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UVic knowlEDGE

Research and discovery at the University of Victoria

Genome detective

A UVic biologist probes the genetic mysteries of the human immune system

by Valerie Shore

Imagine trying to use a dictionary filled with three billion letters, but no words and no definitions.

In a sense, that's what scientists were handed last year when two international research teams announced to the world that they'd mapped the human genome — the three billion bits of genetic code that define who and what we are.

It was a huge milestone for science. But while presidents and prime ministers waxed poetic about "one of the most wondrous maps ever produced by mankind," genetic researchers were far more cautious. The real work, they stressed, has just begun.

"What we have now is a working draft of the genome," says UVic biologist Dr. Ben Koop, who was a participant in the Human Genome Project, one of the two international research networks. "It gives us a string of code in letters but we have no idea which letters represent which genes, and following that, what they do."

As an evolutionary geneticist, Koop seeks to understand how living things change over time. His eclectic research interests — on species as diverse as bats, wolves, sea snails and humans — all focus on the common theme of molecular evolution. "I'm intrigued by variation," he explains, "and it can all be traced back to the genes and their interactions with the environment."

Each of the 100 trillion cells in the human body (except blood cells) contains the entire human genome — all the genetic information necessary to build a human being. Inside each cell nucleus are 23 chromosome pairs, each of which contains the DNA for approximately 30,000 genes, the basic unit of heredity.

Genes, in turn, carry instructions for making proteins, essential components of all organs and biochemical processes. "Proteins are the body's workhorses," says Koop, "and specific genes tell them what to do and what their characteristics will be."

Koop's contribution to the Human Genome Project involved the identification of genes associated with T-cell receptors — key proteins that recognize and destroy foreign invaders such as bacteria, viruses and cancer cells. It's fundamental research that he plans to continue indefinitely.

"Many people think the genome is now complete, but there are still a lot of holes, many of which are enormously interesting in terms of disease," he explains. The immune system is particularly intriguing because that's where a huge family of genes has evolved to help the body recognize and fend off infection and disease.

"From one common ancestor, these genes have duplicated and specialized to the point that they can create billions of different types of T-cell receptor proteins," says Koop. "It's why our immune systems work so well."

But sometimes immune systems go haywire, and understanding why is the key to treating and perhaps preventing serious disease. Koop is also interested in a gene-rich but fragile area of the human genome known as 7q22. "It's very prone to breakage and re-arrangement," says Koop, "which can result in various types of cancers." It's also sensitive to substances such as pesticides, arsenic and caffeine.

Koop

Why this area is so vulnerable to mutation is puzzling. "From an evolutionary viewpoint, it doesn't make sense, which stimulates our interest even further," says Koop. "We need to find out why variation in this area seems to be so important."

Koop hopes to identify all of the genes in the 7q22 neighbourhood and what they do. "Ultimately, we want to know what genes cause cells to lose control over normal growth and death processes, and what role the environment plays."

facts from the EDGE

- Dr. Ben Koop is one of six Canadian scientists to be awarded a 2001 Steacie Fellowship from the Natural Sciences and Engineering Research Council. The award provides funding for two years of research uninterrupted by teaching or administrative duties.
- Koop is chair of the biology department and deputy director of UVic's centre for environmental health, which conducts research on the impact and influence of the environment on genetic organization and expression.
- Koop has been studying immune system genes for more than 10 years. He's looked at humans and mice, and he's about to investigate cows. As grazers, cows routinely deal with massive amounts of bacteria.

sharpen your knowlEDGE

- Browse the human genome for yourself via the National Center for Biotechnology Information, a division of the U.S. National Library of Medicine and the National Institutes of Health. It's the Web bible for all things genomic. **www.ncbi.nlm.nih.gov**
- What's a genome? A chromosome? And what is DNA, anyway? One of the features of the National Human Genome Research Institute Web site is a handy glossary of genetic terms. **www.nhgri.nih.gov**

on the EDGE of your seat

Roderick Haig-Brown, A Legacy
May 24 – July 6
Maltwood Art Museum & Gallery. Info: 721-6562
Exhibit on the life and times of writer and conservationist Roderick Haig-Brown (1908–1976), including books, artifacts, and his fly-fishing tackle collection.

UVic Alumni Association AGM and Awards Night
Wednesday, May 30. AGM: 6 p.m., dinner: 7 p.m.
University Club (formerly the Faculty Club)
Dinner tickets: $30. Reservations and info: 721-6000
At the dinner, Distinguished Alumni Awards will be presented to Kirsten Barnes (BA '93), Tim Price (BA '64), and Eden Robinson (BFA '92).

EDGEwise Going fishing

Ben Koop will soon have a big fish story to tell.

Koop is co-leader of the Genomics Research on Atlantic Salmon Project (GRASP), which will explore and map the genome of the Atlantic salmon and use the information to improve fish husbandry techniques, evaluate the health of wild populations, and enhance environmental monitoring from freshwater to ocean conditions.

The multi-million dollar project involves universities, government agencies, research institutes and industry from B.C. and across Canada, and ties into international genomics research programs taking place in Ireland and Norway.

The first step is to define the genome of Atlantic salmon by building a salmon gene "chip," a 1 x 3 inch glass slide on which about 40,000 genes will be placed and monitored to see how they're expressed.

"From the chip we can determine what the various genes do in different conditions," Koop explains. They'll be able to see which genes are turned on and off in, for example, fresh and saltwater environments, or upstream and downstream from an industrial site, or in fast and slow-growing fish, or healthy and sick fish.

What they find out will be useful for all species of salmon. "All the salmonids, which include Pacific salmon and trout, are so closely related that the information we get from one is applicable to the others," says Koop.

Several other UVic researchers are involved in the project — all from the department of biochemistry and microbiology. They are: Dr. Bob Olafson, who will use advanced proteomics technologies to identify key salmon proteins and their genes; Drs. Bill Kay and Terry Pearson, who will investigate the relationship between salmon genes and pathogens; and Dr. Caren Helbing, who will adapt the chips for monitoring gene expression in response to various environmental conditions.

GRASP is being funded by Genome Canada and is conditional on its B.C. arm, Genome BC, raising matching funds from the provincial government and other sources.