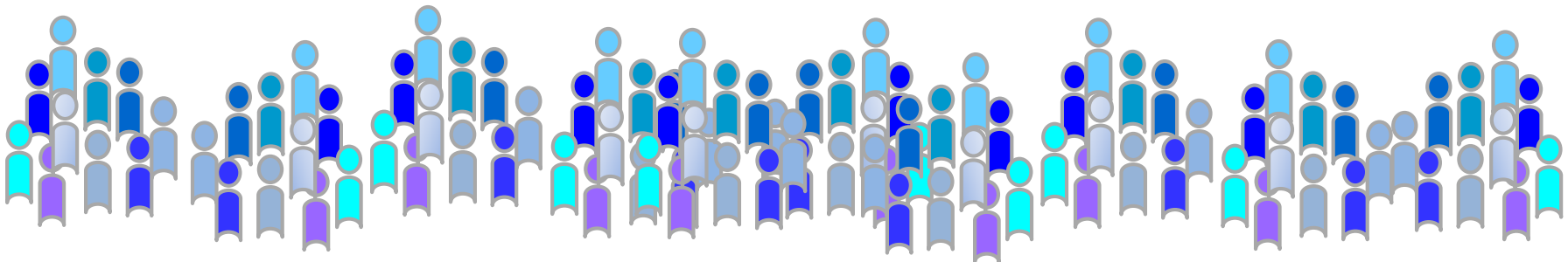
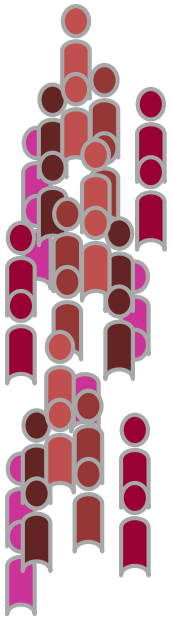


Fragile X syndrome



National Institutes of Health
Turning Discovery Into Health

Centers for Collaborative Research in Fragile X

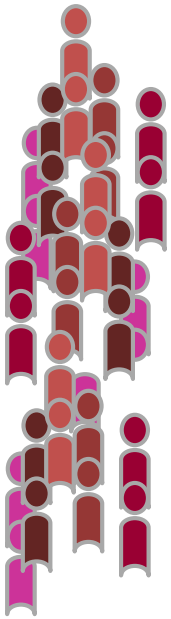
Kimberly M. Huber, Ph.D., University of Texas Southwestern Medical Center

Joel D. Richter, Ph.D., University of Massachusetts Medical School

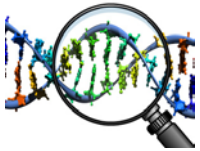
Stephen T. Warren, Ph.D., Emory University

Centers for Collaborative Research in Fragile X

Fragile X syndrome



FX-MOD: Modifiers of Fragile X-Associated Disorders



…tracking down genes that interact with *FMR1*

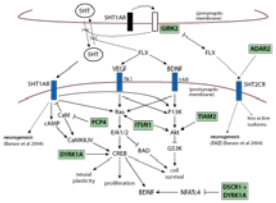
People with FXS

vs.

No seizures **Seizures**

Environmental factors ⟷ Genetic factors

Identify affected biological pathways



Develop interventions that target imbalance

Fragile X syndrome

NATIONAL **FRAGILE X** FOUNDATION

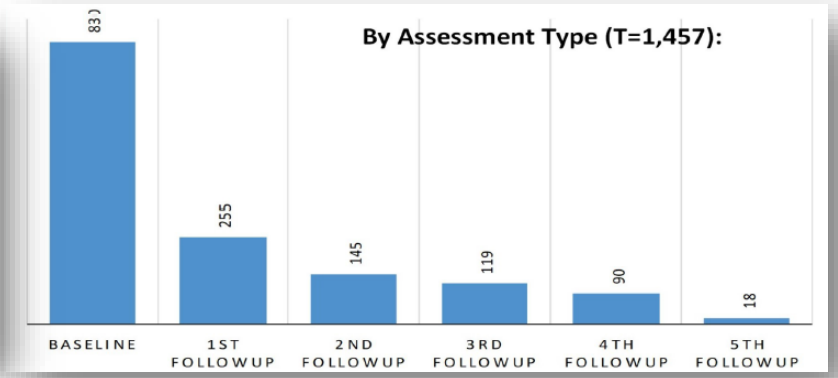
FRAGILE X CLINICAL & RESEARCH CONSORTIUM

With support from Centers for Disease Control and Prevention

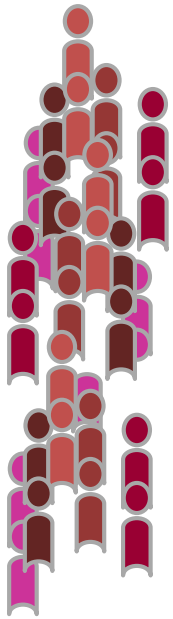
FORWARD

FRAGILE X ONLINE REGISTRY WITH ACCESSIBLE RESEARCH DATABASE

FORWARDFX.org



Fragile X syndrome



NATIONAL **FRAGILE X** FOUNDATION

FRAGILE X CLINICAL & RESEARCH CONSORTIUM

Collaborative Biomarker Research Project

Towards precision medicine for people with intellectual and developmental disabilities (IDD)