

Discussion

What a research agenda for autism and the environment might look like?

Framework/Infrastructure

Multidisciplinary teams are essential

Epidemiologists (assessments, medical records, questionnaires, biol sampling)

- Case control (typically developing, DD, other?)
- Longitudinal exposure-based
- Cross-sectional design
- Occupational Exposure
- focus-populations with lower risk for autism

Psychologist, Pediatrician, Trained Assessors

(endophenotypes)

- administer behavioral/cognitive assessments
- medical exams for co-morbidities
- formal instrument to data mine med records

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Exposure assessments-(Exposure expert, analytical chem,engineers)

- prioritize which chemicals/physical agents
agricultural community? Urban environment?
- optimize environmental sampling (stabilize analytes)
- implement/develop biosensors
- optimize biological sampling (stabilize biomarkers)
- implement/develop analytical methods
Metals: ICP-MS, LA-ICP-MS,
Organics: GC-MS, LC-MALDI-TOF, nanoscale ELISA

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Molecular Genomics (on primary cells)

- SNP analysis (500k chips)
- CNV (low copy repeats/microdeletions, etc)
- Epigenetic (DNA methylation)
- total genome sequence
- Other?

Metabolomics/proteomics/lipomics -

- develop/validate rapid throughput
(LC-MS, GC-MS, LC-MS-MS)

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Toxicologists, cell biologist

(expertise in immunity, neurodevelopment, metabolism, endocrinology)

- Identify biomarkers that are selective or unique to autism
 - immune profiling (primary PBMCs from epi study)

cell type-specific activation markers

intracellular cytokines

antigen recall, LPS challenges, xenobiotic challenges

autoantibodies to brain protein(s)

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- Identify biomarkers that are selective or unique to autism
 - immune cell signaling (e.g., B cell, CD8+ T cell, DC, macr.)

Focus on direct and convergent signaling pathways implicated in autism

MET--->Grb2, Gsb-1, **PI3K**

CaV1.2 ----> CRUs, **PI3K**, CREB, mTOR

PTEN ---> akt/PKB, **PI3K**, NF κ B,

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Animal Models

Genetic susceptibility models (must be relevant to autism!)

- transgenic, knockin, knockout mice
- conditionals (timed expression of susceptibility allele)
- “autistic” dog line

Environment susceptibility models (must be relevant to autism!)

-Develop autism “surrogate”

autism IgG model

PKU model

Poly IC model

oxidative stress model (folate pathway enzymes)

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Data validation, Integration, modeling

Urgent Needs:

- Randomized controlled trials of novel therapeutics and innovative interventions
 - chelation
 - antioxidants (protocol?)
 - vitamin supplementation (example folate or B12 supplementation)
 - docosahexanoic acid (DHA)
 - other?

- combinatorial therapeutics?