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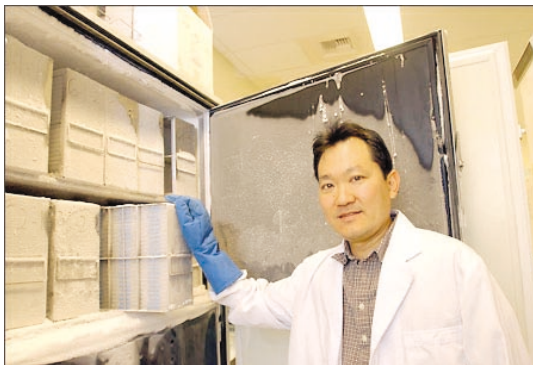
Seattle lab designing key to unlock genetic secrets

The human genome project has given rise to a new kind of science in which animal genomes are compiled for use as tools to understand human genetic code.



Ron Wurzer / P-I

Researcher Chris Amemiya displays containers holding genome libraries of a crocodile, top, and an armadillo at his lab at Benaroya Research Institute.

By CAROL SMITH
SEATTLE POST-INTELLIGENCER REPORTER

Chris Amemiya's personal human genome project arrived earlier this month, a few days late but with all the requisite baby parts: 10 fingers, 10 toes, a tiny nose and a string of DNA 3 billion units long.

While baby Amemiya (rhymes with mama mia) gets used to working those parts, her daddy is busy figuring out how all the parts work.

Amemiya, 43, is one of the founding fathers of a new breed of genetic science called comparative genomics. A genome contains all the DNA data of a given organism, but much of it is genetic jabberwocky — long sequences signifying nothing.

With comparative genomics, however, scientists are creating a kind of genetic Rosetta stone, giving them a way to interpret the vast string of decoded letters unraveled by the human genome project.

"The human genome is only useful if you have something to compare it to," said Amemiya. "Otherwise it's almost meaningless."

To help decipher the code, his lab at the Benaroya Research Institute at Virginia Mason Medical Center is making genome "libraries" of various creatures, one of only three places in the country doing this highly specialized work.

By comparing these gene sequences to those of humans, scientists will be able to learn where genes are located and more about what each one does and how it's controlled.

"There's a lot of black magic that goes into this," said Amemiya, winding his way through lab benches where he and his 14 lab partners have teased apart the instruction codes for everything from armadillos to African elephants.

"Sometimes it works, and sometimes it doesn't."

Amemiya's unassuming manner belies both the enormity of the task ahead of him and his reputation as the man to do it. If he were to sit and read a transcript of the human code to his newborn daughter, it would take him nearly a decade.

The trick is figuring out which segments are code for genes and which are filler. (This is the equivalent of figuring out which lines in the book you can skip before your little one catches on.)

"The vast majority is non-coding," he said. When comparing two genomes side by side, most of the sequence will appear random and won't match up. But certain areas will be similar, indicating likely spots for genes.

Scientists are also especially interested in the snippets on either side that turn them on and off.

Amemiya, who is also an accomplished jazz musician and golfer, has a reputation for being both deft and creative at coaxing the libraries into shape.

"My running joke is, we wouldn't have gotten this grant if it didn't have his name on it," said University of Washington biology professor Scott Edwards, who is working with Amemiya to build libraries of some ancient reptile species and the emu, a large flightless bird.

To create these archives, Amemiya and his lab workers break the DNA into fragments, cloning each chunk into a strain of bacteria. These "Bac-libraries" are stored in trays stacked in fancy freezers with each location on the tray given a Dewey Decimal-like locater code.

Amemiya, a former geneticist in the pediatrics department

at Boston University Medical School, was recruited to Seattle two years ago to help launch Benaroya's program.

"We wanted someone on the leading edge, technically," said Pat Concannon, director of the molecular genetics program at Benaroya. "He has an insightful mind — he can connect disparate pieces of information."

For his part, Amemiya was drawn to this new field by chance.

"I was beginning to be interested in more basic kinds of questions," he said. And Seattle had become a hotbed for genomics research.

Lee Hood, who helped invent some of the technology that made DNA sequencing possible, was spearheading the ambitious Institute for Systems Biology to address the complexities of deciphering the genome. In addition, the University of Washington and Fred Hutchinson Cancer Research Center were ramping up their genome work. So far, in addition to the armadillo and the elephant, Amemiya's archive includes genomes for the alligator, bat, opossum, rat, shark and coelacanth, a "dinosaur fish" once believed extinct and long thought to be the missing link between land and sea creatures.

This esoteric zoo wasn't chosen at random.

"Every organism being proposed (for a library) has some facet of biological development of interest to the study of human health," he said. Armadillos, for example, are the only animal, besides humans, that get leprosy.

Rats are of keen interest because they've been used for so much pharmaceutical work. And the coelacanth, which was rediscovered in the 1930s, intrigues people who study limb development.

"It's literally a living relic from another time," he said. "The fossil record can only tell you so much."

The coelacanth (pronounce seal-a-kanth) is sometimes called "Old Four Legs" because its fins look much like limbs. Understanding how genes turn into fins in that species, but legs in another, could one day give scientists ideas about ways to induce tissue regeneration.

Amemiya goes beyond just cataloging genomes, however. He also sometimes retrieves them. He just returned from a six-week stint in Antarctica tracking down the eerie "vampire fish," so called because of its white flesh and clear blood.

The fish lack the red blood cells that other animals need to carry oxygen because they're able to absorb oxygen directly from supercold water. Understanding it better could one day help scientists create synthetic blood.

Fishing off an ice breaker was a long way from the warm waters of Hawaii where he grew up and did his formative specimen collecting.

"I was always bringing things home," said Amemiya, the youngest of five children. "I thought I was going to be the next Jacques Cousteau." But a college epiphany convinced him the future lay in the study of genes.

When Amemiya was born, scientists had only recently discovered that DNA was shaped like a double-helix. The idea of decoding the whole genome was a dream as distant as a galaxy.

Now as his first child enters the world, people are already talking about understanding how to control the 30,000-some genes that run the human body.

"It's mind-boggling," he said. "Even for those of us in genetics. The sky's the limit."

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