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To the Editor:

In this letter, we describe the Autism Genetic Resource Exchange (AGRE), a resource for the study of autism and pervasive developmental disorder (PDD). Autism presents within the first 3 years of life, is characterized by qualitative impairments in communication and social interaction—in the presence of restricted repetitive and stereotyped patterns of behavior, interests, and activities—and is part of a spectrum of disorders that includes Asperger syndrome and PDD (American Psychiatric Association 1994). Estimates of the prevalence of autism in the general population ranges from 0.4% to 0.1% (Bryson et al. 1988; Gillberg et al. 1991). Twin and family studies have demonstrated that the genetic contribution to autism and PDD is significant, with an MZ-twin concordance of 60%-90% and a 45- to 150-fold increase in risk to siblings (Ritvo et al. 1989; Jorde et al. 1990; Bailey et al. 1995). Thus, molecular genetic studies of autism-spectrum disorders are likely to contribute significantly to our understanding of this condition, as the recent results of several independent genome scans suggest (International Molecular Genetic Study of Autism Consortium 1998; Barrett et al. 1999; Philippe et al. 1999; Risch et al. 1999).

AGRE has been developed as a joint effort of the Cure Autism Now (CAN) Foundation and the Human Biological Data Interchange (HBDI), to facilitate collaborative genetic research into the etiology of autism and PDD and to make biomaterials from well-characterized families with autism widely available to the scientific community, so as to accelerate research. Since genetic studies of complex neuropsychiatric conditions are limited by the large sample sizes needed to attain adequate power (Lander and Kruglyak 1995; Risch and Merikangas 1996), the consolidation of large numbers of families into one collection that is made available to researchers at a fraction of the cost originally incurred
in their ascertainment and collection is of great value to the community.

One unique feature of AGRE, which has enabled the rapid ascertainment of large numbers of families, has been the development of a protocol and the infrastructure to conduct the majority of the evaluations and blood draws in the families’ homes. This process may prove useful for more-rapid family ascertainment in studies of other neuropsychiatric conditions (AGRE Web site). To date, ~400 multiplex families with autism and PDD are in various stages of clinical evaluation, with DNA collection completed (table 1). Both an online and a hardcopy catalogue are available, containing the pedigrees in the collection, with notations of affection status and basic phenotypic features, such as language delay. A sample pedigree is depicted in figure 1. Biomaterials from 343 of these completed families are currently available to the scientific research community, and this resource continues to expand, with the goal of 500 families by the end of the year 2001. Family biomaterials for the AGRE program are housed at the HBDI Repository at Rutgers University, under the direction of Jay Tischfield. Quality-controlled samples, including immortalized cell lines (1 × 10⁶ cells/ampoule), 20-μg aliquots of DNA, and 50-μl aliquots of sera, are available to the research community by simple application, which requires proof of institutional review board (IRB) approval. Samples are available to academia and industry, and significant discounts, as well as limited grants to support academic use of the resource, are available to academic researchers through the CAN Foundation. To facilitate collaboration, free samples are available to researchers who deposit their collections in AGRE through the Sharing Researcher Program.

Scientific oversight for the program is provided by a Steering Committee, which includes researchers from the fields of genetics and autism. Human subjects protection oversight is provided by the IRB at the University of Pennsylvania School of Medicine. In addition to providing researchers with biomaterials, a major effort has been undertaken to develop a state-of-the-art, Internet-accessible database of detailed clinical information. Phenotypic assessment is ongoing and includes the two examinations that are completed by all of the NIH autism collaborative groups: the Autism Diagnostic Interview—Revised (ADI-R) (Lord et al. 1994) and the Autism Diagnostic Observation Schedule (ADOS) (Lord et al. 2000). ADI and ADOS raters undergo ongoing reliability checks to prevent any drift in diagnosis (Lord et al. 1994, 2000). In addition, photographic dysmorphology, physical and neurological examination, and medical and family history are being collected by pediatric neurologists. Probands with possible secondary autism resulting from perinatal trauma, from an identified genetic syndrome, or from other medical causes are noted, although this is only a small percentage of cases. Currently, the ADI data and a subset of the ADOS data, both coded for confidentiality,
are available online for researcher access through the AGRE Web site. Online phenotypic databases for the remainder of the data collected are being developed and will be available in <6 mo. More information on the timeline of data and material collection is available at the Web site. We are striving to improve the utility of AGRE, and user feedback is an important element in this process. Fragile-X testing is conducted in all families (Brown et al. 1986), and cytogenetic analysis—including FISH for 15q and telomere screening—is commencing. Of 220 families tested, 3 have subjects that carry a fragile-X expansion (1.3%; W. T. Brown, unpublished data). A genome scan at an average 10-cM resolution has been completed on the first 132 families in the collection (T. C. Gilliam, personal communication), and genotype data from 188 families are available online at the AGRE Web site. As genome scans on additional families are completed, these data will be updated regularly, and investigators accessing these data will be notified of the updates automatically. More information regarding this resource, including pricing of samples and access to the resource, can be obtained from the CAN Foundation and AGRE Web sites, or by contacting the authors.

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Electronic-Database Information

The URLs for data in this article are as follows:


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