Question 7 Draft Updates for the IACC 2011 Strategic Plan

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Question 7. What Other Infrastructure and Surveillance Needs Must be Met?

What is new in this research area and what have we learned this past year?

Data sharing

This year, the Autism Informatics Consortium (AIC) was formed with the goal of accelerating scientific discovery by making informatics tools and resources more useful to, and usable by, autism researchers. The consortium is charged with identifying information technology solutions, harmonizing major informatics frameworks, and developing standards in the field for working with research data. The consortium is comprised of representatives from both public and private institutions that are responsible for the development of major autism informatics tools and resources. Current members include Autism Speaks (Autism Genetic Resource Exchange), Kennedy Krieger Institute (Interactive Autism Network), Simons Foundation and Prometheus Research (Simons Foundation Autism Research Initiative), and the National Institutes of Health (National Database for Autism Research). The AIC held its first workshop on August 26-27, 2010 at the NIMH offices in Rockville, MD. In attendance were representatives from 12 major research institutions. The objective of the meeting was to explore short term (1-2 years) and intermediate term (2-5 years) priorities for increasing the utility and harmonization of major autism research informatics resources, identify ways to best pursue those priorities, and determine ways to measure progress toward achieving them.

Biobanking

The Autism Treatment Network (ATN), a collaboration among 14 academic medical centers providing clinical services for children with ASD, collects and stores common, extensive phenotypic data on children with autism in a central patient registry. This year the ATN was funded by the National Institute of Mental Health to collect DNA, plasma, and urine from four of the 14 sites as a beginning step toward establishing a comprehensive biorepository for the ATN. One goal of establishing the repository is to provide a platform for conducting comparative effectiveness research that can utilize biomarkers to predict response to treatments.

In 2010, the Autism Tissue Program established a neurological tissue genetic repository from brains donated to the program. Sample tissue from each selected brain was carefully removed, its DNA isolated, stored in small aliquots and are now made available to approved researchers. To date, genetic analysis has been conducted on cortical samples from 50 brains utilizing both 1M Illumina and Affymetrix 6.0 DNA chips, providing both copy number variation (CNV) and small nucleotide polymorphisms (SNP) data provided free of charge to researchers accessing this repository.

With funding from the NIH and in collaboration with the scientific community, the ATP is also working to create a near limitless source of neurological tissue to enhance cell and molecular biology studies in autism by helping to create, curate and steward an ASD stem cell repository. Both skin samples from individuals with autism and cell samples taken directly from fresh post mortem brains donated to the ATP, are being collected and genetically engineered to induce a "stem cell" or pluripotent state (iPSC's).

With these newly formed iPSC neuronal cells, researchers will be able to directly study laboratory created living autism "brain cells".

Surveillance

One area which has progressed is the establishment of systems to identify and monitor the prevalence of ASDs in the US. The ADDM Network (2009) and report from the National Survey of Children's Health reported ASD prevalence of around 1% of children with an average increase of 57% from 2002 to 2006 in 10 areas of the US covered by the ADDM Network. CDC, 2009; Kogan et al., 2009) While some of the increase was attributed to improved identification of particular subgroups such as Hispanic children and children without cognitive impairment; a true increase in risk is also possible. (CDC, 2009) Several other recent studies have also indicated that multiple identification factors contribute to, but do not fully explain the rising ASD prevalence (Hertz-Picciotto and Delwiche, 2009; Saemundsen, 2010; King and Bearman, 2009; Rice et al., 2010; Van Meter et al., 2010; Mazumdar et al., 2010). Concerted efforts are now needed to evaluate the reasons behind these changes.

Information and Communication Dissemination

Of particular importance is the rapid translation of research findings as they apply to intervention and the dissemination to families and practitioners in the community in a way that is easy to access and understand. There have been several reviews of intervention quality and effectiveness (http://www.impaqint.com/files/4-content/1-6-publications/1-6-2-project-reports/finalasdreport.pdf) (Lang et al., 2010) and several states have developed state plans for ASD and other DD services based on the current state of knowledge.
http://www.aucd.org/template/event.cfm?event_id=2456&id=547&parent=547

Research Workforce Development

What gap areas have emerged since last year?

Data sharing

The AIC identified several short term and long term priorities for increasing the utility and harmonization of major autism research informatics resources, identifying ways to best pursue those priorities, and determining ways to measure progress toward achieving them. Examples of gap areas identified include the need for improved options for data federation, query interfaces and languages, genetic visualization tools, file and data set management, data quality and validation rules and algorithms, data dictionaries and ontologies, standardizing GUID usage. procedures for maintaining phenotype resources with associated biospecimens (imaging, genetics, etc) , defining a core (clinical) phenotype battery, working with publishers of copyrighted assessments, and addressing concerns about intellectual property.

Biobanking

In the absence of biological markers, current approaches for stratification of individuals with ASD into clinically meaningful subgroups have relied on behavioral characteristics. However, the variability of behavioral, medical, and developmental concerns that affect individuals with ASD has made it extremely difficult to predict which treatments work best for which individuals. The integration of biologic information into phenotype selection algorithms can help to guide the development and evaluation of more targeted and effective therapeutics and significantly improve the prediction of a therapeutic response. To this end, there is a need for the establishment of a robust network of clinical research sites offering clinical care in real-world settings that can collect and coordinate standardized and comprehensive diagnostic, biological (e.g. genotype), medical, and treatment history data that would provide a platform for conducting comparative effectiveness research and clinical trials of novel autism treatments. Currently, there is a need high-throughput screening tools to quickly evaluate gene-environment interactions relevant to ASD. Lack of progress in this area has made identification of potential exposures of interest difficult and driven by anecdotal evidence.

Surveillance

Moving forward, there is a need to understand how multiple identification and potential risk factors have influenced the increasing estimates of ASD prevalence. Further analyses of existing datasets are needed to examine any relationship between changes in ASD prevalence and changes in potential risk factors in the population. Surveillance cohorts also provide the opportunity for communities and policy makers to use these data for resource allocation in addition to characterizing population-based identification patterns and gaps.

Communication and Information Dissemination

There have been several reviews of intervention quality and effectiveness and several states have developed state plans for ASD and other DD services based on the current state of knowledge. This information and these plans should be easily accessible to other communities.

Research Workforce Development

The need for on-going investment in developing research expertise and facilitating research careers in autism research is needed, especially in the emerging areas of health services research, translational research, and international collaborative studies.

What new research opportunities and research objectives have emerged?

- Revise Objective B: Conduct an annual "State of the States" assessment of existing state programs and supports for people and families living with ASD by 2009 and make this information as well as state plans developed regarding ASD and other DD services available on a single "ASD Services and Supports" web location. *IACC Recommended Budget: $300,000 each year.*

- Revise Objective D: Establish and maintain an international network of biobanks for the collection of brain, fibroblasts for pluripotent stem cells, and other tissue or biological material, by acquisition sites that use standardized protocols for phenotyping, collection, and regulated distribution of limited samples by 2011. This includes support for post-processing of tissue such as genotyping, RNA expression profiling, and MRI. (Deleted: This includes developing fibroblast repositories to produce pluripotent stem cells). Protocols should be put into place to expand the capacities of ongoing large-scale children's studies to collect and store additional biomaterials, including newborn bloodspots, promoting detection of biological signatures. Support should also be provided to develop an international web-based digital brain atlas that would provide high resolution 3D images and quantitative anatomical data from tissue of patients with ASD and disease controls across the lifespan, which could serve as an online resource for quantitative morphological studies by 2014. *IACC Recommended Budget for establishing biobanks by 2011: $10,500,000 over 2 years. IACC Recommended Budget for maintaining biobanks: $22,200,000 over 5 years.*

- Revise Objective M: Support 10 "Promising Practices" papers that describe innovative and successful services and supports being implemented in communities that benefit the full spectrum of people with ASD, which can be replicated in other communities by 2015 and make these available on the "ASD Services and Supports" web portal. *IACC Recommended Budget: $75,000 over 5 years.*

New Objectives:

A. Establish a robust network of clinical research sites offering clinical care in real-world settings that can collect and coordinate standardized and comprehensive diagnostic, biological (e.g. DNA, plasma, fibroblasts, urine), medical, and treatment history data that would provide a platform for conducting comparative effectiveness research and clinical trials of novel autism treatments by 2012.

B. Encourage programs and funding mechanisms that expand the research workforce, enhance interdisciplinary research training, and recruit early career scientists into the ASD field by 2013. IACC Recommended Budget: $5,000,000 over 3 years.

C. Create an information resource for ASD researchers (e.g. PHEN-X Project) to share information to facilitate data sharing and standardization of methods across projects. This includes common protocols, instruments, designs and other procedural documents and should include updates on new technology and links to information on how to acquire and utilize technology in development. This can serve as a bidirectional information reference, with autism research driving the development of new resources and technologies, including new model systems, screening tools, and analytic techniques by 2013.

D. Provide resources to centers or facilities which develop promising vertebrate and invertebrate model systems and make these models more easily available or expand the utility of current

model systems, and support new approaches to develop high throughput screening technologies to evaluate the validity of model systems by 2013.

References

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