What Causes Autism?

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Goals:
• To identify genes and biological pathways or functions for targeted therapies
• To identify diagnostic biomarkers of ASD
• To develop a "systems level" understanding of the pathobiology of ASD

Experimental strategy: Grouping individuals according to severity of behavioral symptoms ⇒ Subtype-dependent diagnosis & treatment

- Deficiency in RORA impacts many autism susceptibility genes

Subtype-dependent genetic differences

Subtype-dependent gene expression

Intrinsic and extrinsic environmental factors (e.g., hormones, pesticides)

Genetics (Hardware)
- Mutations
- Copy number variants
- Chromosomal abnormalities

Epigenetics (Software)
- DNA methylation
- MicroRNA expression
- Histone modification
- Chromatin remodeling

Gene expression profile: level of gene activity

ASD phenotypes: brain circuitry, behaviors and symptoms

An integrated genomics approach to autism spectrum disorders

A hierarchical view of the multiple factors that cause or affect risk for autism. In this view, the components of each level can influence those shown below.

Effects of male and female hormones on RORA explain increased testosterone levels and why males may be more susceptible to ASD.
Publications

Research articles
- Autism Research
- Molecular Autism
- FASEB Journal
- Genome Medicine
- PLoS ONE
- BMC Genomics
- North American J. of Medicine and Science

Reviews/perspective/editorial/editorial/commentary
- Future Neurology
- Child Development
- Pharmacogenomics
- Disease Markers
- NeuroToxicology
- MicroRNAs in Toxicology and Medicine (book chapter)
Autism spectrum disorder (ASD) has rapidly become one of the most prevalent of the neurodevelopmental disorders affecting both children and adults. Despite the rapid rise in the number of cases reported and the high heritability associated with ASD, there is still very little understanding of its etiology and lifelong progression as well as the many factors, both intrinsic and environmental, that may increase risk for ASD. Currently, there are neither validated biomarkers for diagnostic screening nor pharmacologic therapies specific for ASD. Diagnosis is primarily based upon reports of functional and behavioral abnormalities, with medical treatment taking a mostly trial-and-error approach, since the pathology affecting most individuals with ASD is unknown. This uncertainty is in part due to the significant clinical and phenotypic heterogeneity associated with ASD. Yet, progress is being made in identifying genes, metabolic pathways, and cellular/tissue functions disrupted by autism, and there is evidence that targeted treatment of some of these genetically-defined conditions or dysfunctional pathways has led to improved outcomes for subgroups of individuals on the spectrum.

This book focuses on the emerging and expanding areas of research on ASD and their potential to lead to better diagnosis and more effective therapies. These patient-focused research areas include innovative and integrative approaches to genetic/genomic analyses and investigations of epigenetic contributions, including the role of noncoding RNAs, DNA methylation, alternative splicing, RNA editing, and faulty translation in gene regulation and expression, metabolic and immune dysfunction, co-morbidities, as well as hormonal and gene-environment interactions that may increase risk for ASD.

Within each chapter, experts review cutting-edge research as well as provide their perspective on the future of research in their respective areas, including the challenges involved and the types of studies or advances that are necessary to move the field forward to achieve predicted translational goals.

Since many of the chapters are projecting research towards novel therapeutic strategies and other practical interventions, it is anticipated that this book will be of value not only to established investigators and students engaged in autism research, but also to the general population, especially families of individuals affected by ASD and their professional caregivers.
Selected References


More at: http://www.gwumc.edu/smhs/facultydirectory/profile.cfm?empName=Valerie%20Hu&FacID=2046028605