What is our goal?
The CHARGE study is a project of the NIEHS/EPA Center for Children’s Environmental Health at UC Davis, that has been designed by parents and researchers committed to understanding the causes of autism and other neurodevelopmental disabilities. These serious, lifelong disorders interfere with a person’s ability to function in everyday activities. By studying children with different patterns of development we will learn more about factors that can increase risks for these disabilities.

What kinds of causes do we study?
We are investigating:
- Environmental toxins
- Medical history
- Lifestyle factors both before and after birth

We also look at susceptibility factors that may affect brain development, including:
- Metabolites such as lipids, sugars and amino acids
- Cell to cell communication molecules
- Gene activity
- Immune system function and status

Who participates in the CHARGE study?
Three groups:
- Children with autism
- Children with mental retardation/developmental delay but not autism (MR/DD)
- Children with typical or expected development (GP)

Who is eligible to participate?
- Between the ages of two and five
- Born in selected areas of California
- Parents speak either English or Spanish
- Living with at least one biologic parent

Typically developing children (n=700) randomly sampled from California live births occurring in same birth years and counties as cases

Children with autism (n=700) from State of California

Children with mental retardation/developmental delay (n=600) from State of California Regional Center System

Typically developing children (n=700) randomly sampled from California live births occurring in same birth years and counties as cases

Regional Center Locations

Data Collection
- Regional Center Record Abstraction
- Maternal Interview
  - Demographic and lifestyle factors, medical, reproductive, occupational and residential histories
- Clinical Assessments
  - Cognitive, Behavioral and Medical
- Specimen Collection
  - Blood, urine, buccal swab and hair
- Medical Record Review
  - Obstetric, labor-delivery, neonatal, pediatric, dental
- Take-home Questionnaires
  - Aberrant Behavior Checklist, Multiple Language Questionnaire, Sleep and GI Survey

Preliminary Results

Subject Enrollment

<table>
<thead>
<tr>
<th></th>
<th>Number of Families in Clinical Process</th>
<th>Number of Families Completed Clinical Process</th>
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</thead>
<tbody>
<tr>
<td>Autism Group</td>
<td>126</td>
<td>118</td>
</tr>
<tr>
<td>MR/DD Group</td>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>Typically Developing Group</td>
<td>36</td>
<td>26</td>
</tr>
<tr>
<td>Total</td>
<td>181</td>
<td>164</td>
</tr>
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Biological Sample Analysis (highlights)

Analytical Core (Core I) is attempting to cast a wide net and use the electrospray time of flight mass spectrometer to look in a semi quantitative way at a large variety of metabolites in urine and serum of autistic children including:

- Tryptophan metabolites (serotonin is a tryptophan-derived neurotransmitter)
- Neuroactive peptides, such as casomorphin from casein or gliadinomorphin form gluten (neuroactive peptides that exert an "opioid-like" effect in the brain)
- Oxilipins (oxidized lipids derived from the arachidonic acid and linoleic acid cascades) which are recognized as mediators of inflammatory and proliferative responses.

The Analytical Core is also measuring blood Hg and a wide range of other metals using ICP-MS (Inductively Coupled Plasma Mass Spectrometer) technology.

Cellular Activation/Signaling Core (Core II) is profiling serologic samples from autistic and matched control children to:

- define blood levels of key neurotrophins and neuropeptides in plasma.
- ascertain what tissue-specific antibodies are found in sera of patients with autism using a variety of neuronal antibodies by immunoblot.

Molecular Biomarkers Core (Core III) is applying expression microarray and single-gene approaches to identify patterns of altered gene expression that form significant associations with autism in human populations, or which are coupled to specific environmental factors in animal models. Specifically the core is examining the association between autism and single-gene polymorphisms at six loci:

- Adenosine Deaminase, Serotonin transporter (S-HT), Glutathione S-transferase, Reelin, dopamine beta-hydroxylase, and monoamine oxidase A.