Translational Research in Autism: A national perspective

Alycia Halladay, PhD
Sr. Director of Clinical and Environmental Sciences
Overview of presentation

- Translational research in autism – skip through
- Mechanisms of support
  - Outside LLC (Delsia)
  - ATN
  - Investigator-Initiated awards
A little about Autism Speaks

- 2013 - $24M research funding
  - Grants, initiatives, resources,
Translational Research

What is it, and why is it critical to our mission?
**trans-la-tion:** (n) The process of converting scientific discovery into applications that provide real-life benefit for individuals living with ASD.

<table>
<thead>
<tr>
<th>Bench</th>
<th>Development</th>
<th>Bedside</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetics</td>
<td>Cell Biology</td>
<td>Medicines</td>
</tr>
<tr>
<td>Biochemistry</td>
<td>Physiology</td>
<td>Devices</td>
</tr>
<tr>
<td>Imaging</td>
<td>Behavior</td>
<td>Diagnostics</td>
</tr>
</tbody>
</table>
Intellectual Disability

Language Impairment

Social Deficits

Sleep Deficits

Mood

Anxiety

Attention

Hyperactivity

Tantrums

Self Injury

Aggression

Seizures

GI Disorders

Immune Dysfunction

Core Clinical Features

Associated CNS Symptoms

Somatic Symptoms

Approved by FDA: 2006
For use in children ages 5 to 16

Risperdal
Risperidone

Approved by FDA: 2009
For use in children ages 6 to 17

Abilify
Aripiprazole
Understanding the Translational Research Space

Bench
- Basic Research
- Discovery
- Pre-Dev

Development
- Phase 1
- Phase 2
- Phase 3

Bedside
- Commercialization

↑ Regulatory oversight
↑ Scale of investments
↑ Exposure to liability
↑ Complexity of agreements/contracts
↑ Opportunity for financial obligation or return
Potential approaches

- Investing in business ventures to accelerate science
- Supporting academics targeted on “bench to bedside research”
- Creating infrastructure and a platform for clinical research
Postdoctoral awards - 4 main areas:

1. Biomarker Discovery:
2. Outcome Measure Development:
3. Preclinical Target Validation:
4. Experimental Therapeutics:
Number awarded each year

<table>
<thead>
<tr>
<th>Year</th>
<th>Number Awarded</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>10</td>
</tr>
<tr>
<td>2012</td>
<td>10</td>
</tr>
<tr>
<td>2013</td>
<td>6</td>
</tr>
</tbody>
</table>
Examples

- Small molecule compounds to “wake up” the dormant paternal allele in Angelman Syndrome mice
- RCT of oxytocin
- Autism in a dish: inserting genetic mutations into human cell progenitors
Integration with other translational research programs:

- Understanding the etiological significance of attentional disengagement in infants at-risk for ASD
Challenges for patients

- Many children with autism cannot describe pain or may show discomfort behaviorally.
- Disruptive behaviors make careful and thorough examination for medical issues difficult.
- Failure to accurately diagnose underlying medical conditions could likely lead to more serious health problems.
- Doctors have attributed medical symptoms to the individual’s autism.
- Parents were traveling all over the country to piece together a medical team to address their child’s needs.
A Model for Comprehensive Care
Autism Speaks Autism Treatment Network

- 17 children’s hospitals with teams of doctors and specialists who understand autism and who work together across several subspecialty areas to treat the medical issues.
- Each center has a team that includes pediatricians, psychologists, sleep medicine, GI doctors, psychiatrists, genetics/metabolics and neurology
- Support a comprehensive integrated model of care focusing on the whole child
- Family-Centered
- Address the medical issues that individuals with autism face
- Develop guidelines for associated medical conditions
- Raised the bar among the medical community to recognize the importance of medical issues in autism
- 34,000 children served **annually**
- > 6300 patients in registry
- **NIMH-funded bio-repository** (473 individuals)
- Serving as the **HRSA-funded Autism Intervention Research Network for Physical Care (AIRP)**
- Over 18 toolkits and resources for families and physicians released
- 24 **peer-reviewed** papers
- **First published evidence-based guidelines** for medical treatment of GI, sleep, and ADHD (*Pediatrics*, 2012)
## Tool Kits and Resources

<table>
<thead>
<tr>
<th>ATN/AIR-P Tool Kit</th>
<th>Number of Downloads</th>
<th>Month of Release</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation Guide for Parents</td>
<td>506</td>
<td>2013 - July</td>
</tr>
<tr>
<td>Safe Medication Use</td>
<td>3,404</td>
<td>2013 - June</td>
</tr>
<tr>
<td>Sleep Quick Tips for Parents</td>
<td>293</td>
<td>2013 - February</td>
</tr>
<tr>
<td>Applied Behavioral Analysis</td>
<td>11,122</td>
<td>2012 - June</td>
</tr>
<tr>
<td>Introduction to Behavioral Health Treatments</td>
<td>5,922</td>
<td>2012 - June</td>
</tr>
<tr>
<td>Toileting</td>
<td>8,343</td>
<td>2012 - June</td>
</tr>
<tr>
<td>Dental Provider’s Guide</td>
<td>3,474</td>
<td>2012 – February</td>
</tr>
<tr>
<td>Sleep Parent Booklet</td>
<td>8,362</td>
<td>2012 – February</td>
</tr>
<tr>
<td>Visual Supports</td>
<td>15,003</td>
<td>2011 - November</td>
</tr>
<tr>
<td>Blood Draws – Guide for Parents</td>
<td>3,210</td>
<td>2011 - September</td>
</tr>
<tr>
<td>Blood Draws – Guide for Providers</td>
<td>1,606</td>
<td>2011 - September</td>
</tr>
<tr>
<td>Medication Decision Aid</td>
<td>7,910</td>
<td>2011 - September</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ATN/AIR-P Tool Kit</th>
<th>ETA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivering Feedback Video for Professionals</td>
<td>August 2013</td>
</tr>
<tr>
<td>Feeding Guide for Parents</td>
<td>September 2013</td>
</tr>
<tr>
<td>PICA Guide for Parents</td>
<td>Fall 2013</td>
</tr>
<tr>
<td>Vision Exam Video for Professionals</td>
<td>Fall 2013</td>
</tr>
</tbody>
</table>
Moving forward – what will the ATN look like in the future?
New funding opportunity/ expanding the resource

- **Expand access to the ATN Care Model** for the increasing numbers of children and youth with ASD
- **Expand care** through collaborative partnerships with community-based **provider networks**.
- Enhance the care model by **strengthening family support**, **enhancing training** for healthcare professionals, and incorporating **adult transition**.
- **Provide greater integration** with Autism Speaks local chapters, advocacy and awareness activities, and fundraising efforts (ex. Light It Up Blue).
- Continue to **support research** through public and private partnerships (i.e. AIR-P).
Bottom Line – network model to accelerate development

• The ATN is a **live captive audience** for translational research
  – Well characterized, standardized protocols
  – Willing to participate in additional studies

• It can leverage on existing resources, infrastructure and funding
  – Ready made clinical trial network
  – AS contribution per site modest ($140k per year per site)

• Simultaneous functions: resources, research and recruitment