
ROYALTY-FREE/CORBIS

A jumping off point

The recent flood of genome sequences has given evolutionary genetics a boost. **Ricki Lewis** takes a sharp look at a varied field.

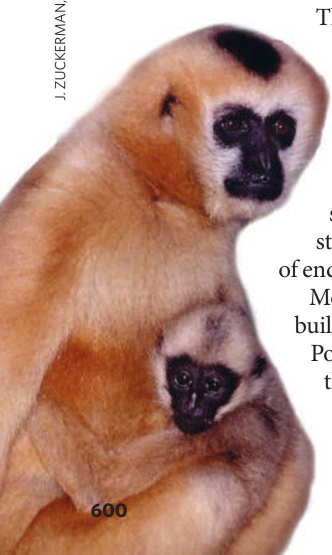
The field of evolutionary genetics is itself in the midst of astonishingly rapid evolution. For decades limited largely to theoretical considerations and a gene-by-gene focus, the field blossomed after the first genome was sequenced in 1995. Since then, researchers have been able to pose new types of questions and pursue the answers with experiments barely imaginable a generation ago.

Armed with hundreds of sequenced genomes, today's evolutionary geneticists tackle problems as diverse as tracing the origins of infectious diseases, explaining rampant obesity and conserving endangered species. The field actually embraces two research areas: how genes underlie evolutionary processes, and how genes and genomes themselves evolve.

Such broad questions invite comparisons across species and data sets, says Kateryna Makova, a biologist at the large Center for Comparative Genomics and Bioinformatics at Pennsylvania State University in University Park. Even a small department will offer varied research opportunities.

The five-member School of Population and Evolutionary Genetics at the University of Nottingham, UK, for example, investigates bacteria, insects, snails, slugs and a 'frozen ark' of stored DNA from thousands of endangered animal species.

Modern evolutionary biology is built on a foundation of genetics. Powerful new tools complement the imaginations of researchers intent on teasing out clues to the past from genes and genomes. And there is no shortage of data to mine. As of September 2006, a total of 429 complete genome sequences have been published, according to the Genomes OnLine Database, and ongoing projects will add another 1,000 (see 'The role of genomics'). "It will be very interesting to adapt the longstanding theoretical understanding of the interactions among selection, migration, genetic drift, mutation and demographic change to deal with these very large data sets," says John Brookfield, an evolutionary geneticist at the University of Nottingham.


J. ZUCKERMAN, GIBBON CONSERVATION CENTER

From the lynx to the gibbon: today's study of genes and evolution is wide-ranging.

In the money

Funding is robust. In 2006 in the United States, for example, the National Human Genome Research Institute (NHGRI) budgeted $133 million for its five-centre large-scale sequencing research network, according to agency spokesman Geoff Spencer. The spectacular growth of The Institute for Genomic Research (TIGR) in Rockville, Maryland, launched in 1992, illustrates just how dramatically the field is booming. A not-for-profit research organization funded by private and government sources and home of the first genome sequence — that of *Haemophilus influenzae* — TIGR's Comprehensive Microbial Database now boasts more than 300 sequenced genomes.

The time element distinguishes evolutionary genetics from much of biology. Most geneticists are concerned with how present-day adaptations protect individuals. An evolutionary geneticist, explains Brookfield, looks backwards, hypothesizing how modern gene or genome structure reflects selection driven by past environmental factors. "Evolutionary genetics gives us a 'common yardstick', a scale that applies to all measurements of genetic change," says David Lunt, a molecular ecologist at the University of Hull, UK.

Makova says that evolutionary geneticists need the "ability to integrate complex concepts from

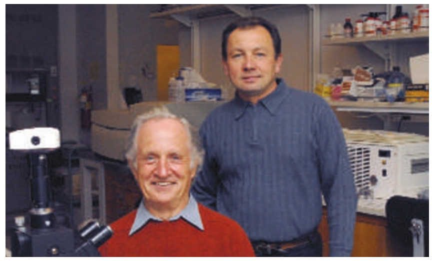
THE ROLE OF GENOMICS

Today's young evolutionary biologists may not remember a time when genome sequences weren't readily available. However, having such sequences at one's fingertips is not an endpoint in the research process, but a new type of beginning. Creativity and imagination are still key to success in evolutionary genetics.

Eventually the correlative data obtained through evolutionary bioinformatics will have to be rigorously tested in experimental models, notes Petr Tvrdik, a postdoctoral fellow at the University of Utah. Still, he emphasizes that genome sequences are critical in filling out the branches of evolutionary trees.

Angus Davison of the University of Nottingham has designed several courses in evolutionary genetics; he has found expressed sequence tags (ESTs), which herald protein-encoding genes, are more useful than entire sequenced genomes. He works on molluscs, not one of which has so far had its genome sequenced. "It is not just the sequenced genomes that are providing the impetus — the sheer volume of sequences, especially ESTs, from non-model organisms has had a big impact," he says.

Although he appreciates what genomics has done for biology, evolutionary biologist David Lunt challenges its value in evolutionary research. "Although genomic projects produce a truly impressive quantity of data, they have not been designed to address evolutionary questions," says Lunt, based at the University of Hull, UK. "I think we have got wrapped up in sound bites and buzzwords and vague possibilities for the future without really seeing what it can actually do for us now." **R.L.**



Petr Tvrdk (right) and his lab chief Mario Capecchi.

different disciplines, such as biology, statistics and computer science". And just as a species survives because of its ability to adapt, a successful evolutionary geneticist must adapt to a "diversity of software and computer platforms", says Blair Hedges, a biologist at Pennsylvania State University. Other skills are vital too. "It takes persistence. I think the most important skill is to read a lot, understand and remember," says Lunt.

Research bridging evolution and genetics may take place at a computer or lab bench, or in the field. A project at the University of Utah School of Medicine in Salt Lake City illustrates the creativity that can drive experimental research. Postdoctoral fellow Petr Tvrdik has reversed what may have happened over evolutionary time, by generating mice with a non-functioning homeobox (*hox*) gene that would normally control facial expression, then restoring it by adding the regulatory region of a related *hox* gene.

His experiments tests the long-held theory that members of gene families duplicated and diverged from a single gene over time, some members retaining the ability to affect others. "Our example shows that critical theoretical information is required in combination with experimental expertise to tackle the complex questions of evolutionary genetics," says Tvrdik.

Diverse directions

Research in evolutionary genetics takes many forms. For instance, any experiment that uses a gene in a model organism to discover a similar gene in a different species (such as our own) uses an evolutionary genetics approach. Genome similarities have driven the NHGRI to include diverse species in the genome sequencing projects it funds. The most recent candidate, a gibbon, will join five other non-human primates. Also slated for genome sequencing are ten modern species whose ancestors straddle the boundary between unicellularity and multicellularity.

Many aspects of human health and disease have arisen from the temporal tango engaged in by our genomes and the environment. Current epidemics of diabetes and obesity, for example, may reflect natural selection of gene variants that fostered nutrient storage during long-ago famines. Understanding viral diversity and evolution has helped identify the cause of severe acute respiratory syndrome (SARS). "If we can sequence a gene, put it into a tree of life, and find its close relatives, we can then begin to understand what type of beast our new disease is," says Lunt. Even Tvrdik's reconstruction of a half-billion-year-old gene in mice may have an impact on human health care by suggesting therapy that coaxes one gene to rescue another.

Marianne Bronner-Fraser and Angus Davison revel in the field of evolutionary genetics.

Conservation biology also uses evolutionary genetics. At the University of Uppsala in Sweden, evolutionary biologist Hans Ellegren and his group reconstruct histories of endangered wolves and lynxes from DNA in the excrement and hair of modern animals and 200-year-old museum specimens. The Swedish Research Council has funded him to found a Centre of Excellence in Evolutionary Genomics.

And the discipline is aiding our understanding of cancer. Marianne Bronner-Fraser, who heads the Centre for Excellence in Genomic Science at the California Institute of Technology in Pasadena, is examining neural-crest formation in zebrafish and chickens — models for more complex vertebrates. Human diseases that stem from neural-crest anomalies include melanoma, neuroblastoma and neurofibromatosis. The funding for the centre is $18 million over the next five years.

Branching out

In training for a career in evolutionary genetics, the department name is not as important as faculty interactions. "A narrow group, such as our 'population and evolutionary genetics' group, within a broad department, is probably best," says Angus Davison of the Institute of Genetics at the University of Nottingham. Brookfield suggests joining a genetics department that offers different subdisciplines, such as developmental genetics and palaeobiology. And Makova thinks that getting faculty members actively interacting and working in the area is key. "It can be in the same department, but it doesn't have to be. We have a centre with weekly meetings," says Makova, who draws from biology, biochemistry and molecular biology, anthropology, plant pathology, entomology and animal-science departments.

A career in evolutionary genetics weds the application of new tools and technologies to the imaginative exploration of how biodiversity came to be — an enticing goal. "The really important breakthroughs come from understanding a problem in a way nobody else does, and that is rarely accomplished by examining the minutiae more closely than others," says Lunt. "It's a holistic approach that is true of science in general." ■

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