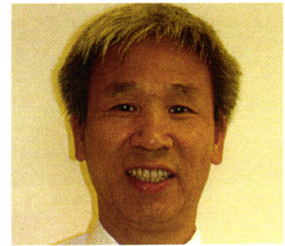


NARSAD Researchers in the News



Xiangning Chen, Ph.D.

NARSAD-Funded Research Identifies New Gene Candidate for Schizophrenia

Schizophrenia has long been known to have a large inherited component – generally estimated by scientists to be as high as 80 percent. This past September, two NARSAD investigators reported the results of a novel kind of genetic study of schizophrenia in *Molecular Psychiatry*.

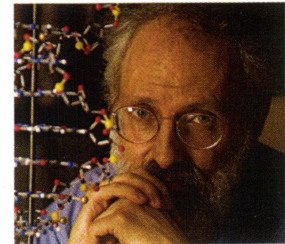
NARSAD Independent Investigator Xiangning Chen, Ph.D., and others were joined by NARSAD Scientific Council member Kenneth S. Kendler, M.D., – one of the leaders in the field – in identifying a gene called CMYA5 that was not previously known to be associated with elevated risk for the illness. This is an important result, but it was the method of the study that brought it to light that is most noteworthy.

The most popular form of genetic study into schizophrenia's causation has been an approach called the genome-wide association study, or GWAS. By searching the entire genome of thousands of individuals and looking for differences in the genes of healthy people and people suffering from a given illness, "gene candidates" can be identified and examined further. There are gene candi-

dates for such illnesses as type-two diabetes, most forms of cancer and heart disease. GWAS studies have also generated many candidate genes for schizophrenia – many hundreds from among the total set of 21,000 human genes – and yet this rich harvest has not yet correlated with advances in our ability to diagnose and treat schizophrenia (unlike cancer, for example).

The reason: Different studies, using different populations of both patients and healthy controls, turn up different genes seeming to signal elevated risk of the illness. Yet, it is the strong conviction of Drs. Chen and Kendler (who are, respectively, associate professor and professor at Virginia Commonwealth University's School of Medicine) that "there are genetic markers – genes with true effects – buried within the large number of tested markers" in existing GWAS studies.

The researchers ran a mathematical fine-toothed comb over results of existing GWAS studies. The final results were the product of 25 different samples that included 33,834 people – made up of more than 16,000 healthy people



Kenneth S. Kendler, M.D.

with no family history; more than 13,000 people with schizophrenia; and 4,190 members of 912 families with histories of schizophrenia. The CMYA5 gene, which emerged, "had previously been associated with cardiomyopathy, a kind of heart disease. The gene is expressed not only in the heart but also in the brain; its function remains unknown. The team notes that CMYA5 is involved in a biochemical pathway that includes another known candidate gene for schizophrenia, DTNBP1. Fleshing out that pathway is one likely result of this research in the near term.

A double helix, right, carries DNA genetic information like that carefully analyzed by Drs. Chen and Kendler in their landmark work re-examining existing genome-wide association studies. Through this extensive work including samples of almost 34,000 people, they discovered that the gene CMYA5 is associated with elevated risk for developing schizophrenia.

