

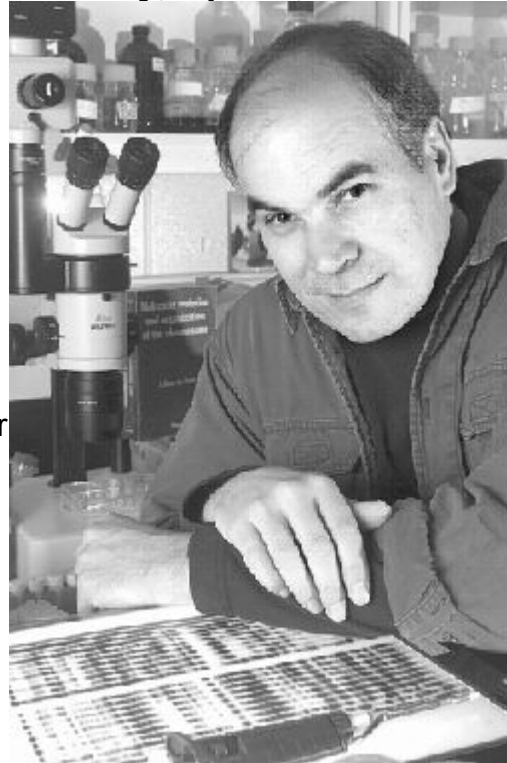
## **The Genome Project - An Uneasy Alliance with Industry** **By Tom Spears, The Ottawa Citizen, Tuesday, April 4, 2000**

The cellphone rings in Prof. Martin Petkovich's office. It's his office calling - his other office, the one where he keeps his alternate identity as a captain of industry.

Dr. Petkovich, cancer researcher, has spent years at Queen's University investigating the molecules that our genes produce, and how they do both good and bad things for us.

Dr. Petkovich, entrepreneur, is the co-founder and vice-president of Cytochroma, Inc. a biotech company partnered with a California pharmaceutical firm that wants to find new cancer drugs.

His Queen's office and his students are in Botterall Hall, a medical research building on campus. His corporate office and 12 employees are a short walk away, across a lawn full of pigeons, in the university's Bioscience Complex. That's the office that calls the cell phone he wears on his belt, reaching him in his academic office.



If this sounds confusing, it can be. Until he founded Cytochroma in 1996, he didn't need a cell phone. His work was research, period.

But like many gene researchers, he found himself frustrated with the lack of opportunity to make that research advance.

He tried going to existing pharmaceutical firms with his insights into the genes and how they work, but no one was interested in funding his work.

"I felt we might as well exploit the opportunities ourselves," he says now.

Spinning off small companies to exploit the fruits of research is increasingly popular for university scientists.

At Queen's alone there are about 11 spin-off companies, all supported with seed capital by Queen's own technology transfer arm - Partners in Technology at Queen's, or PARTEQ.

PARTEQ president John Molloy says about three-quarters of these companies are in life sciences. Some do genetics research, some do biology, others

informatics, instruments or software related to biotech. Many of them have several scientists within a single company.

The reason for the spin-offs is that their discoveries are brand new and unproved in the corporate world.

"It's very difficult to find someone (that is, a corporation) who's already out there and is willing to take on technology in this developmental stage," he says. To get value for new discoveries, "you have to do a lot of the work yourself."

That means setting up a new company that can get funding from a venture capital fund, he said. Their goal is simply to develop what they've learned to a more sophisticated level - one that can then be of use to a mainstream pharmaceutical firm.

"Most of these (PARTEQ) companies will not bring a drug to market themselves."

Dr. Petkovich's business isn't about finding genes just for their own sake. The goal is to design new drugs based on what the gene teaches him. Drugs to attack cancer, to control skin diseases, to help the body make the fullest possible use of ordinary substances such as vitamin A that, because of a genetic problem, it may be unable to use.

But the quest for a new generation of drugs begins with an attempt to find out what our genes do in the first place.

Once a gene is identified, the researchers look at the protein it produces. That's the chemical that genes make and send out into the body to put all this stored DNA code into action. Genes build proteins from amino acids from your food, and each gene builds and sends out proteins with a unique mission.

All of us probably have mutated genes in our bodies, he believes - genes that function poorly or not at all. "In some cases, this contributes to who we are, in some cases it causes a disease state," and in some cases it doesn't affect us because other genes will compensate for what's missing.

While gene therapy tries to find and replace a badly mutated gene, drugs leave the gene alone and focus instead on the protein tool kit it is creating.

The proteins form bonds with other molecules they encounter, such as hormones, the body's chemical signalling systems, and enzymes, which regulate chemical reactions everywhere in the body. The trick is to find drugs that will alter the job done by a protein from a mutated, unhealthy gene, or boost the power of good work done by useful proteins.

Big drug companies use a method called "high throughput screening." This is just

a fancy name for taking tens of thousands of drug ingredients and throwing them all at a protein or an enzyme that interests you to see whether any of the drugs stick to it.

Proteins are like electrical sockets: Each one will only allow a particular kind of chemical to bond with it, in a particular position, just as a socket will only take the right size of plug in the right position, and a light bulb or a foreign country's appliance plug won't fit at all.

So throwing many chemicals at the protein is like trying out many different kinds of plugs to see which ones fit the socket.

If a few chemicals do stick - by bonding with the protein molecule - these are candidates to become drugs affecting how that protein does its job in your body.

Some will inhibit it, plugging up the part of the protein that does the bonding and in effect shutting it down. Dr. Petkovich says this is like putting a child-proof plastic cap into a wall socket so a toddler can't stick a fork into it.

This is useful if it's a "bad" protein - for instance, one produced by a mutant gene that can cause disease.

But in this case it's also used to jam up molecules that destroys retinoic acid, a useful chemical that your body makes from vitamin A. This makes more of the vitamin A available to your body.

Retinoic acid helps the body fight skin disorders including psoriasis and acne, and may be useful in fighting cancer.

Other drug researchers are also using the structure of genes to design new drugs, says Prof. Karen Jackson, chairwoman of biology and marine science at Jacksonville University in Florida.

"Some mutations cause faulty proteins to be made, so they do faulty work."

Sickle cell anemia, for instance, has a misshapen hemoglobin molecule in the red blood cells, preventing those cells from doing a proper job of carrying oxygen.

"The path... to producing a working vaccine is seldom smooth," French microbiologist Xavier Nassif writes in a recent issue of the research journal *Science*. But there is an "enormous potential of bacterial genomics for discovering new therapeutic strategies to fight infectious diseases."

Dr. Petkovich's Cytochroma is now working with Allergan Inc., a big California drug maker, to investigate a "superfamily" of genes that carry the code for

cytochrome P450 enzymes.

Part of the task is to identify the genes and their functions, and then deciding whether blocking their function will be useful.

Change metabolic processes based on P450 enzymes, the company believes, and one can make different tissues in the body more able to use substances such as vitamins, natural steroids and drugs.

Founded in 1996, the firm began with \$350,000 in seed financing from University Medical Discoveries Inc., which is part of the Canadian Medical Discoveries Fund, a venture capital fund.

Then came \$2.1 million last February from three venture capitalists - CMDF again, Working Ventures and GeneChem of Montreal.

"It's a big change in a number of respects. Business has a different culture from science."

"I'm very much a scientist at heart," he adds. But he has to concentrate on making sure the pressure to run a profitable company doesn't get in the way of doing pure research.

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