

A decorative border with ornate corner pieces surrounds the slide. The background features a faint, stylized DNA double helix structure composed of blue dots and lines, positioned behind the main title text.

# **Genetic/Phenotypic Data Repositories & Their Applications in Research**

**Olivia J. Veatch, PhD**  
**Incorporating Genetics into Health  
Outcomes Research (Autism)**

**PCORI Workshop**

**April 7, 2017**



# Outline

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- **Challenges and Opportunities in Autism Genetics Research**
- **Approaches to Precision Medicine Using Big Data**
  - **Current Research Using Ongoing Autism Initiatives**
  - **Current Research Using Ongoing Initiatives in Electronic Health Record and Biorepositories**
- **Engaging Parents/Caregivers in Genetic Research Projects**
- **How Patient-Centered Outcomes Research Projects Can Help Enact Changes in Health Care**

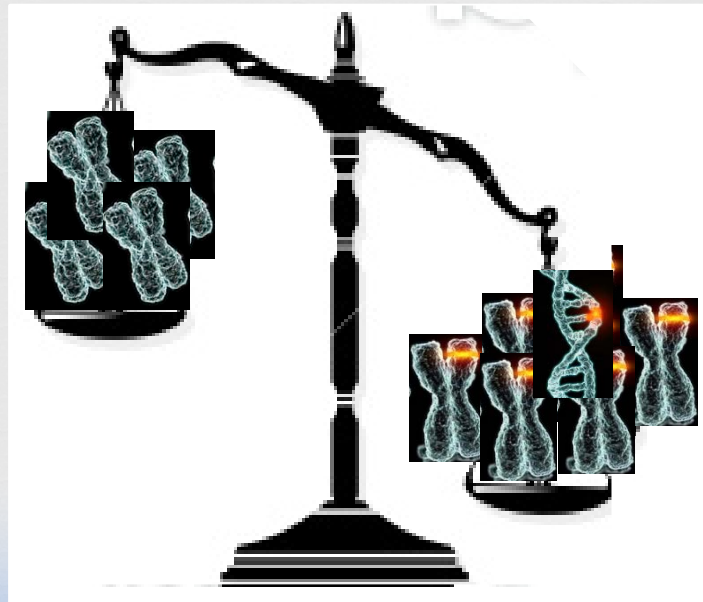


# Autism Genetics:

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## Inherited Hypothesis

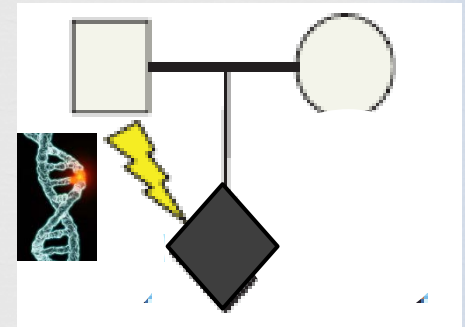
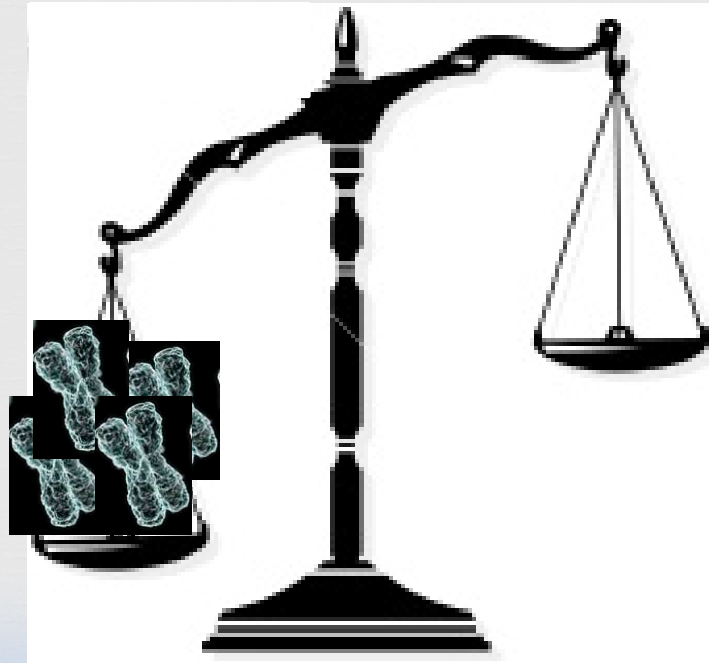
- Mom and Dad both have some genetic differences
- Genetic changes from both parents are passed on to the child
- Autism occurs because many genes are not working properly
- Families with more than one affected child



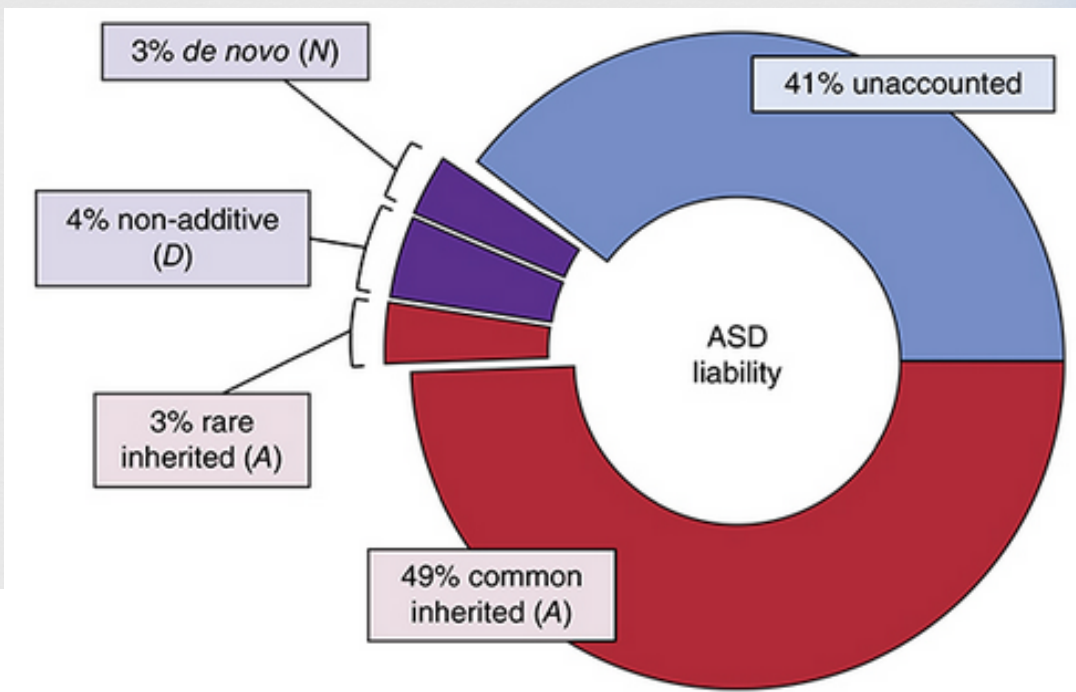


# Autism Genetics: Spontaneous

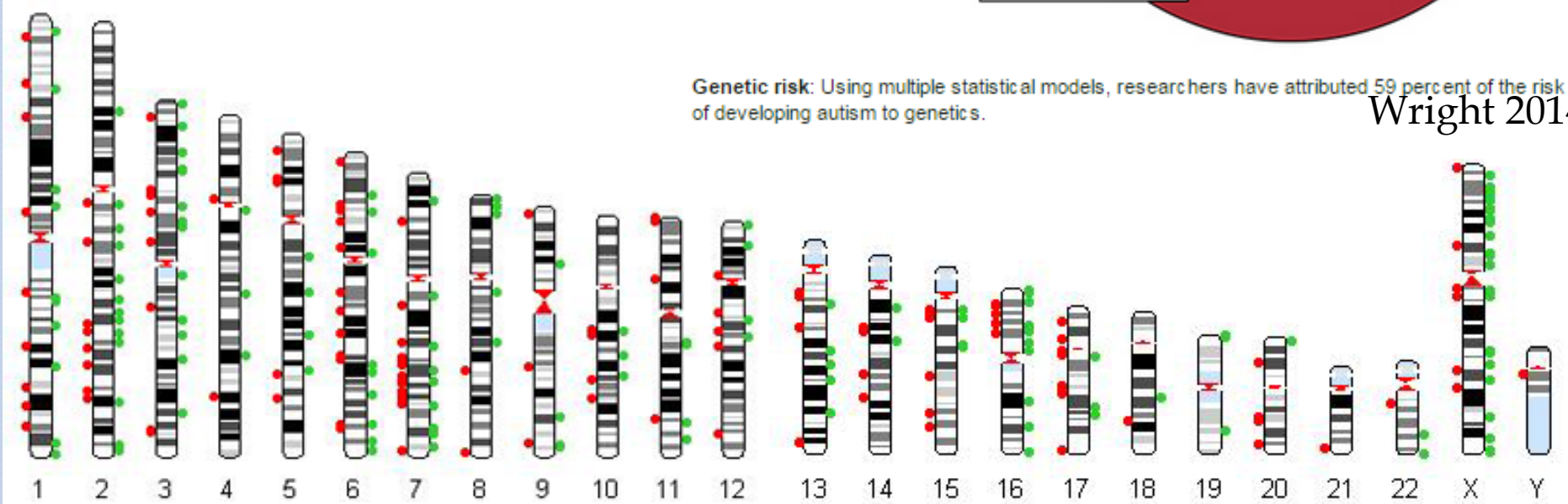
- Autism occurs when one genetic change happens in Mom's egg or Dad's sperm
- Families with only one affected child



# Autism Genetic Landscape



Genetic risk: Using multiple statistical models, researchers have attributed 59 percent of the risk of developing autism to genetics. Wright 2014



**COGNITIVE  
COMORBIDITIES**

**BEHAVIORAL  
COMORBIDITIES**

**GENETICS**

# DSM-5 Diagnostic Criteria

Core autism spectrum disorder symptoms

Impaired social communication/interaction (3/3):

- Social reciprocity
- Nonverbal communication
- Relationships

Restricted/repetitive behavior (2/4):

- Repetitive speech/behavior
- Insistence on sameness
- Restricted interests
- Sensory abnormalities

Language impairment

Intellectual disability

Simple genetic disorders: fragile X, TS, Rett, etc.

Copy number variants: 16p11-p12, 15q11-q13, 22q13, etc.

Rare variants: *NRXN1*, *NLGN4*, *SHANK3*, *SERT*, etc.

Hyperactivity/impulsivity

Agitation/aggression

Anxiety

Severe constipation

Seizure disorder

**MEDICAL  
COMORBIDITIES**

Abnormal EEG

Developmental macrocephaly

Neuroimaging: altered brain region size

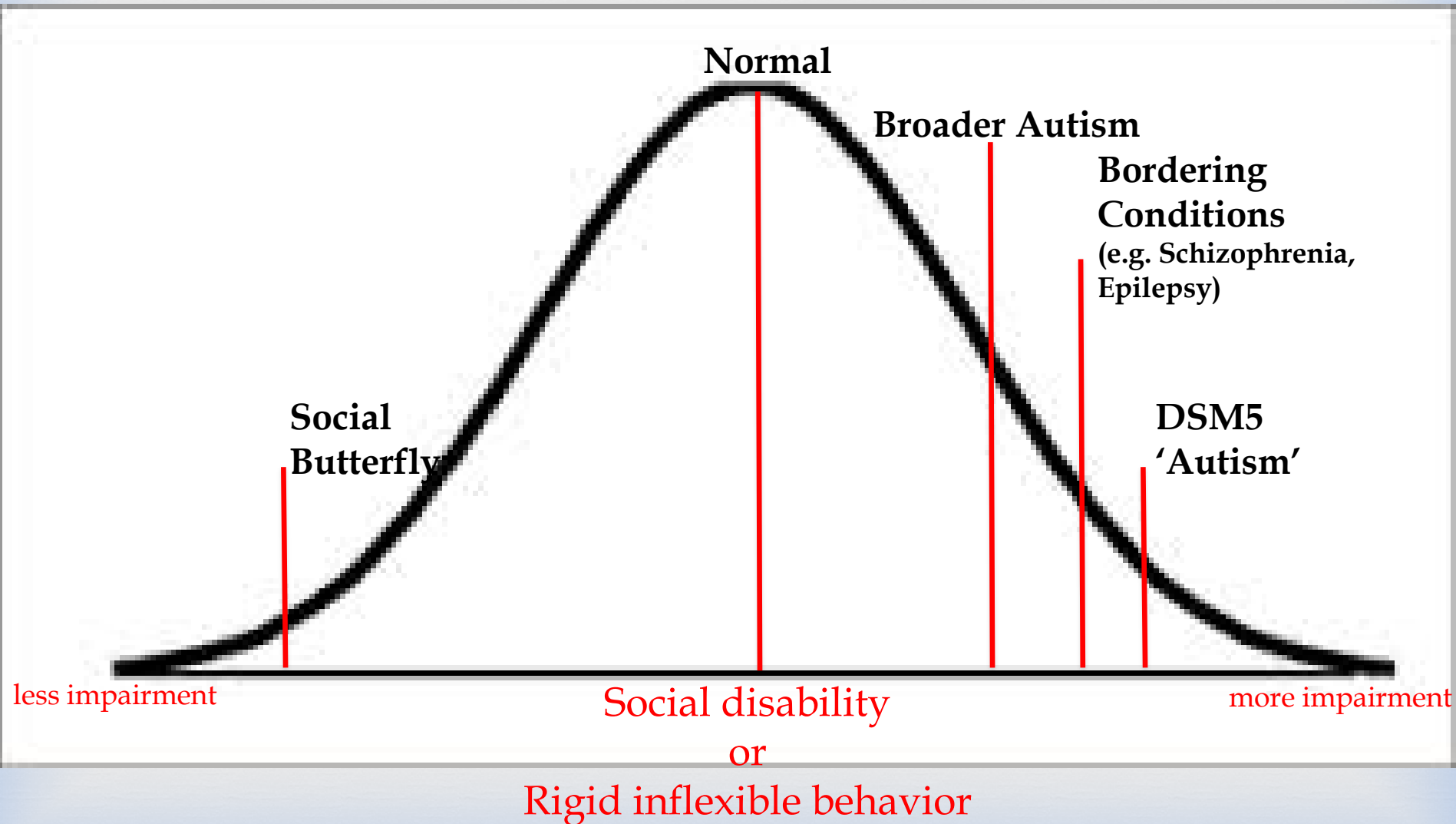
**BIOMARKERS**

Hyper-serotonemia

Altered immune/mitochondrial indices



# Beyond the Narrow, All-Encompassing Definition







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# Autism Speaks/MSSNG

- Clinical data and sequencing of DNA from >10,000 families for research
- Autism Treatment Network-Goal to improve treatment for autism

[www.autismspeaks.org/science/resources-programs/autism-treatment-network](http://www.autismspeaks.org/science/resources-programs/autism-treatment-network)

## Guide for Managing Constipation in Children:



A Tool Kit for Parents



These materials are the product of on-going activities of the Autism Speaks Autism Treatment Network, a funded program of Autism Speaks. It is supported in part by cooperative agreement U43 MC 11054, Autism Intervention Research Network on Physical Health (AIR-P Network) from the Maternal and Child Health Bureau (Combating Autism Act of 2006, as amended by the Combating Autism Reauthorization Act of 2011), Health Resources and Services Administration, Department of Health and Human Service to the Massachusetts General Hospital.

## Strategies to Improve Sleep in Children with Autism Spectrum Disorders



A Parent's Guide



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## An Introduction to Behavioral Health Treatments



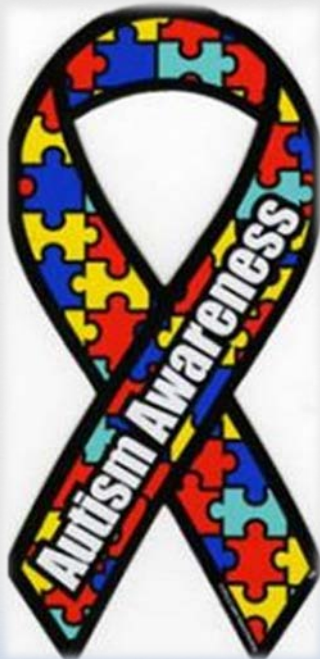
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# Understanding the Connection Between Autism and Sleep



- **Insomnia is very common in children with autism (50-80%)**
- **Sleep is important for proper brain development, when children with autism do not sleep this may have negative long-term effects on brain function**
- **Lack of sleep worsens autism-related symptoms during the day**
- **Genetic information may help to inform treatment for insomnia in children with autism**

# Simons Simplex Collection

- Extensive medical histories and whole-exome sequence data collected in families with only one affected child
- Sleep duration previously found to be a reliable parent-reported insomnia trait (Veatch et al., Behav Sleep Med 2016)

Sleep Problems	Current	Ever
<b>Regularity and Duration</b>		
Regular bed time and wake time?	<input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> Not sure	<input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> Not sure
On average, how many hours/night?	_____ hours	_____ hours
Do you think this is enough?	<input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> Not sure	<input type="checkbox"/> No <input type="checkbox"/> Yes <input type="checkbox"/> Not sure

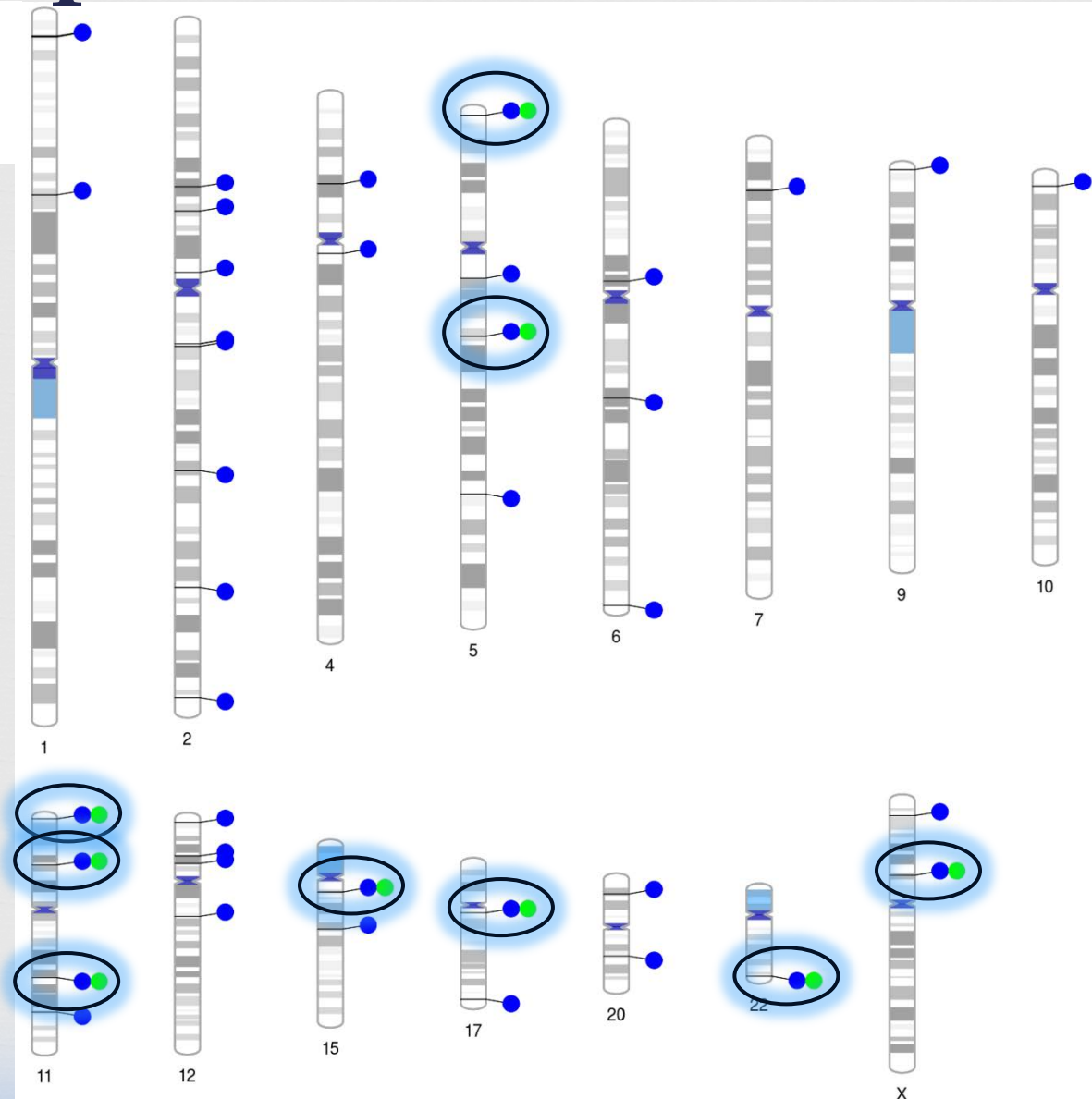
- Shorter amounts of sleep worsen autism-related symptoms
  - Social impairment
  - Problem behaviors
  - Attention Deficit/Hyperactivity
  - IQ scores
  - Depression
  - Obsessive Compulsive Disorder



# Autism Genes Also Have Effects on Sleep: Is There a Connection?

● Insomnia

● Autism







# Outline

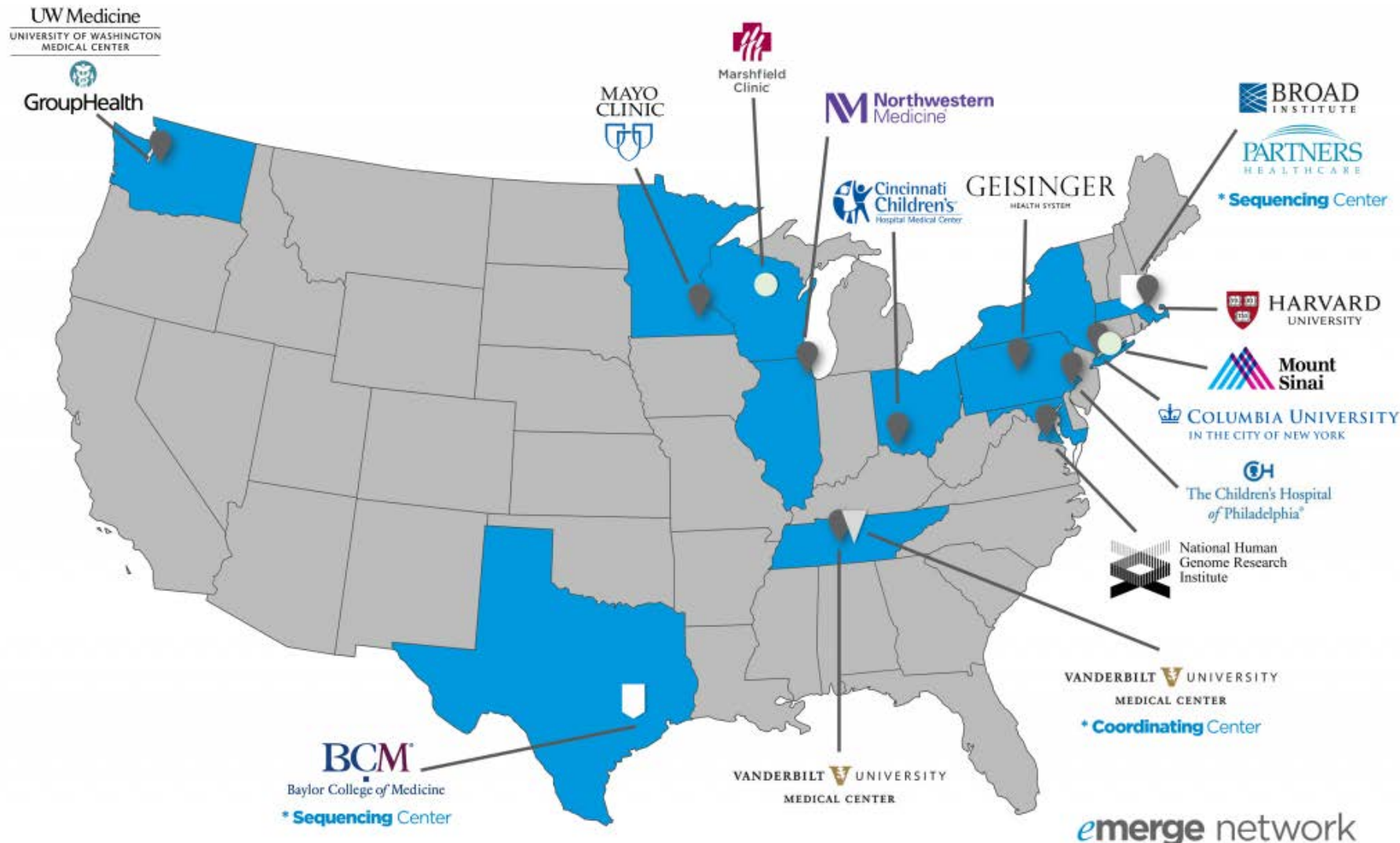
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# The eMERGE Network

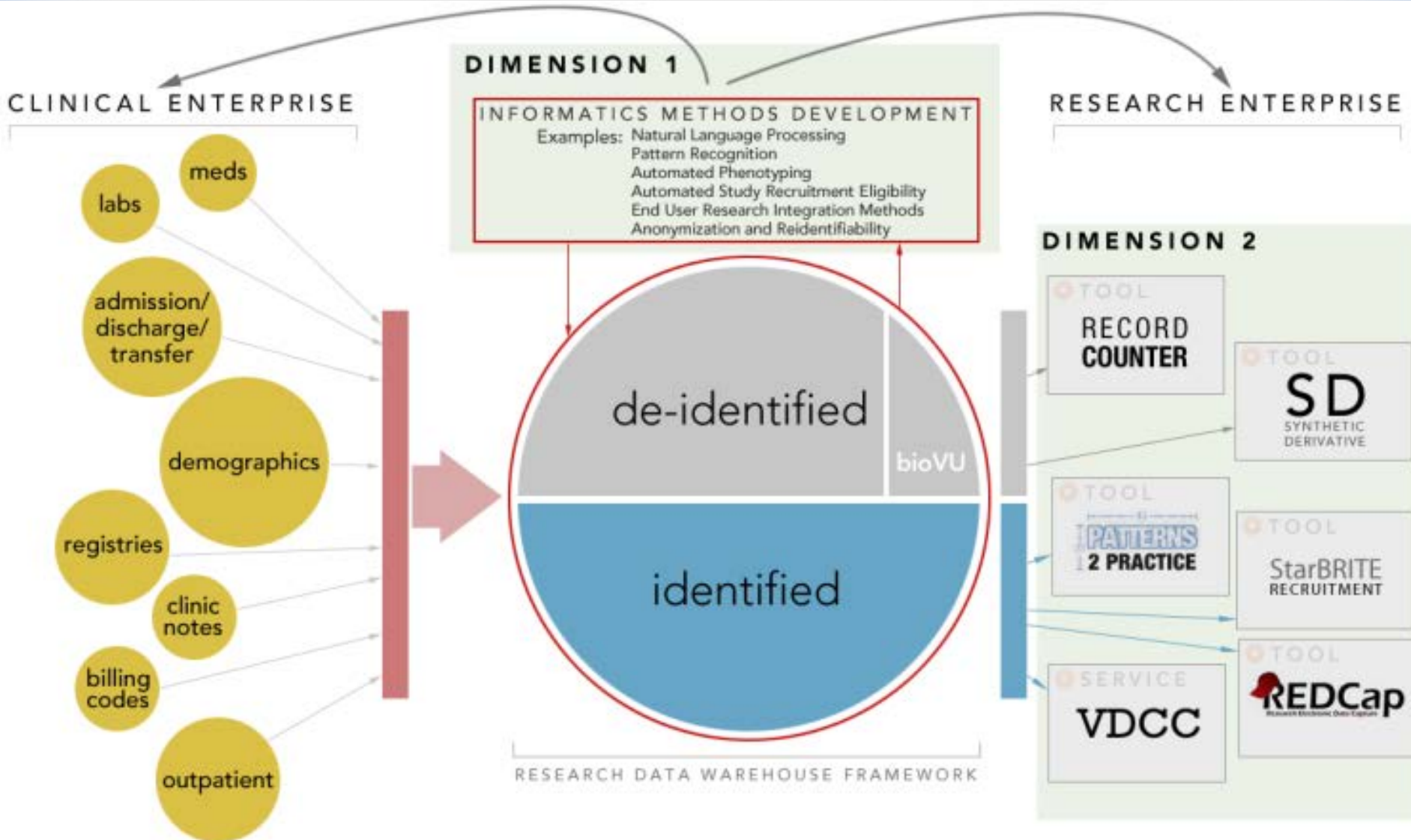
## electronic Medical Records & Genomics

*A consortium of biorepositories linked to electronic medical records data for conducting genomic studies*





# Electronic Medical Data



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# Engaging Parents/Caregivers in Genetic Research Projects

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- Provide patient portals reporting research results
- Understand incentives that are important to research participants
- Offer opportunities for emotional support and information sharing



# How Patient-Centered Outcomes Research Projects Can Help Enact Changes in Health Care

- **Helps identify:**
  - Useful health-related information for clinicians
  - Problem areas in health care access
  - Understudied health problems
- **Helps connect patients to:**
  - Medical experts in specific content areas
  - Clinical trials being conducted
  - Research that offers therapy or progress evaluations



# Acknowledgements

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- Allan I. Pack, MBChB, PhD, FRCP
- Beth A. Malow, MD, MS
- All of the families who generously participated in these projects
- Sarah H. Elsea, PhD
- Diane Fawkes
- Kim Frank
- Suzanne E. Goldman, APRN, PhD
- Carl H. Johnson, PhD
- Terry Katz, PhD
- Brendan Keenan, MS
- Roberta Leu, MD
- Alvin Loh, MD
- Melissa H. Potter
- Ann Reynolds, MD
- James S. Sutcliffe, PhD
- Lily Wang, PhD
- Zachary E. Warren, PhD
- Shelly K. Weiss, MD
- Deborah Wofford
- Amanda Wyatt
- Funding:
- NIH T32HL07713
- Autism Intervention Research Network on Physical Health
- Autism Speaks Autism Treatment Network
- Simon's Foundation
- Burry Chair in Cognitive Development