Overall goals
This meeting will bring together experts in bioinformatics, computational and small molecule screening paradigms with key researchers in the genetics and neurobiology of autism to discuss the possibilities for applying new bioinformatics and screening tools and approaches to advance research on environmental contributors to autism and needed resources to enhance the use of these strategies.

Background
Autism spectrum disorders (ASD) are a collection of heterogeneous conditions that feature qualitative impairments in language and reciprocal social interactions and the presence of restricted and repetitive behavior and interests. Significant progress in elucidating the genetic architecture of ASD has been achieved over the past five years, while research in identifying environmental contributors to ASD, and their relation to genetic risk, is proceeding more slowly. Several obstacles to progress can be identified, including (1) the large number of exposures meriting consideration as risk factors and the lack of an efficient means for prioritizing and selecting exposures for investigation in humans; (2) limited understanding of the critical biologic substrates of ASD; (3) corresponding paucity of in vitro cellular models or well-established whole animal models for mechanistic studies; and (4) lack of robust analytic tools for joint consideration of genetics and environmental data in human population studies.

Recent technologic advances in the development and availability of novel bioinformatics and computational resources provide exciting new opportunities to identify toxicant interactions with signaling molecules and biologic pathways related to human disease and dysfunction. For example, progress is being made in computational methods for data mining and bioinformatics strategies for incorporating prior biological and toxicological knowledge into data analysis algorithms for identification of gene-environment interactions in human studies. The Comparative Toxicogenomics Database provides an example of a public use resource that includes manual curation of peer reviewed data and integration of existing data sets to explore relationships among toxicants, proteins, genes and diseases. A number of federal initiatives, including the US Environmental Protection Agency ToxCast and the National Toxicology Program's Biomolecular Screening Program are underway and aimed at establishing a new paradigm for toxicological testing, based on screening for mechanistic targets active within cellular pathways considered critical to adverse health effects.

While these approaches have not yet been applied to address questions related to autism environmental risk, recent genetic findings demonstrate a convergence on select biologic pathways. For
example, a number of genes and gene products and pathways associated with synapses have been implicated in autism, including those that function in neuronal migration and pathfinding, development of dendritic spines and excitatory or inhibitory synaptic transmission. These provide a new opportunity for exploring complex genetic and environmental contributors using the tools of computational biology.

**Meeting organization**
The meeting is organized around the following themes:

*What is known about autism etiology?*

- What kinds of genetics/genomics data are now available for autism (e.g., GWAS, cnv, candidate gene, family-based studies), how were they generated; what are their limitations; what molecular pathways are implicated?
- What environmental risks for autism are known or suspected?
- How is epigenomics emerging as a potential broker between genetic and environmental influences in autism?

*Bioinformatics/Computational approaches for complex disease etiology*

- What bioinformatics and computational tools are now available for use in understanding complex diseases?
- How could these tools be harnessed for integrating genetics/genomics and toxicology data in autism; e.g., what data are available to explore the interaction of toxicants with autism pathways/molecular targets identified through genetic studies?

*Putting it all together*

- How can genetics and bioinformatics/computational strategies be used to inform (1) data integration of exposure and genetics in human population studies; (2) development of HTS or tiered screening efforts?
  - What new molecular assays are needed to query relevant molecular targets for HTS?
- What is the role for existing autism databases, which are currently gene-centric, in these efforts?
- What additional resources and tools are needed to encourage application of bioinformatics/computational strategies to advance understanding the role of environment, and gene-environment interplay, in autism?
## Agenda
The meeting will be held at Marriott at Research Triangle Park, 4700 Guardian Drive, Durham NC, 27703
Meeting registration is available at [http://tools.niehs.nih.gov/conferences/dert/bioinfo/](http://tools.niehs.nih.gov/conferences/dert/bioinfo/)

### Tuesday, November 29, 2011

<table>
<thead>
<tr>
<th>Time</th>
<th>Session Description</th>
<th>Presenter(s)</th>
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<tbody>
<tr>
<td>7:30-8:30</td>
<td>Registration &lt;br&gt; Continental breakfast available</td>
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<tr>
<td>8:30-8:40</td>
<td>Welcome and introductions &lt;br&gt; Linda Birnbaum, NIEHS</td>
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<td>8:40-8:45</td>
<td>Charge to group &lt;br&gt; Cindy Lawler, NIEHS</td>
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<tr>
<td>8:45-8:50</td>
<td>Session overview &lt;br&gt; Alycia Halladay, Autism Speaks</td>
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<tr>
<td>8:50-9:15</td>
<td>Overview of clinical features &lt;br&gt; Geri Dawson, Autism Speaks</td>
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<td>9:15-9:40</td>
<td>State of the science in autism genetics and genomics &lt;br&gt; Catalina Betancur, INSERM, Université Pierre et Marie Curie</td>
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<td>9:40-10:05</td>
<td>Recent clues from environmental risk factor research in autism &lt;br&gt; Heather Volk, USC</td>
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<td>10:05-10:30</td>
<td>Using phenotypic heterogeneity as a tool to understand autism etiology &lt;br&gt; Dan Campbell, USC</td>
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<td>10:30-10:50</td>
<td>Break</td>
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<tr>
<td>10:50-11:15</td>
<td>Epigenomics as the interface for genes and environment in autism etiology &lt;br&gt; Chris Ladd Acosta, Johns Hopkins University</td>
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<tr>
<td>11:15-11:45</td>
<td>Q &amp; A; Discussion</td>
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<tr>
<td>11:45-11:50</td>
<td>Session overview &lt;br&gt; David Balshaw, NIEHS</td>
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<tr>
<td>11:50-12:15</td>
<td>Using the Comparative Toxicogenomics Database to explore autism &lt;br&gt; Allan Peter Davis, Mount Desert Island Biological Laboratory</td>
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<tr>
<td>12:15-12:40</td>
<td>Metabolomics as a strategy to inform environment-disease linkages &lt;br&gt; Dean Jones, Emory University</td>
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<tr>
<td>12:40-1:45</td>
<td>Lunch</td>
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<td>1:45-2:10</td>
<td>Systems biology approaches to reconstruct pathway maps and causal networks of disease &lt;br&gt; Richard Brennan, Thomson Reuters, GeneGo</td>
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<tr>
<td>2:10-2:35</td>
<td>Using biological knowledge to inform complex genetics analysis &lt;br&gt; Marylyn Ritchie, Penn State University</td>
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<td>2:35-2:55</td>
<td>Break</td>
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## Agenda (cont’d)

**Tuesday, November 29, 2011**

### Panel Discussion

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<thead>
<tr>
<th>Time</th>
<th>Event</th>
<th>Speaker(s)</th>
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<tbody>
<tr>
<td>2:55-3:00</td>
<td>Introduction</td>
<td>Gwen Collman, NIEHS</td>
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<tr>
<td>3:00-5:00</td>
<td>Questions <em>(under development)</em></td>
<td>James Sutcliffe, Vanderbilt University&lt;br&gt;Rita Cantor, UCLA&lt;br&gt;Stuart Lipton, Sanford Burnham Institute&lt;br&gt;Richard Judson, US EPA&lt;br&gt;Scott Auerbach, National Toxicology Program&lt;br&gt;Simon Gregory, Duke University</td>
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<tr>
<td>6:30</td>
<td>Group dinner at <em>Mez</em>, 5410 Page Road, Durham 27703</td>
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**Wednesday, November 30, 2011**

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<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>7:30-8:30</td>
<td>Continental breakfast available</td>
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<tr>
<td>8:30-8:35</td>
<td>Overview of Session</td>
<td>Kimberly McAllister, NIEHS</td>
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<tr>
<td>8:35-9:00</td>
<td>National Database for Autism Research: a model for research collaboration</td>
<td>Dan Hall, NIMH</td>
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<td>9:00-9:25</td>
<td>Autism data integration challenges: examples from AGRE</td>
<td>Dušan Bošnjaković, AGRE</td>
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<tr>
<td>9:25-9:50</td>
<td>SFARI resources and tools for discovery research in autism</td>
<td>Alice Luo Clayton, Simons Foundation</td>
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<tr>
<td>9:50-10:15</td>
<td>Q &amp; A; Discussion</td>
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<tr>
<td>10:15-10:35</td>
<td>Break</td>
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<tr>
<td>10:35-12:00</td>
<td>Prioritization and recommendations</td>
<td>Cindy Lawler, Kim McAllister, David Balshaw, Gwen Collman</td>
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<tr>
<td>12:00-12:10</td>
<td>Wrap up and next steps</td>
<td>Cindy Lawler</td>
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<tr>
<td>1:00</td>
<td>Shuttle leaves for airport</td>
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</table>
Suggested Background Reading

Session 1: Autism--What we know now

**Autism.**
Levy SE, Mandell DS, Schultz RT.
PMID: 19819542 [PubMed - indexed for MEDLINE]

**Etiological heterogeneity in autism spectrum disorders: more than 100 genetic and genomic disorders and still counting.**
Betancur C.
PMID: 21129364 [PubMed - in process]

**The conundrums of understanding genetic risks for autism spectrum disorders.**
State MW, Levitt P.
PMID: 22037497 [PubMed - as supplied by publisher]

**A genomic point-of-view on environmental factors influencing the human brain methylome.**
LaSalle JM.
PMID: 21617367 [PubMed - in process]

**Autism spectrum disorders and epigenetics.**
Grafodatskaya D, Chung B, Szatmari P, Weksberg R.
PMID: 20643313 [PubMed - indexed for MEDLINE]

**Genetic heritability and shared environmental factors among twin pairs with autism.**
PMID: 21727249 [PubMed - in process]

**Epigenetics of autism spectrum disorders.**
Schanen NC.
PMID: 16987877 [PubMed - indexed for MEDLINE]
Session 2

Bioinformatics and computational approaches to complex disease etiology

**In vitro screening of environmental chemicals for targeted testing prioritization: the ToxCast project.**
PMID: 20368123 [PubMed - indexed for MEDLINE]

**The Comparative Toxicogenomics Database: update 2011.**
Davis AP, King BL, Mockus S, Murphy CG, Saraceni-Richards C, Rosenstein M, Wiegers T, Mattingly CJ.
PMID: 20864448 [PubMed - indexed for MEDLINE]

**Methods for investigating gene-environment interactions in candidate pathway and genome-wide association studies.**
Thomas D.
PMID: 20070199 [PubMed - indexed for MEDLINE]

**The Next PAGE in understanding complex traits: design for the analysis of Population Architecture Using Genetics and Epidemiology (PAGE) Study.**
PMID: 21836165 [PubMed - indexed for MEDLINE]

**Interactome networks and human disease.**
Vidal M, Cusick ME, Barabási AL.
PMID: 21414488 [PubMed - indexed for MEDLINE]

**Controllability of complex networks.**
Liu YY, Slotine JJ, Barabási AL.
PMID: 21562557 [PubMed - indexed for MEDLINE]
The druggable genome.
Hopkins AL, Groom CR.
PMID: 12209152 [PubMed - indexed for MEDLINE]

Session 3

Autism research resources

Changing the landscape of autism research: the autism genetic resource exchange.
Lajonchere CM; AGRE Consortium.
PMID: 20955925 [PubMed - indexed for MEDLINE]

Fischbach GD, Lord C.
PMID: 20955926 [PubMed - indexed for MEDLINE]

SFARI Gene: an evolving database for the autism research community.
Banerjee-Basu S, Packer A.
PMID: 20212079 [PubMed - indexed for MEDLINE]