Gene Expression May Be ‘Therapeutic Target’ for Stroke

BY BETSY BATES
Los Angeles Bureau

SAN DIEGO — Characteristic patterns of gene expression in blood samples can now identify patients with migraine, Tourette’s syndrome, neurofibromatosis type 1, tuberous sclerosis type 2, Down syndrome, and early ischemic stroke, among other diseases, Dr. Frank Sharp said at the annual meeting of the American Neurological Association.

The notion that genomic expression can provide a fingerprint of a disease is increasingly proving to be true, although the patterns in blood are not as robust as those found in tissue and are sometimes seen in complex combinations, said Dr. Sharp, who is professor of neurology at the M.I.N.D. Institute, University of California, Davis.

The findings in stroke are particularly intriguing, however, with profound implications for better understanding the timing and nature of inflammatory responses to acute stroke, which in turn could aid in early diagnosis, prognosis, and treatment. Dr. Sharp and his associates have seen a biologic response to a disease in blood cells in response to ischemic stroke, reflecting the release of proteins, cytokines, and growth factors that are needed to repair the dead brain or unhappy brain. It’s valuable for much more than just diagnosis. In my mind, every single one of these genes is a potential therapeutic target for stroke.

Polyomaviral clear leukocytes and monocytes drive the distinguishing genetic profile of ischemic stroke. But genetic expression of CD8 and natural killer cells are more pronounced in the fingerprint for Tourette’s syndrome. For migraine, monocyte platelet genes are the ones to watch. “It turns out that for autism, lupus, and rheumatoid arthritis, we can map these genes onto these cell types and they all differ.”

You can see a profile in every muscular disease. What we don’t know is how specific these profiles are,” he said. Not every disease will be equally amenable to categorization. Five genes in the blood differentiate neurofibromatosis type 1 and tuberous sclerosis type 2, for example.

The profile of Down syndrome involves 200 genes, and the genetic fingerprint looks different still in Down syndrome patients with congenital heart disease.

Dr. Sharp acknowledged the contribution of many colleagues in his pursuit of an understanding of blood genomics, including Dr. Yang Tang, who is also at the University of California, Davis.

Physicians, Others Face Greater Risk of Developing Parkinson’s

BY MARY ELLEN SCHNEIDER
Senior Writer

Physicians and individuals with 9 or more years of education are at an increased risk of developing Parkinson’s disease, according to a study by Dr. Roberta Frigerio of the Mayo Clinic in Rochester, Minn., and her colleagues.

Individuals such as construction and heavy workers, production workers, medical workers, and engineers who have more physically demanding jobs are at a reduced risk for the disease, the researchers found (Neurology 2005;65:1575-83).

The researchers examined the education levels and occupations of 202 individuals in Olmsted County, Minn., who developed Parkinson’s disease from 1976 through 1995. Each case was matched by age and sex to a general population control who was free of Parkinson’s disease and living in the same county. Of those individuals, 16 were able to obtain medical records for 196 cases and 196 controls. In addition, they obtained data from telephone interviews available for 149 cases and 149 controls.

The researchers compared the education and occupational status of patients with those of controls and also examined the history of taking medications known to be linked to Parkinson’s disease. They found that nonphysicians and people with less education were significantly more likely to be cases than controls. Physicians and individuals who had graduated from college were significantly less likely to be cases than controls.

The study was supported by grants from the Parkinson’s Foundation and the National Institutes of Health, among others, and was published in the November 29 issue of Neurology. Dr. Frigerio said that the findings do not mean that physicians do not get Parkinson’s disease. Rather, she said, the findings support the idea that there are more than one cause of Parkinson’s disease.

“More research is needed to figure out what these findings mean. For example, the findings could mean that being a physician or having more education is not a risk factor for the disease, which all female sex and personality. Parkinson’s disease is marked by a deficiency of dopamine, which is important to personality. A deficiency of dopamine could shape personality in a way that makes a person more inclined to sit at a desk and study, he said.

prior to their strokes had a significantly different genomic expression of 143 genes when their blood samples were compared with samples from patients who were not taking aspirin prior to enrollment in the Combined Approach to Lytic Evaluation of Fibrinolysis and rt-PA in Acute Ischemic Stroke (CLEAR trial).

“This is, in fact, a biologic response to dying tissue … white [blood] cells sensing dead brain or unhappy brain. It’s [valuable for] much more than just diagnosis. In my mind, every single one of these genes … is a potential therapeutic target for stroke.”

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