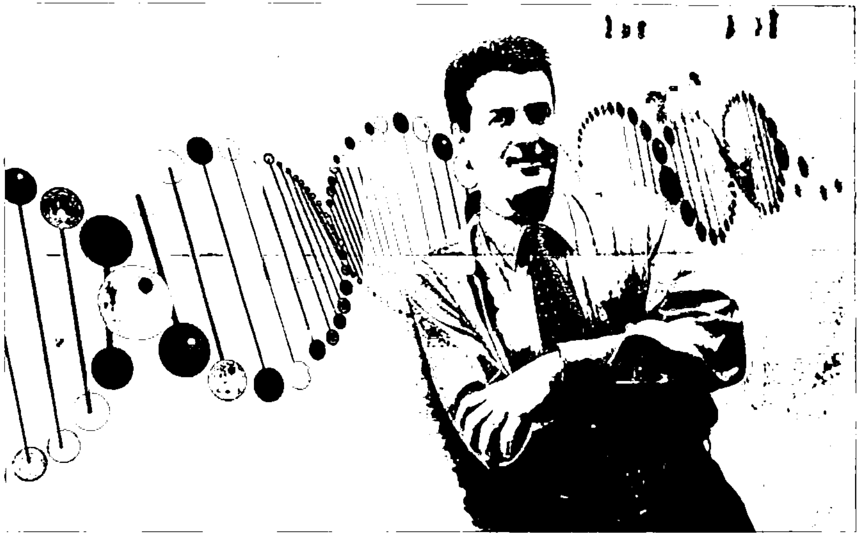


'EUREKA MOMENT': Windsor native Steve Scherer is a researcher at the Hospital for Sick Children in Toronto and is a Canadian member of a U.S.-British-Canada-Japanese research team which has found major variations in DNA among individuals.

Toronto Star photo: Carlos Osorio

Scientists redraw the genetic map

Windsor native at forefront of research

BY CRAIG PEARSON
STAR STAFF REPORTER

After two weeks of long hours early in 2004 and a flurry of new DNA experiments, producing seemingly odd results, researcher Steve Scherer did not yet know his Toronto team's work would help change our perception of human genetics.

The inkling that they had spotted something big came in his Hospital for Sick Children office a few weeks later, after a symposium on gene research when he met with one of the presenters and a fellow Canadian, Charles Lee, from Harvard University. The pair tiptoed around their recent research until they realized that each had independently discovered the same surprising results.

Their groundbreaking conclusion: humans differ genetically from one another more than previously thought.

"That's when we had the eureka moment," Scherer, a 42-year-old Windsor native, recalled this week. "After the workshop, we sat down and were just kind of looking at each other. So I kind of hinted at what we were seeing and he jumped in and said he was seeing the same thing. So we thought, it must be real because it has been replicated in two places."

After comparing their data, gathered using new technology called Array CGH (comparative genomic hybridization), or DNA microarrays, which Scherer likens to a "molecular microscope," the two agreed to combine their work. Their first article appeared in the summer of 2004 in Nature Genetics, though the two scientists felt they needed to confirm and expand their hypothesis.

So the two Canadians hatched a plan that would take two years, $6 million, and teams from Sick Kids Hospital, the Harvard Medical School, the Wellcome Trust Sanger Institute in England, the University of Tokyo, and the California-based Affymetrix Corp.

On Nov. 23 the international consortium, which included British project leader Matthew Hurles, published their findings in Nature, Nature Genetics, and Genome Research — sparking media coverage around the world. Instead of humans being 99.9 per cent alike, it turns out they're more like 99.5 per cent alike, enough of a margin to open realms of research.

Scherer's DNA findings could help scientists isolate the causes of certain diseases and perhaps abilities.

"It helps us understand ourselves better as humans, certainly helps biomedical science, and helps the social sciences as well," he said. "It's exciting."

The so-called Book of Life, the sequence of the human genome which scientists completed in 2004, reflected a blueprint of humans. Differences seemed no more than a typographical error here and there, a few switched letters in an otherwise exact textbook. Now, it appears, phrases, paragraphs and even pages of the Book of Life may be duplicated, missing or reversed.

HUMANS REDEFINED

- The Toronto team led by Windsor native Steve Scherer at the Hospital for Sick Children in Toronto was comprised of 12 researchers. Worldwide about 100 scientists, including Canadian Charles Lee of Harvard University, joined the two-year project.

Charles Lee

- In the 1980s, scientists began talking about the ultimate genetic goal: the complete sequencing of the human genome. A first draft of the Human Genome Project came in 2000 followed by another version in 2004.
- Recent DNA research supersedes some principles of human genetics developed since the days of Gregor Mendel, the 19th-century father of Mendelian genetics who studied pea plants, and of Jim Watson and Francis Crick, who discovered the DNA double helix in 1953

Scherer's team uncovered many copy number variants (CNVs), a once-obscure scientific term that has gained sudden notoriety. Prior wisdom held that humans inherit 23 pairs of chromosomes — one each from the father and the mother — which form the instructions that make people who they are. Their research shows we can actually receive two, three or more copies of chromosome segments and, in rare cases, none of other segments, and still be healthy.

The group studied the genomes of 270 volunteers from African, Asian and European ancestry and found that 12 per cent of the genome was variable in these samples.

Adrenalin rush

"Any time in science you have a new discovery, big or small, it leaves you with quite a thrilling feeling," Lee said this week about the excitement he felt examining DNA. "You're the first ones in the world to see this. That's what keeps us in science: the adrenalin rush when you see for the first time something no one else has seen."

As is common when exploring new horizons, Scherer and Lee's work is expected to raise ethical questions in various disciplines such as evolutionary biology and medicine, since we must rethink the concept of normality.

As the Independent in London said: "Scientists have discovered a dramatic variation in the genetic makeup of humans that could lead to a fundamental reappraisal of what causes incurable diseases and could provide a greater understanding of mankind."

"Now the feedback I'm getting is that this really changes our understanding of human genetics, and the implications are so widespread," said Lee, 37, who immigrated to Canada from Korea at age one, grew up in Grand Prairie, Alta., and now works as director of cytogenetics at the Harvard Cancer Center. "At the press conference in London, half the questions were on understanding genetic biology. The question that was asked a couple of times was, 'Does this mean there could actually be more genetic variations between humans and chimpanzees?' And I said, 'Absolutely.'"

Scientists previously considered chimpanzee DNA 98.5 per cent similar to its human counterpart. Now the guess is more like 96 or 97 per cent.

Whatever the DNA dissimilarities, the international consortium co-led by Scherer altered the way biologists will teach.

"I'm already changing my lectures for next semester," said Andrew Hubberstey, an associate professor of biological science at the University of Windsor. "This is huge. The theory used to be that you got one gene from each parent. This changes the way we look at that. Maybe that's not the case.

"This paper will be a major part of what I teach, there's no doubt about it."

Hubberstey says the research has affected language and perception.

"CNVs are a new term and yet they're talked about all the time, just since the paper came out," Hubberstey said. "The prevalence of CNV regions is what's interesting. If we differ with all these different genes, how can we ever say someone's normal?"

One potentially troubling area revolves around bioethics. If it has been proven that our genetic recipes differ greatly, even between cultures, then someone might try to argue that certain traits or certain people are inherently better.

But Scherer says such arguments would miss the point.

"I think what's going to happen, as always happens whenever there's a study on genetic variation, is that some people try to use the information to identify differences and to stigmatize certain populations," said Scherer, who in 2001 at age 37 became one of the youngest people ever to receive an honorary doctorate from the University of Windsor. "But our study, while it does show we are more different than we thought, genetically it also emphasizes that we are very, very similar. So 99.5 per cent of us is still identical.

"The beauty of it is it still confirms our common humanity."

Scherer, Lee and colleagues are now hard at work on Phase 2. They hope to develop technology to view individual nucleotides, instead of nucleotides in chunks, in order to take an even better snapshot of the human genetic map.

They might even shoot for an X Prize, which in 2004 awarded $10 million to the first private space flight. Now it will offer $10 million to the first team to successfully map 100 human genomes in 10 days, with the hope of ushering in a new era of personalized preventive medicine.

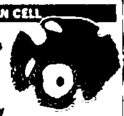
Copy number variants, after all, may help explain why most people with similar conditions react the same way to specific medication, but 10 per cent behave differently.

"What's going to happen maybe in five years down the road, we will have the ability to sequence a baby's genome before they actually leave the hospital," said Scherer, who attended Riverside high school before moving on to the University of Western Ontario and then the University of Toronto, where he earned a PhD in genetics and where he now teaches. "This will become one of the standard norms of medicine."

THE HUMAN GENOME

All of the genetic information carried inside a cell.

THE HUMAN CELL

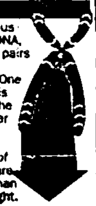


Some 100 trillion cells make up the human body. They compose every bodily substance such as blood, hair, bone, etc.

CELL NUCLEUS

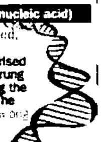
Inside every human cell (except red blood cells) is a ball-shaped structure called the nucleus — the control centre of the cell.

CHROMOSOME



Inside the nucleus are strands of DNA, packaged in 23 pairs of rod-shaped chromosomes. One half of the pair is inherited from the mother, the other from the father. It's now known that segments of chromosomes are more variable than previously thought.

DNA (deoxyribonucleic acid)



A double-stranded, spiral-shaped molecule comprised of chemicals strung like beads along the DNA "ladder." The order of codes along the ladder give directions to make the molecules that are essential for life.

GENE

A gene is a segment of DNA that carries the code for making one specific kind of protein. There are about 30,000 genes in a human DNA.

NUCLEOTIDES

A C T G

Chemicals that form the building blocks of DNA. These chemicals are represented by the letters A, C, G and T. A stands for adenine, C for cytosine, G for guanine and T for thymine. One letter sits at the end of each rung on the ladder of DNA so that A joins to T and C to G, forming a base pair. The letters, or nucleotides, spell out the recipe for a gene that encodes a protein.

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