

Canadian scientists discover giant gene

It may regulate brain development

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MEDICAL REPORTER, TORONTO

On the ninth floor of the Hospital for Sick Children, a team of young scientists crammed in a small warren of rooms has made a very big discovery.

Toiling elbow-to-elbow at computers capable of sifting through billions of bits of DNA, researchers suspect they have unearthed the largest gene that humans possess.

Its chemical recipe — expressed in letters of A, G, T and C — is so massive they were reluctant to print it out. On paper, the giant gene stretches like wall-to-wall carpet from one end of a hospital corridor to the other. It has about 100 times more chemical ingredients than the average gene.

To scientists, its impressive size makes sense: They suspect this Fat Albert of genes actually contains instructions to build the wondrous framework of the human brain.

And discovering it brings scientists a sizable step closer to understanding how the fetal brain develops. It also offers a distant hope that one day there will be ways to fix neurological problems that begin in the womb.

"Based on its function of regulating development in the brain, we can speculate that it also plays a role in certain diseases... and that there may be something we can do about those," says Steve Scherer, senior scientist at the hospital.

For example, researchers suspect that a defect in this gene may cause one form of hereditary deafness, in which children are born without hearing in both ears.

The Toronto scientists are now collaborating with researchers in France who are rounding up families with a history of the rare hearing disorder.

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THE GLOBE AND MAIL

CANADA'S NATIONAL NEWSPAPER • FOUNDED 1844 • GLOBEANDMAIL.COM • SATURDAY, FEBRUARY 10, 2001

THE GLOBE AND MAIL • SATURDAY, FEBRUARY 10, 2001

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Huge gene 100 times average known size

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The hope is that with the families' DNA samples, the Toronto group will be able to spot a mutation in the giant gene that accounts for their deafness.

"But because this is such a large gene, identifying these things will take a long time," Dr. Scherer says.

The giant gene is at the bottom end of chromosome seven, one of the 23 pairs of chromosomes in each human cell and the focus of the research. It represents the fifth in the family of genes that are believed to encode operating instructions for the human brain. All are larger than average genes and scientists suspect that they will ultimately discover that up to half of the entire human genetic blueprint is devoted to the 1.5-kilogram protoplasm between people's ears.

"It makes sense, that as the most complex organ — more complex than the heart or the liver — the brain is utilizing the most number of genes," Dr. Scherer says.

While scientists have pinpointed



Dr. Kazuhiko Nakabayashi holds a printout of the massive gene he helped discover at Toronto's Hospital for Sick Children. Dr. Steve Scherer, senior scientist at the hospital, holds a printout of an average gene.

the giant gene in human DNA, clues to its function have actually come from studies in mice. Proteins that the gene appears to produce, for example, are believed to be crucial in the first moments of life.

The brain begins as a hollow clump of cells in the weeks after conception. From the centre, cells begin duplicating exponentially and drifting to the outer edges of the clump, one generation after another. Eventually, these early brain cells become neurons and set up

camp in specific locations in what rapidly becomes the newly formed brain.

"[The gene] seems to control the signalling process between neurons in the brain, telling neurons where to go," Dr. Scherer said. Indeed, the 16 hours it takes for this gene to produce its protein suggests it controls a mission that takes weeks — not unlike pregnancy. Most genes can manufacture proteins in less than an hour.

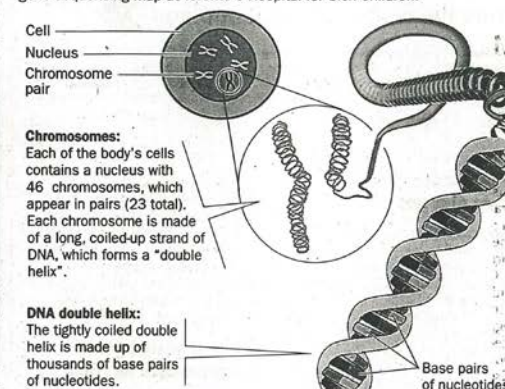
It was a Japanese postdoctoral fellow who identified the first

pieces of the massive sequence last summer. It is tricky, in his 21-month-old second language, for the young Kazuhiko Nakabayashi to describe how he feels about the accomplishment, which is to be published this week in the journal *Genomics*. "This could be largest gene in genome!" he said, "It was fun for me."

There's no guarantee, however, that Dr. Nakabayashi's find will stick in the record books. Thousands more genes are likely yet to be discovered.

A lesson in genetics

Scientists have discovered a new "super gene", thanks to a specialized gene-sequencing map at Toronto's Hospital for Sick Children.



Genetically superior

A gene is a sequence of base pairs (20,000 - 50,000), some of which make up proteins. There might be thousands of genes in a single chromosome.

The newly discovered gene is 100 times the size of an average gene, and made up of at least 2.3 million base pairs. Scientists suspect it contains the instructions to build and help operate the human brain from conception onward.

Sources: Graphic News

TRISH McALASTER/The Globe and Mail