

## **Assessment and Quantification of Risk for the Development of Schizophrenia**

### **Background**

Schizophrenia is a developmental disorder caused by brain damage in a fetus due to maternal genetic and environmental factors. The genetic factors have not been definitively identified despite extensive linkage analysis due to several factors: 1) involvement of more than one gene 2) uncertainty in the mode of inheritance 3) a high frequency of the allele being tested in the population being screened. The environment around the developing fetus is contributed by maternal components and there is a growing appreciation that a combination of fetal environmental and maternal genetic factors during the second trimester of pregnancy contributes to the development of schizophrenia. A resolution of the precise nature, components, and manner of interaction of the genetic and environmental factors could lead to the prevention of this disease and other developmental disorders that are believed to share common etiological factors.

As per National Institute of Mental Health, about 2.2 million Americans over the age of 18 suffer from Schizophrenia, with men and women being affected equally. In the United States, the annual cost to treat schizophrenia has been estimated to be \$18.6 billion in direct medical costs and \$46.5 billion in indirect costs. The lack of reliable screening and testing schemes for the prevention and treatment of developmental disorders pose considerable healthcare costs. Thus, there is a significant unmet medical need to screen populations and identify individuals prone to developmental disorders as well as individuals susceptible to giving birth to schizophrenic individuals. Additionally, strategies that avert the risk of susceptible individuals from developing these diseases and therapeutic modalities that provide symptomatic relief would be medically beneficial.

### **Description of the Technology**

A 19 base pair deletion mutation in the enzyme dihydrofolate reductase (DHFR) has been shown to have a significant predictive value for the identification of individuals at risk for the development of schizophrenia. Models for the determination of gene inheritance pattern using patient derived tissue samples have been developed. Further, the dietary content of folate, cobalamin, and pyridoxine of pregnant and susceptible individuals has been determined to be predictive of the susceptibility to schizophrenia.

Binary logistic regression analysis was performed using the data obtained from PCR analysis for the detection of the 19 base pair deletion in DHFR and the 677C→T polymorphism in the methylenetetrahydrofolate (MTHFR) genes using blood samples drawn from schizophrenic patients and family members of the patients. These analyses revealed that the presence of a double dose of the 19 base pair deletion in DHFR in the mother, but not in the father, of schizophrenic patients increased disease risk in the offspring. However, polymorphism in the MTHFR gene, either in single or double dose, in the mothers of schizophrenic patients was not a genetic risk factor for the child while the polymorphism was a risk factor for the mothers.

In terms of environmental factors contributing to the risk of susceptibility, a significant percentage of normal controls carried the polymorphism in DHFR and MTHFR genes, but did not have the disease, indicating that interaction between genetic and environmental factors contribute to the development of schizophrenia.

**Advantages**

- No reliable risk assessment and quantification methods are currently available.
- Overlapping etiological elements in developmental diseases such as Autism and Attention Deficit Hyperactivity Disorder opens the possibility for using the current method for the assessment of at risk patients.

**Applications**

- To screen and identify individuals genetically susceptible to give birth to schizophrenic individuals
- For the assessment and quantification of risk for the development of schizophrenia
- For the development of a database of environmental reference sets for the identification of environmental factors capable of triggering the disease in genetic carriers or genetically prone individuals or their offsprings.
- For the development of treatment modalities for individuals identified as susceptible to develop developmental disorders

**Patent Status**

- United States patent issued on April 3, 2001. Patent number US 6,210,950 B1

**Licensing Opportunity**

- This technology is available for exclusive license.

**Contact**

Mr. Peter Golikov, M.S., M.B.A.  
University of Medicine and Dentistry of New Jersey  
335 George Street, Suite 3200  
New Brunswick, NJ 08901  
Office Phone: (732)-235-9355  
Fax: (732)-235-9358