Does the fragile X gene protect against cancer?

Some genes considered deleterious can also be protective, and a new study suggests that this is true of the Fragile X gene mutation.

Fragile X, the most common inherited form of mental retardation, often causes autistic-like symptoms. The disorder occurs when a defective FMR1 gene on the X chromosome results in the absence of the protein FMRP. The defective gene contains far more repeats of a trinucleotide sequence than does the non-mutated gene.

Soren Schultz-Pedersen and colleagues recently used data from the Danish Cytogenetic Registry and the Danish Cancer Registry to calculate the incidence of cancer in 223 people with fragile X syndrome, comparing this to the incidence in the general population. The researchers identified four cases of cancer among the Fragile X group, while 11 cases would have been expected based on typical rates. They conclude that the cancer risk of individuals with Fragile X is only 28% that of the general population.

The researchers note that an earlier study investigating causes of death in a Fragile X population found that only 13 of 83 subjects died of cancer, a much lower rate than would normally be expected.

Schultz-Pedersen et al. say their data suggest the possibility that "the expanded trinucleotide repeats in fragile X syndrome protect against cancer," and that this finding could lead to insights into genetic mechanisms that protect against malignant transformations in cells.

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"Evidence of decreased risk of cancer in individuals with fragile X," Soren Schultz-Pedersen, Henrik Hasle, Jorgen H. Olsen, and Ursula Friedrich, *American Journal of Medical Genetics*, Vol. 103, No. 3, August 2001, 226-230. Address: Soren Schultz-Pedersen, Norrebrogade 20 4th floor, 8000 Aarhus C, Denmark.

Secretin's role in amygdala, cerebellum revealed

(continued from page 2)

themselves after depolarization. These cells are large neurons that appear to be responsible for communications between different tissue layers in the brain. Previous post-mortem studies have reported abnormal numbers and sizes of Purkinje cells in the autistic cerebellum, and researchers have created a rat model of autism by selectively destroying cerebellar Purkinje cells.

> The researchers say secretin appears to modulate the activity of GABA, a neurotransmitter, in the cerebellum. "These novel actions of secretin, which are distinct from those on the endocrine system, strongly support the hypothesis that secretin serves as a neuropeptide in the rat brain," they say.

"Our results... provide a link for the speculative relationship between secretin, cerebellum, and autism," the researchers say, "as well as an explanation for the potential use of secretin as a drug to treat this disease." They add that the effects of secretin probably extend beyond the cerebellum, because secretin and its receptor are also expressed in other brain regions.

"We are extremely excited," Chow says, "to see that our work supports strongly the role of secretin in the cerebellum and a connection between secretin and autism."

In additional research, scientists at Repligen demonstrated that secretin injected into the bloodstream of mice can cross the blood-brain barrier. This indicates that secretin injections can affect the functioning of the central servious system because, Herlihy says, "secretin is directly accessing the brain."

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"Neural expression of Fos protein in the central amygdala after intravenous injection of secretin," M. Goulet, P. Shiromani, W. A. Banks, R. Boismenu, and J. Rusche, presentation to the International Meeting for Autism Research (IMFAR), November 9 and 10, 2001, San Diego, CA. Address: Repligen Corp., Needham, MA 02494.

—and—

"Secretin facilitates GABA transmission in the cerebellum," Wing-Ho Yung, Po-Sing Leung, Samuel S. M. Ng, Jie Zhang, Savio C. Y. Chan, and Billy K. C. Chow, *Journal of Neuroscience*, Vol. 21, No. 18, September 15, 2001, 7063-8. Address: Dr. Billy K. C. Chow, Department of Zoology, Kadoorie Biological Sciences Building, University of Hong King, Pokfulam Road, Hong Kong, bkcc@hkusua.hku.hk.

—and—

"Secretin neurobiology," report of the Repligen Corporation, November 2001.

—and—

"The science of secretin," John Travis, *Science News*, Vol. 160, November 17, 2001.

Wakefield (cont. from p. 1)

the British government issued a report which concludes that the possibility that MMR vaccination causes autism in susceptible children cannot be ruled out based on current evidence. In addition, Harvard researcher Timothy Buie recently reported evidence supporting Wakefield's finding of an autism/gut dysfunction link (see page 2).

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"Autism parents left stunned as Wakefield is forced out," Lorraine Fraser, UK *Telegraph*, December 2, 2001. Dr. Wakefield will speak at the May and October Dan! Conferences.

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Melatonin may ease TD

The hormone melatonin can reduce symptoms of tardive dyskinesia, according to a new Israeli study of schizophrenics.

Tardive dyskinesia (TD), a serious movement disorder often caused by psychotropic drugs, causes involuntary facial and limb movements, tremors, and stiffness. Symptoms generally cannot be treated with medication, and cannot always be reversed by discontinuing drug treatment. (Several studies do show, however, that the use of vitamins E and/or B6 is often helpful in reducing TD—see ARRI 13/3, 12/4, 12/3, 10/2).

Eyal Shamir and colleagues tested the effects of melatonin on 22 schizophrenics with TD, with each subject undergoing six weeks of a placebo and six weeks of melatonin treatment (10 mg daily). Half of the subjects received the melatonin first, while half received the placebo first, with a four-week "washout" period between the two phases.

The researchers report that nine subjects exhibited a 30 percent or greater reduction in the severity of their TD symptoms, while 7 showed a more than 3-point drop in symptoms on the Abnormal Involuntary Movement Scale—a result considered significant. No adverse effects were reported.

"It remains to be studied," the researchers say, "whether the efficacy of melatonin will further increase with longer treatment or with larger doses of the hormone." They believe melatonin's effects may be related to its antioxidant properties, or to its effects on dopaminergic activity.

Melatonin, a hormone produced by the pineal gland, is available as an over-the-counter supplement, and studies show that it can reduce autistic children's sleep problems. The hormone appears to promote growth rates and general health, and reduces seizures in some children but may exacerbate seizures in others (see ARRI 13/4).

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"Melatonin treatment for tardive dyskinesia," Eyal Shamir, Yoram Barak, Irena Shalman, Moshe Laudon, Nava Zisapel, Ricardo Tarrasch, Avner Elizur, and Ronit Weizman, *Archives of General Psychiatry*, Vol. 58, No. 11, November 11, 2001, 1049-52. Address: Eyal Shamir, Abarbanel Mental Health Center, 15 KKL St., Bat-Yam 59100, Israel.

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"Melatonin may treat side effects of antipsychotics," Reuters, November 21, 2001.