to redefine genetic testing. "We will be identifying risk at the level of the potential child, … not at the level of donor or client," Morriss and Silver write in an e-mail. But they admit that identifying risk in a potential child might implicate a parent. If someone wants to know more, GenePeeks "will provide raw genotype data to donors or clients" upon request, "and we will encourage them to have it interpreted." The company plans to consult with its lawyers to determine whether the informed consent already signed by sperm donors is enough to cover the deeper sequencing they plan to do. They also plan to partner with biomedical ethicists, although they decline to name anyone who might participate.

Standards now vary for gene testing of sperm and egg donors across the industry. California Cryobank, a large sperm bank headquartered in Los Angeles, follows guidelines of the American College of Medical Genetics and Genomics, which recommends that anyone planning a pregnancy be tested to see if they carry mutations for cystic fibrosis, spinal muscular atrophy, or eight other diseases in a panel associated with Ashkenazi Jewish ancestry. California Cryobank also performs additional genetic testing in certain circumstances. For example, if a female client knows she carries a mutation for a particular disease and hopes to use a donor, the bank may ask the donor if he is willing to be tested for carrier status for that disease as well.

"We probably coordinate about 100 requests like that a year" and always check back with the donor for additional informed consent, says Pamela Callum, a genetic counselor at California Cryobank. "We never want to turn around and say to a donor, 'Hey, we tested you for this and we didn't tell you.' " All donors are offered the chance to learn their genetic testing results.

Callum worries about ever-expanding gene testing panels, especially when the results may be tough to interpret. "It's really hard to give consent" if the test provider says, " 'We're going to look at all your DNA, [but] we don't really know what it means.' "

With genetic technology advancing fast, a company like GenePeeks may be inevitable, some say, to help sperm- and egg-donor operations keep pace. But how far will the company go as its testing strategy develops? "Are they going to test for albinism, risk of deafness, risk of being short?" Caplan wonders. "Once you get into this, you're quickly sitting face to face with the value question of what counts as a difference that should be classified as a disease, what counts as a difference that should be worth disclosing."

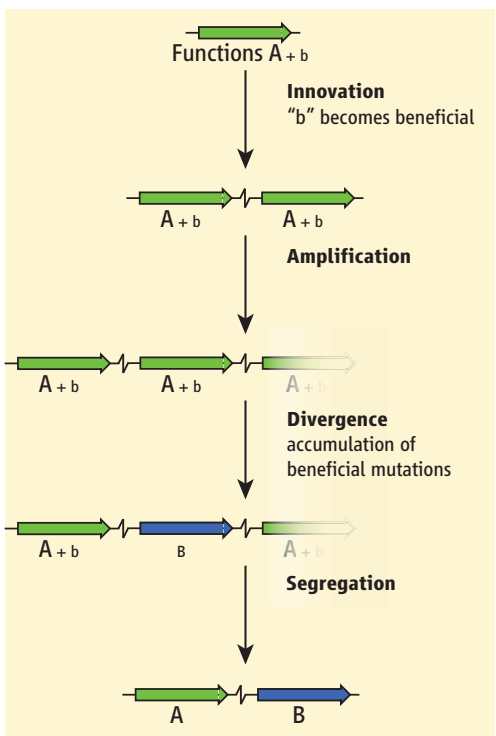
–JENNIFER COUZIN-FRANKEL

EVOLUTION

Gene Duplication's Role in Evolution Gets Richer, More Complex

In 1970, geneticist Susumu Ohno proposed a simple, yet elegant, idea: New genes arise when a hiccup during cell division produces an extra copy of an existing gene, and that spare copy is free to mutate and take on new functions. This mechanism, he argued, is the single most important factor in evolution. His book, *Evolution by Gene Duplication*, quickly became a classic that's still cited today, 12 years after his death.

No one is casting aside Ohno's tome, but some say it's time for an update.



Expanding the genome. Selection on double-duty genes helps prompt gene duplication.

An experimental evolution study in bacteria, presented on page 384, shows that at least some genes take another route to giving an organism new functions. And other recent work has established that partial copies of genes—rather than complete duplications of genes or genomes, the focus of Ohno's work—regularly become useful. All told, a growing body of research demonstrates that Ohno's ideas were a little too simple. "In the past decade, we've realized there's additional complexity" to evolution by gene duplication, says Richard Meisel, an evolutionary geneticist at Cornell University.

In 1932, about 20 years before scientists demonstrated the structure of DNA, evolutionary biologist J. B. S. Haldane suggested that gene duplications might be important to evolution. Ohno greatly elaborated on the idea. He proposed that mutations could accumulate in a complete copy of an existing gene because it would not be under natural selection to remain unchanged. In most cases, the extra gene eventually disintegrates, but sometimes the mutations would impart a new function on the copy's protein product. If that function was beneficial, then natural selection would kick in to preserve that copy and its useful sequence.

In the late 1990s, Michael Lynch, an evolutionary biologist now at Indiana University, Bloomington, proposed that twinned genes would also both stick around if they divided the original gene's work between them: Each might be expressed to a lesser degree or in different tissues, or code for distinct parts of the original protein. Several studies bore out his "subfunctionalization" theory.

But John Roth, a microbiologist at the University of California, Davis; Dan Andersson, a microbiologist at Uppsala University in Sweden; and their colleagues weren't completely satisfied with those explanations. Given natural selection's tendency to purge unnecessary genes, how would the gene copy stick around long enough to take on a new or subfunction? In 2007, this team proposed a different model for evolution by gene duplication, one in which selection prompted the temporary formation of gene copies.

In their scenario, the best candidate for gene duplication is a gene whose single protein product not only performed its primary job but also could carry out a secondary, nonessential function. If new conditions arose that made the secondary function crucial for survival, it would become advantageous for a duplicate gene, even multiple copies of the gene, to arise to meet the need for more of that protein. Once a mutation in one extra copy improved the resulting protein's efficiency in performing this secondary function, that duplicate's perpetuity would be guaranteed, and other extra copies

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would disappear, they suggested. The original gene would continue carrying out the primary function.

Now Andersson, his postdoctoral fellow Joakim Näsvall, Roth, and colleagues have documented this process in bacteria. Näsvall first screened mutant *Salmonella* for one that could still make a little tryptophan even though the researchers had disabled the gene for an enzyme, called TrpF, normally needed for the amino acid's synthesis. Tests showed that this ability arose in *Salmonella* because its version of the gene, *HisA*, for making the amino acid histidine, encodes a protein that could also craft tryptophan from its precursors.

Näsvall put this dual-function gene and a gene for yellow fluorescent protein into *Salmonella* bacteria lacking typical *HisA* and *TrpF* genes and grew them on media lacking both those amino acids—an environment that should select for microbes able to make both substances on their own. The intensity of the yellow fluorescent protein was a quick indicator of the increase in gene copy numbers.

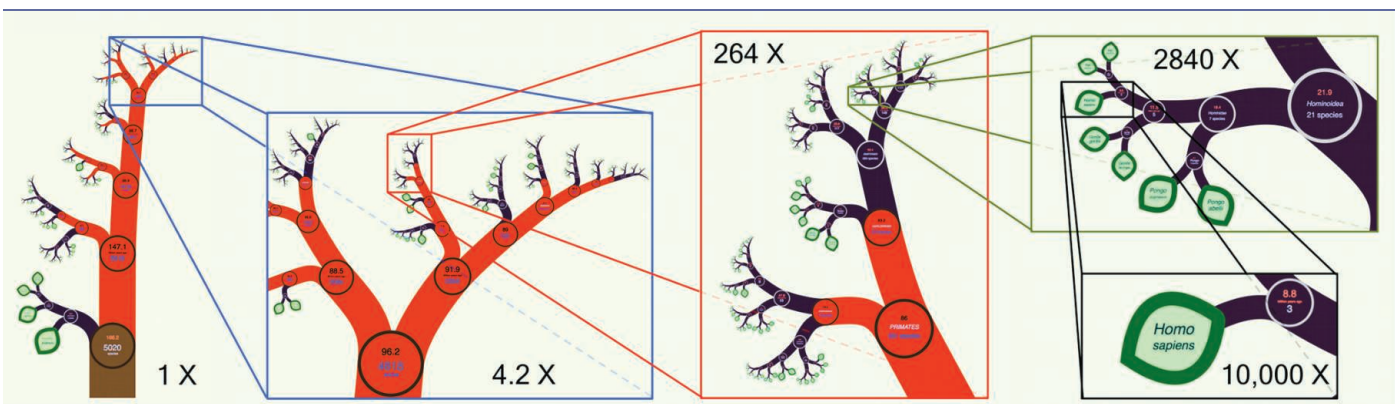
At first, the bacteria grew slowly, taking 5 hours to double their population. But in several hundred generations, that doubling time plummeted to about 2 hours. Over the course of a year—and 3000 bacterial generations—Näsvall periodically examined the genome of the microbes. He found that the single introduced copy of the dual-function *HisA* gene became amplified into multiple copies. And in some strains, one copy mutated to become much more efficient at making tryptophan and another excelled in making histidine, evidence of the evolutionary process Roth, Andersson, and their colleagues had proposed.

"Ohno will go down as a very important historical figure, but Andersson has the new model for how genes duplicate," says Antony Dean, a microbial evolutionary biochemist at the University of Minnesota, Twin Cities. "His theory is square one."

Other researchers have previously explored the idea that multifunctionality in genes can promote duplication, Meisel says, but this "is a nice, elegant experimental system, and the model seems to be supported." He cautions, however, that this process might be limited to bacteria and viruses. But Dean and Austin Hughes, an evolutionary biologist at the University of South Carolina, Columbia, suspect it's more common. No matter what, Näsvall's experiment will encourage more experimental tests of gene-duplication scenarios, Hughes says.

In a review in the September *International Journal of Evolutionary Biology*, evolutionary geneticist Vaishali Katju of the University of New Mexico, Albuquerque, drew attention to another simplification by Ohno. She documents numerous cases in which partial duplications of a gene, some of which acquire additional DNA, perhaps during the copying process, have become key precursors to novel genes. The work "enriches Ohno's theory by showing that two gene copies need not be identical at birth," says Jianzhi Zhang, an evolutionary geneticist at the University of Michigan, Ann Arbor. "Ohno would be pleased with these additions and modifications."

–ELIZABETH PENNISI



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BIOINFORMATICS

New Way to Look at Life

Ever since Charles Darwin, biologists have been building trees to show how organisms are related to one another. Now, computational biologist James Rosindell of Imperial College London and his colleagues have come up with a tree that outdoes all trees. Called OneZoom, the approach works like Google Maps: A user can drill down the tree's trunks, branches, and tips to view ever-finer details, and the structure can incorporate an infinite amount of information. (See www.onezoom.org.)

The concept is based on fractal geometry, in which patterns repeat themselves at different scales. Rosindell's open-source program embeds biological data—text, graphs, etc.—he and Luke Harmon of the University of Idaho in Moscow reported this week in *PLoS Biology*. "It seems to be a very elegant solution to a problem that's been widely recognized in evolutionary biology: how to have a tree of life that's visually appealing and accurate," says Richard Ree, an evolutionary biologist at The Field Museum in Chicago, Illinois.

Researchers can use the program to view their own phylogenetic data and can add information to the nodes, such as references, links to other Web sites, and even whether a species is endangered. OneZoom is for computers only, however. The simplest way to represent the bacteria, if printed out, would be 2000 kilometers long, Rosindell says. Over the next year, a large-scale project sponsored by the National Science Foundation called the Open Tree of Life plans to produce one tree encompassing 1.8 million named species. "Until I saw [OneZoom], I was apprehensive about how we were going to do this," Ree says. But he thinks OneZoom may offer a solution.

–ELIZABETH PENNISI

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