MEETING EVOLUTION '99

Development Shapes Evolution

MADISON, WISCONSIN—Once rarely considered in evolution discussions, development was a hot topic for researchers here for the Evolution '99 meeting, held from 22 to 26 June.

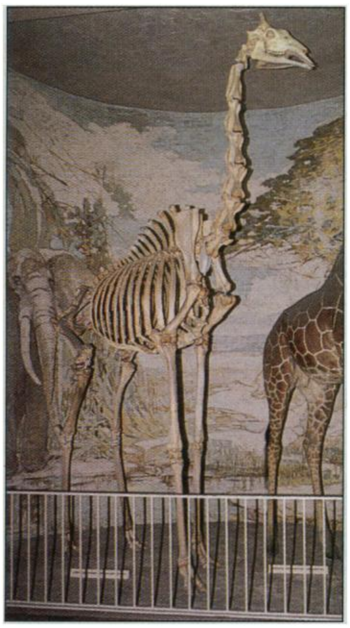
Why Most Mammals Are Neck And Neck

Bats and giraffes look nothing alike and live very different lives. Despite that, they and most other mammals have exactly the same number of neck vertebrae: seven. Generations of biologists have puzzled over this strange consistency. Many other skeletal components do vary according to the needs of the individual organism, and the number of neck vertebrae can vary dramatically in other animals, such as birds. A swan, for example has about 25, while swifts have just 13. Now, Frietson Galis, a functional morphologist at Leiden University in the Netherlands, may have ferreted out the reason why mammals have maintained a seven-vertebra neck over millions of years of evolution.

Based on her searches of the scientific literature, she proposes that a serious developmental constraint limits change in mammalian neck vertebrae. As Galis reported at the meeting, any alteration of the genetic program responsible for generating those seven chunks of backbone greatly increases the risk for embryonic cancers—those arising because embryonic tissue continues to proliferate instead of specializing into a particular organ. The constraint, she argues, operates in mammals but not in other, less cancer-prone animals. Gunter Wagner, a developmental biologist at Yale University in New Haven, Connecticut, says the proposal is "the first rational explanation for a phenomenon that has never really made sense." (The work also appears in the spring issue of *Molecular and Developmental Evolution*.)

Galis first began to consider the cancer connection after a colleague who studies neuroblastomas, a type of brain tumor that arises from embryonic neural tissue and usually occurs in children, mentioned that many neuroblastoma patients also have congenital rib abnormalities. And when she searched the medical literature, she discovered that others, including R. Schumacher of the University Children's Hospital in Mainz, Germany, and Steven Narod of the University of Toronto, had also noted an association between skeletal abnormalities and childhood cancers.

Galis then learned that researchers had found that mouse strains tend to develop abnormal ribs when one or another of the *Hox* genes, which help set up the organization of the backbone and other parts of the embryo, is inactivated. And other studies in mice had linked the inactivation of *Hox* genes or their regulators to cancer. For example, some found increased rates of leukemia and related cancers when the *Hox* gene regulator M11 was inactivated or when the *Hoxb-8* gene was overactive; others found an increase in intestinal cancer when another *Hox* regulator, Cdx2, was missing. Taken together, these findings are making it "much clearer that *Hox* genes can serve a dual function," helping promote cell growth as well as tissue organization, says Narod.



Seventh (vertebrae) stretch. Most mammals, even giraffes, have seven neck vertebrae.

Consequently, Galis says, mutations in the genes would be highly deleterious, especially if combined with other mutations that lead to cancer. As a result, *Hox* gene changes affecting neck vertebrae number are unlikely to persist, even if they make a neck better suited to a particular organism's way of life, Galis concludes.

Reptiles aren't subject to this constraint, she proposes, because they have lower metabolic rates than mammals and are thus less likely to produce highly reactive oxygen free radicals that can damage the DNA and produce mutations that, in conjunction with altered *Hox* gene activity, lead to cancer. And neither are sloths and manatees, which also have lazy metabolisms—and six to nine neck vertebrae. That leaves birds, which also have high metabolic rates, but vary their neck vertebrae as freely as reptiles.

Apparently, high metabolism in birds doesn't exact the same mutational cost, Galis learned. Studies show that pigeon and canary cells do not generate the large numbers of reactive oxygen molecules that mammalian cells do. Perhaps as a result, the cancer rate in birds is about half that in mammals, and most of the cancers that do develop are caused by viruses. "The difference is really striking," Galis says.

Galis will have a difficult time proving that cancer risk limits the number of mammalian cervical vertebrae to seven. Even so, notes evo-devo biologist Jessica Bolker of the University of New Hampshire, Durham, "she's done a good job of pulling together some really diverse kinds of data to come up with a really convincing hypothesis."

Sex and the Single Cockroach

Most of us don't even want to think about cockroaches that can clone themselves. But evolutionary biologist Allen Moore of the University of Manchester in the United Kingdom and his colleagues cherish one such creature, the African cockroach *Nauphoeta cinerea*, as an opportunity to learn more about why so few organisms reproduce asexually, even when they could make do without a mate.

As Laura Corley, a former graduate student in the Moore lab, reported at the meeting, the roach shows that asexual reproduction is a hard road. Working with Moore and his wife, developmental biologist Patricia Moore, when the team was at the University of Kentucky, Lexington, Corley found that only a few *N. cinerea* females—those with the most varied genetic makeup—are able to reproduce without sex, and they generate few offspring.

Quite a few sexual species, particularly insects, can sometimes switch to parthenogenesis, in which their unfertilized eggs develop into new individuals. Evolution should favor the process, because it allows an individual to pass all of its genes to each progeny, instead of the 50% they transmit by sexual reproduction (*Science*, 25 September 1998, p. 1980). But even in insects that can make the switch, asexual reproduction is rare—posing a long-standing puzzle in biology.

One reason, Corley and her colleagues found in *N. cinerea*, may be that only a few individuals within a species are capable of parthenogenesis. They first separated out immature female cockroaches from their lab colonies to prevent them from mating. Only 14% to 44% of these virgin females produced young. The researchers then looked at the genetic makeup of the females that could

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not reproduce on their own and also that of the females that could and their offspring.

They focused on six genes that they found to be polymorphic, meaning that they exist in several different versions. The researchers found that the two copies of each gene were much more likely to be different in females able to reproduce parthenogenetically than in other *N. cinerea* females. The single moms "were a very specific subset of the population," says Corley, who is now at the University of Wisconsin, Madison. "It suggests that it's good to be genetically variable; it allows those individuals to be more flexible."

The researchers don't know why that is, although they speculate that, as in so many other species, individuals with a varied genetic makeup are less likely to suffer from genetic defects that reduce their vigor. After all, as Corley found, parthenogenesis is a struggle even for roaches that can pull it off. The females reared alone produced no live young from their first two batches of eggs, and when they finally did give birth, had just six or so progeny over their lifetimes. In contrast, females reproducing sexually have well over 100 lifetime offspring. "The difference in fitness is dramatic," Corley notes.

Sex is best. This cockroach can make clones, but with a partner it produces many more young.

Rudolf Raff, a developmental biologist at Indiana University, Bloomington, attributes the poor asexual reproduction to the reproductive machinery being "very creaky." It's set up to produce gametes with half the genome, he notes, and thus only rarely can individuals generate eggs with the full number of chromosomes. Thus, once sex evolves in an organism, going back to asexual reproduction becomes very difficult.

Neither Moore nor Corley know just why, but having both sexual and asexual behavior within a species should make the problem easier to study, Corley notes. Raff agrees: "[The cockroaches] could be quite useful for further studying this phenomenon."

–ELIZABETH PENNISI

U.S.–CHINA TIES

Biomedical Group Lobbies NIH

A delegation of Chinese scientists, some working in the United States, is urging NIH to boost its funding of research in China

LEXINGTON, MASSACHUSETTS—Adopting U.S.-style lobbying techniques, Chinese biomedical researchers are pressing the U.S. National Institutes of Health (NIH) to support a skein of collaborative projects aimed at advancing science and mending frayed relations between the two countries.

Last week a delegation of scientists from the United States and China met with top NIH officials in Bethesda, Maryland, to discuss such ideas as high-tech methods of analyzing traditional Chinese herbal medicines, research on human genetic variation, a scheme to create a genetic knockout mouse production center in China, and AIDS vaccine trials. The ideas were developed at an extraordinary gathering here the previous weekend, where more than a score of Chinese researchers met U.S. counterparts, along with NIH head Harold Varmus, to discuss research plans, renew contacts with expatriates, and make new connections. "Biomedical science can break the ice" produced by "an early winter between our two countries" brought on by recent allegations that Chinese scientists helped steal U.S. nuclear secrets, says Yiming Shao, an AIDS researcher from the Chinese Academy of Preventive Medicine, who attended both meetings.

Planting a seed. China's Peng Yu hopes Gerald Keusch and NIH colleagues will support research on traditional Chinese medicines such as the saw palmetto.

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The delegation, headed by deputy minister of public health Peng Yu, departed from NIH with no specific commitments from the Americans. But Varmus offered some encouragement when he said that science can bridge political differences. And Gerald Keusch, director of NIH's Fogarty International Center and organizer of the group's visit to Bethesda, described the 14 July talks as a "first step" that may lead to "concrete" agreements. "The way we left things," he says, "is that they would do some thinking about their highest priorities and we would think about ours."

Prospects for collaboration on genetic studies are already good, aided by new guidelines governing the export of genetic material, which the Chinese government adopted last fall (*Science*, 18 September 1998, p. 1779). Ming Tsuang, a psychiatric geneticist at Harvard University, announced at the Lexington meeting that he has been approved to receive samples and that "the system is working well." Since then at least one other transfer has been approved, according to Xiping Xu, a Harvard School of Public Health epidemiologist who, as president of the Boston, Massachusetts–based Association of Chinese Professionals in Biomedicine, helped organize the meeting.

To get a closer look at what China can bring to collaborative ventures, Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, is heading to Beijing in September, and Keusch will be joining a group of National Science Foundation officials going to China in October. Last week Varmus announced plans to go to Beijing in November to join other Nobel laureates in celebrating the 50th anniversary of the Chinese Academy of Sciences.

But Chinese scientists are eager to get projects moving sooner. They tried to persuade Varmus during his visit here that NIH should invest more research dollars in China. Varmus listened politely but made no commitments. Keusch notes that NIH already backs several major collaborative projects in China, including a tropical diseases research center in Shanghai, a national study of cardiovascular disease, and AIDS prevention.

Although the mood in Lexington was optimistic, attendees acknowledged the tension between China and the United States. Cardiology researcher Jie Wang of Columbia University said he had been questioned by an FBI agent in February about his involvement with a group of Chinese scientists interested in drug development. He said he had ignored the incident on the advice of his university, but he asked Varmus what a person should do if "harassed" by an FBI agent over participation in "meetings like this."

Varmus responded forcefully: "Just let me know ... I am ready to speak out." The words pleased the Chinese scientists, who hope that scientific collaboration will also warm the climate between the two countries.

–ELIOT MARSHALL