Evolution: Constant Change and Common Threads
Lecture Two—Selection in Action
David M. Kingsley, Ph.D.

1. Start of Lecture 2 (00:17)

[ANNOUNCER:] *From the Howard Hughes Medical Institute. The 2005 Holiday Lectures on Science. This year's lectures— "Evolution, Constant Change "and Common Threads" will be given by Dr. Sean B. Carroll, Howard Hughes Medical Institute investigator at the University of Wisconsin, Madison and Dr. David M. Kingsley, Howard Hughes Medical Institute investigator at Stanford University School of Medicine. The second lecture is titled "Selection in Action." And now to introduce our program, the Vice President for grants and special programs of the Howard Hughes Medical Institute, Dr. Peter Bruns.*

2. Introduction by HHMI Vice President Dr. Peter Bruns (01:10)

[DR. BRUNS:] Welcome back to the Howard Hughes Medical Institute for our 13th Holiday Lectures on Science. Now over the years we've created, we have a whole series of very interesting lectures but we've created a lot of other resources that go along with those, and we've put all of that material, the lectures, animations virtual labs and so on, on a special web site called BioInteractive.org. And I encourage you to go over to that web site at some point and see what else is there, BioInteractive.org. Our next speaker in this series is Dr. David Kingsley an HHMI investigator from Stanford University. David is well known in the scientific community for developing molecular tools to study natural populations of sticklebacked fish. But before he talks about that sort of form of natural selection, David is going to first talk about selection as artificial selection for a number of organisms, including, for example, the dog. So here is a short video to introduce David.

3. Introductory interview with Dr. David Kingsley (02:30)

[DR. KINGSLEY:] I was interested in lots of things when I was in early school. I had loved dinosaurs as a kid, most kids are fascinated by big bodies and interesting structures when they're small. From that time on I was fascinated by shape and morphology and vertebrates. So right now my whole lab works on skeletal development and we've used a variety of organisms to look at that. About seven or eight years ago we got very interested in trying to use the same genetic techniques that had been so successful in studying lots of other hard problems, to study a really hard problem which is the genetic basis of vertebrate evolution. We ended up having found this small fish called the three spined stickleback which has undergone one of the most spectacular evolutionary radiations on earth, lots of interesting populations can be found here in California and that makes it possible to go fishing nearby, collect organisms that have undergone incredible morphological change in the last 10,000 years, bring them in the laboratory and actually look at the genetic basis of what has made them different. A lot of people think evolution is just sort of this curiosity-driven science and it's much more than that a lot of current medicine is based on what we know about evolution. Every time you're treated with antibiotics because you have a bacterial infection, the physician and you are facing an evolutionary arms race between the bacteria that's in your system, a drug that's killing the bacteria and the bacteria's attempts to evolve to avoid the drug that's killing most of the bacteria. That's evolution. I hope that by the end of the holiday lectures people will have a new appreciation for both the diversity of living things, but at the same time the common origin of living things. Evolution is all around us. Evolution is what has generated the foods that we eat, the pets that we keep the strategies for treating infectious disease in the hospital, it isn't just a historical process. It's something that continues all around us today and in the most relevant ways possible.

4. Natural selection and artificial selection (05:04)

Welcome back everybody. Sean gave you a great introduction to both Charles Darwin and the idea of natural selection. Darwin originally coined the term natural selection by analogy to a process of artificial selection. It's well known by human breeders. Human breeders take natural variants that occur all the time, choose traits that they're particularly interested in, breed selectively from the plants or animals that show those traits and by doing so develop new breeds that can look very different from the original animals. Darwin and Wallace realized that a very similar process would happen in nature. So wild plants and animals vary in all sorts of random ways, but animals, many more are produced than can possibly reproduce or survive. So inevitably more offspring will be generated from those random variants that are the best adapted to a particular environment. As Sean emphasized, environmental conditions on the earth change all the time and so animals are constantly being selected for those that do the best in changing environmental conditions, and Darwin and Wallace proposed that would produce major changes in nature just as humans have done in artificial selection.

5. Artificial selection created corn (maize) (06:25)

People, I think are always surprised at just how much plants and animals can be changed by the simple process of selecting for random variants that occur so I think it's worth going through a couple of examples because it is true that the products of selection are all around us. Selection has generated what we eat, the kinds of pets that we keep, and I'll give one example today from the plant world and one example from the animal world. So let's start with corn. Corn's a great example, it's one of the major agricultural crops in the U.S., a major food source for both people and animals around the world. So there's words for corn and maize in every language around the world. Corn is planted on every continent of the world except for Antarctica and despite that widespread distribution it all arose from domestication events that occurred originally in North America. That's summarized in the next video.

6. Video: Corn and ancestral teosinte (07:23)

So although now widely planted around the world, corn was originally developed as a local agricultural crop by Native Americans in Mexico. These people are harvesting corn, notice the tall stalks the large ears that grow, you can pull these off and each ear has hundreds of kernels. Corn was originally developed by these people's ancestors who recognized the potential of a wild plant to give rise to a useful agricultural crop. Interestingly, that wild plant, teosinte, looks very different from modern corn. So the seeds look completely different, the overall architecture of the plant also looks quite different. Wild teosinte has a bushy like appearance, corn grows in these tall stalks. So very dramatic alterations in the architecture of the plant, really all of its features, bushy or tall and its seeds as well.

7. Ancient breeders selected seed and stalk traits (08:15)

Let's look in greater detail at the seed structure in this wild ancestor, teosinte. So this wild plant is native to valleys in Mexico and Central America. Its seeds are shown here, actually just has a few seeds. So typically a fruiting body of teosinte might have five or twelve kernels that are completely encased in a stony fruit case that's shown there as the brown structures on the left. In teosinte those stony fruit cases actually break off into individual seeds that can be swallowed by animals and pass through the digestive tract to spread the seeds. Ancient breeders selected for major changes in seed and cob morphology in the course of turning that original stony fruit cases into what's seen today in maize. So essentially what the ancient breeders had to do was turn the original stony fruit cases inside out to reveal the corn kernels inside, which are displayed on the surface of a corncob. The stony fruit cases also softened and turned into the interior of the corncob instead of the hard outer case. Similarly major changes in overall branching architecture. So teosinte is a wide, bushy plant. Corn is a tall plant, the ears of the corn are supported on the central stalk, and the tall plant makes it possible to pack in lots and lots of corn stalks when you're planting an agricultural field.

8. Genetic archaeology: How corn was bred (09:48)

So how did ancient agriculturists achieve these major transformations? Well there's an archeological record of corn, so you see the first evidence of sort of corn- like maize cobs appearing maybe six to nine thousand years ago. Those can actually be dated, the earliest sites are in southern Mexico near the sites where wild teosinte grows. That's one form of archaeology. There's another type that can be done this is genetic archaeology. So in an attempt to try to identify key genetic events that are responsible for the major differences between teosinte and corn you can actually today set up crosses between the original wild ancestor and today's highly-derived derivative. The plants are still so closely related to each other that you can generate fertile F1 hybrids and in the next few slides, teosinte chromosomes will be shown in red maize chromosomes will be shown in blue.

9. Mendelian inheritance pattern: A one-gene trait (10:44)

So you cross these two different plants and in the first generation, the F1 hybrids, you'll have one teosinte and one maize chromosome for every chromosome in the plant. If you intercross those F1 hybrids to generate a grandchild or second generation, an F2 generation you'll start to put together different chromosome combinations based on Mendel's laws. As you all know from your genetics classes for a simple Mendelian trait, you typically will take from the hybrids randomly, either the teosinte or the maize chromosomes so a red type or a blue type in the seeds and the pollen of each hybrid. You put them back together during fertilization to generate the F2 grandchildren that are shown in the squares. A quarter of the offspring will randomly inherit two teosinte-like chromosomes. Another quarter of the offspring will inherit two maize-like chromosomes. So in this grand total generation you're generating different combinations that bring back together some of the chromosomes of the originals or still a mixture of maize- and teosinte-like chromosomes. Okay, so that principle can be used to try to roughly estimate the number of genetic factors that underlie the major architectural differences between maize and teosinte.

10. How many genes result in maize/teosinte differences? (12:05)

In the simplest possible world, if all the differences between maize and teosinte were due to a simple Mendelian gene, you'd expect when you did one of these crosses that 25% of the F2, the grandchildren plants would look like either the maize or the teosinte parent. It turns out it's not that simple. So what would happen if the differences were controlled by two genes? So you have to have two different genes on different chromosomes together to produce the differences. Well then instead of seeing maize or teosinte in a quarter of the offspring, you would see them in one quarter by one quarter, or one sixteenth of the offspring. So that's the chance of getting two maize-like chromosomes of gene number 1 and two maize-like chromosomes at gene number two for example. Three genes it gets even worse, a quarter by a quarter by a quarter is one 64th, four genes, et cetera. So the major conclusion from these kinds of tables is that if the genetic differences between forms are controlled by a large number of genes, it's very difficult to get all of the chromosomes back together in the right combination to regenerate the parental traits when you do this sort of genetic crossing, because you're down to one in thousands if the traits are controlled by lots of genes. Conversely if traits are controlled by relatively few genes, then you regenerate parental-like phenotypes in a substantial fraction of the offspring, as many as 25% for a simple Mendelian character.

11. Only 4 to 5 genes changed to make corn form teosinte (13:30)

George Beadle actually carried out a very large cross of this type. He raised 50,000 F2 grandchildren from a cross between maize and teosinte. What he found was that about one five hundredth of the plants looked like the maize or the teosinte parent and that suggests something on the order of between four and five genes that might be involved in controlling the dramatic differences in plant architecture and seeds. So what are these genes? Well geneticists can now do lots more than just calculate ratios. In fact, sophisticated genetic maps have been developed for all of the chromosomes in maize. You can do these sorts of crosses and isolate DNA samples from each of the F2 plants, measure all of the traits in the plants and then type those DNA samples with molecular markers that make it possible to monitor whether a given plant inherited teosinte- like or maize-like chromosomes for any marker in the genome. When you do that, what you find is that there are particular chromosomes regions that control particular aspects of plant morphology, so there's a chromosome region that controls flowering, one for branch pattern, open seeds. These aren't simple Mendelian traits, in fact there's usually a major gene that controls a lot of the difference and a few minor genes. But it's now also possible when you've mapped the major factor that goes to a particular chromosome region to reach into that chromosome region, sequence the DNA found in an area that's controlling the given trait identify all of the genes in that region and try to find the particular candidate genes that may actually be controlling differences.

12. Single genes can radically change an organism (15:11)

The conclusion from a bunch of experiments of that type is that single genes make major changes in the course of generating the key traits that have occurred in maize domestication. For example, mutations in a single gene called teosinte branched 1 can take a single linear-like corn stalk and produce a more bushy plant that looks like teosinte. Conversely there's a second gene called *Tga1* that plays a key role in seed and fruit case morphology. If you introduce the maize version of the *Tga1* gene into teosinte, those stony fruit cases begin to open up soften up, you get rid of the stony covering and you begin to turn the kernels inside out in exactly the way that breeders need it to produce the exposed kernels on an ear of corn. Okay, so I think that's a great example of how by selecting for genetic alterations, you can completely transform the architecture of a plant. How about in animals? For this example of artificial selection I'd like to talk about dogs which I think are a wonderful example they're introduced in the next short video.

13. Video: Dogs and selective breeding (16:23)

Dogs vary in all sorts of interesting traits, colors hair textures, sizes, behaviors that are interesting and useful to humans. DNA studies suggest that all those different modern dog breeds are derived from wolves. Wolves have lived near humans for thousands of years. In the earliest archeological evidence of domesticated forms of wolves or dogs is found about 10,000 years ago in human settlements. At that time the skeletons of domesticated dogs looked fairly uniform and similar to wolves. By the time of the Egyptians you can see these specialized breeds being developed that have long limbs and long muzzles, that breed actually still lives today in an ancient breed called the Saluki. Other breeds have been developed for hunting retrieving, herding animals, pointers and retrievers and sheep dogs are great examples of taking ancestral tracking and hunting behaviors that were present in wolves and turning them into selective behaviors that are useful for humans. So how is it possible to take an ancestral animal and turn it into this broad diversity of different forms? Let's actually listen to a couple of human dog breeders describe how they look at an animal and how they decide what it is they want to do.

[BREEDER:] I think that his neck is a little bit too short. He's got great strength in the neck, but I'd like to have it just a smidgen longer. I also would like to have a little more muscle definition in the rear.

[MS. MCGOWAN:] We really enjoy the ability to take the gene pool and use it like paints. It's our art. This is my art. I made this beautiful dog that I enjoy. I made her. I chose her sire and her dam, I chose several generations to make this beautiful dog. I'm very proud of her.

14. Breeding has generated many dog varieties (18:18)

[DR. KINGSLEY:] Okay, so I think that is a great description of what breeders do. They choose dams and sires, they do so for multiple generations, they pick traits that they're interested in and they develop animals that look different to match what they're interested in. So that process, extended by lots of breeders over lots of time has generated an incredible diversity of different dog breeds that are shown here on this slide. We also have a couple of skeletons from different dog breeds here on the stage. This is actually the skeleton of a German Shepherd and this is the skeleton of a Boston Terrier. You see all sorts of dramatic skeletal differences between the two dog forms. The most obvious is maybe the much longer length of the legs here in the German Shepherd than the terrier. There's also dramatic changes in the jaws, so the muzzle of the German Shepherd is much longer than the short muzzle of the Boston Terrier. If you come at the break you can actually count teeth. There's more molars in the German Shepherd than found here. The length of the vertebral column also differs. There's twice as many vertebra in the tail of the German Shepherd as found here in the Boston Terrier. So Darwin pointed out that if a paleontologist found these skeletons he would definitely have named them different species because of the dramatic changes, and yet these are examples of dramatic transformations that have been achieved by human breeders.

15. The genetic basis of different dog skeletons (19:45)

Okay. So what's actually happened to transform all of these different skeletal structures? Exactly the same sorts of genetic approaches can be used to study this problem as we introduced for the corn and teosinte problem. So some very interesting genetic experiments have been done trying to look at the genetic basis of producing skeletal differences. One of my favorite forms of this experiment because it was one of the largest was done in the 1920s and 30s by a man named Charles Stockard. Stockard got a big grant from the Rockefeller Foundation and used it to buy a farm in upstate New York, so he called this the Cornell Anatomy Farm and for about a dozen years he got in all sorts of different dog breeds and carried out interesting crosses to try to look at the genetic basis of form and behavior in dogs. Let's look at some of these crosses.

16. A German shepherd – basset hound cross (20:35)

This is a cross that Stockard set up between the German Shepherd and the Bassett Hound. Again the German Shepherd has long legs, Bassett Hounds have short legs. The F1 hybrids of this cross also have short legs. That suggested there may be a dominant factor in the Bassett breed that causes short leg length. If you intercross the F1's and make the F2 grandchild generation, the dogs come out with a mixture of either short or tall legs and even in the small numbers of animals that were generated here in the dog litters you can see that short and long legs occur in almost a Mendelian three to one ratio. In the dominant traits only a quarter of the offspring show the long legs that are characteristic of the German Shepherd parent. So these sorts of results are consistent with a single Mendelian gene that controls the difference in leg length between these dog breeds. Okay, here's another cross. This one was set up between the Boston Terrier and the Dachshund, the wiener dog. So if you cross these two animals, the F1 hybrid again looks intermediate. Looks a little more maybe like the Dachshund than the Boston Terrier. If you intercross the F1's, put the chromosomes together in different combinations you get very interesting sorts of F2 dogs coming out. So this is one of my favorite F2's. It has the tummy blaze of the Boston Terrier, it has ears that are the size and the shape of the Dachshund but they're held in the upright position of the Boston Terrier. Okay now so that already suggests different genes controlling ear shape and ear elevation, but remember something else from the table that we went through before for corn and teosinte if the traits were controlled by very large numbers of genes it's almost impossible to get back in a small number of animals, any that will show the chromosome types and traits of the original parents. What's seen here is that very small numbers of animals you're getting back F2's whose ear shape looks like the Dachshund or whose ear elevation looks like the Boston Terrier. Again that suggests relatively few genetic factors controlling those different traits.

17. Genetic control to muzzle shape in dogs (22:41)

Okay, one last cross, this was one of the more dramatic ones on the Cornell Anatomy Farm. It was set up between the Saluki, so the Saluki is that long-muzzled, long-limbed dog that we showed earlier in the Egyptian photo, this is actually the skull of a Saluki dog. You can see that it has a very long muzzle, much longer than is present in the Pekinese, which of course is a very short dog, very squashed-in face almost no muzzle at all, and very short legged. This was one of the hardest crosses that was tried on the Cornell Anatomy Farm. Again he was able to generate a few F1 hybrids, they look intermediate between the two parents. So if you intercross the F1's, you get some very interesting F2 dogs come out. Turns out that the length of the upper and lower jaw is inherited independently in the cross so some of the dogs come out with lower jaws that are longer than the upper jaws, some of the dogs have good match between the upper and the lower jaw, and then this dog in the lower right has the opposite problem its upper jaw is so much longer than its lower jaw that it has a constantly protruding tongue. So again those are very much like the ear results, it's clear there must be different genes for different traits. So upper jaw genes and lower jaw genes are different but it's also clear that you can get shorts and longs coming out on a very small number of F2 animals which again suggests for a given bone that the number of genes involved are likely to be small.

18. Summary of dog genetics (24:10)

Okay, so a summary then of a lot of different dog genetics. The genetics of individual traits can be relatively simple simple Mendelian gene for leg length, for example relatively small numbers of genes likely controlling several of the other differences, at the same time different genes controlling the growth of different bones and I think it's that combination of factors that makes it possible for breeders to do what they do. There's different genes acting on different body parts they have major effects on morphology. You can pick a body part that you want to modify. Choose variants that occur and selectively breed from those in order to generate dramatically different forms. So for both teosinte and for dogs, selective breeding can generate very large changes in a short amount of time.

19. Q&A: How much does modern genetics guide breeders (24:56)

So let's stop there and I'll be happy to take questions. Yeah.

[STUDENT:] For, like, modern-day breeders when they're breeding dogs, do they look a lot at genetics or is it more physical features that they're trying to cross as pictures.

[DR. KINGSLEY:] So the question is how much molecular genetics guides current dog breeding? I think that the breeders that you saw interviewed here weren't using results from DNA to try to decide the particular dam and sire that they were going to choose for the next generation. You could do that now, so in an organized program if you wanted to try to speed the process you could use molecular markers to try to screen progeny for those that might carry a chromosome of particular interest but historically it's all been done based on just looking at animals and choosing, phenotypically, the ones that have a little more muscle definition in the rear or taller ears, shorter ears, et cetera.

20. Q&A: Why different genes for upper/lower jaw formation? (25:51)

Yeah?

[STUDENT:] You said that dogs have different genes that control the upper and lower jaws.

[DR. KINGSLEY:] Right.

[STUDENT:] Is there any evolutionary advantage to that?

[DR. KINGSLEY:] Is there an evolutionary advantage to choose to change different bones differently? So I think the question for jaws is an interesting one because you're worried about the mismatch between the teeth on the upper jaw and the lower jaw and you would think that normally those two traits would go together. In fact, if you look at the amazing variations in bones and patterns that vertebrates are able to achieve, they achieve that because they have a modular genetic control over what's happening in each little bone throughout the skeleton and that makes it possible to tweak and change cartilage and bone into all kinds of useful adaptations for running and hopping and swimming and flying and chewing and running faster, et cetera, you'd have to be able to encode those differences some how in the genome so it's done by a very scattered genetics system with selection deciding, that's a fit combination, or that's a fit combination and thereby producing the overall forms that are seen in animals.

21. Q&A: How did corn breeders know what genes to change (27:08)

Yeah.

[STUDENT:] I understand like how to get from teosinte to the regular maize corn, however, how do you make, like, different varieties of that corn and was maize available, like, back then like, how did they know what genes that could make the teosinte be a maize corn?

[DR. KINGSLEY:] Right, so again, Sean got several questions too about whether the mutations and the variations know what they're going to have to become. They don't, so the variation occurs at random in all different directions. It's really either artificial selection by humans or natural selection, looking for fit variants that decides out of all of the random variations that occurred this one is a feature that a human breeder would like or this is one that has survived better left more offspring, may only be a small survival difference, five or ten percent as Sean mentioned but that random variation and then choosing based on appearance or based on fitness is what generates the different breeds or stocks naturally and then in modern-day times, people are hard at work trying to improve corn yields using all sorts of genetic techniques including breeding and monitoring chromosomes and sometimes now inserting genes that might improve resistance to pests that consume the crops et cetera. So the modifications we see today are a mixture of old and new techniques, but the old techniques have already been able to achieve remarkable things.

22. Q&A: What problems arise from inbreeding dogs? (28:40)

Yeah.

[STUDENT:] You'd think that the upper and lower jaw genes would be linked, but they're not. Do any problems arise when breeding dogs or even corn with those genes?

[DR. KINGSLEY:] So that's a great question about whether the kinds of mismatches that can sometimes come up in these different dog breeds create a problem. It actually is true that there are dog breeds that now have such morphological extremes that if it weren't for humans helping them along either with food, or there are some dog breeds that now are usually delivered by cesarian section because of the mismatch between the offspring and the birth canal of the parents for example. So it is true that artificial breeds are sometimes selected for traits that would reduce their overall viability, which actually is a great transition into what we're going to talk about in the next section, so I think, thanks for all the questions and we'll

23. Can natural selection create variation as breeders do? (29:39)

start the next section because in the next section we're going to talk about selection under a full range of fitness constraints, in the wild okay. So in nature, there isn't the human there helping you along to be born or to serve you a particular kind of food, you really have to be fit and more fit than anybody else in order to survive and adapt. And that brings us back to Darwin's key analogy. He knew that artificial breeders had been able to achieve major changes in body form by selective breeding and he argued that natural species would also be able to change in dramatic ways and that natural selection would be able to transform wild plants and animals based on differences in fitness.

24. Video: The stickleback on "Jeopardy!" (30:29)

So for the rest of the talk I'd like to focus on evolution not in human cornfields or in dog kennels, but evolution subject to a full range of fitness constraints in natural environments and to introduce the organism that we'll be talking about, I have a short video. This actually is an actual episode of Jeopardy that aired two or three weeks ago.

[ANNOUNCER:] This is Jeopardy! And now Alex Trebek!

[MR. TREBEK:] Chris is looking at me like I'm weird because we're going into Double Jeopardy with these categories. These are going to be fun. World Capitals, followed by Movies to the Max, Almost Assassinated, American Women, Furred, Feathered, Finned.

[JOHN:] And finish the category $2000.

[MR. TREBEK:] It may ring a bell that this capital of Belize also starts with Bel, B-E-L. John?

[JOHN:] What is Belmopan?

[MR. TREBEK:] Belmopan, that's right.

[JOHN:] Let's try Furred, Feathered, Finned for $400 please.

[MR. TREBEK:] The brown type of this pouched bird plunges from the air to fish, the white one scoops up fish as it swims. John?

[JOHN:] What's a pelican?

[MR. TREBEK:] Right.

[JOHN:] Furred for $2000.

The dorsal spines give this fish seen here its name. And it is a stickleback stickleback fish. John?

[DR. KINGSLEY:] Okay, now I've got to ask you guys. How many of you would have known the pelican? How many of you would have known the capital of Belize? You should get a t-shirt. How many of you would have known the three spine stickleback? A few. Okay, so let's talk more about this small fish that's now famous enough to have actually made it onto Jeopardy, but on the other hand was the $2000 rather than the $400 question on Jeopardy, and was obscure enough that it stumped all of the contestants, even the ones who knew the capital of Belize.

25. Ancestral sticklebacks spawned in freshwater streams (32:32)

Okay, so this stickleback is a small fish. The ancestral form is found in oceans about three inches long. Sticklebacks, although they live in oceans, are like salmon so they migrate into fresh water streams every year to spawn, so these ocean fish are constantly migrating and probing fresh water environments along the coast. That lifestyle has been key to an enormous evolutionary radiation of the fish that actually plays upon one of the factors that Sean mentioned in the first lecture and that's the enormous environmental changes that have occurred in the earth over time. What's shown in blue here are these huge ice sheets that used to cover North America, during the time of the La Brea tar pits for example, ice age animals that Sean was showing. So about 15,000 years ago those large ice sheets started to melt and that set off an evolutionary radiation that's summarized in the next environmental video.

26. Video: Environmental pressures led to stickleback evolution (33:35)

Okay, so during the ice age these huge sheets covering lots of land mass. Ice was incredibly thick, so a mile wide thickness of ice piled on top of land and then the earth starts to warm. So wide spread melting of those ice sheets begins and the glaciers recede leaving in their wake environments that used to be completely buried under ice but are now exposed. If you go into areas like for example around British Columbia you'll find that the islands around Vancouver are dotted with fresh water post- glacial lakes in these formerly ice covered regions. Those fresh water lakes, if you look in them, very frequently have sticklebacks that have come in from the ocean but then adapted to the local environmental conditions in the lake. That adaptation includes decisions about how to avoid predators. This shows a trout trying to eat a stickleback. You can see the sticklebacks sometimes get away so the armor that they have can be very useful. Sticklebacks are also eaten by insects. The preying strategy of an insect is actually to reach out and grab onto things like spines of sticklebacks reel them in and then munch them from the sides. So depending on the kids of predators that you're encountering in different lakes, it may be better or worse to have or to lose armor.

27. Adaptive radiation from ancestral form (35:02)

That's just one example of the kinds of environmental factors set off by this widespread change in climate, but then an adaptive radiation as an ancestral marine form colonizes and evolves to the ecological conditions in different lakes. The ancestral marine fish is shown here, they're not usually this red, this fish has actually been stained with a dye called alizarin red which highlights all of the skeletal structures. The marine fish completely covered with armor plates from head to tail. It has the three prominent spines that Alex Trebek mentioned. You can also see a spine down here on the belly region that we'll come back to. That ancestral form has radiated in different fresh water lakes and streams throughout the northern hemisphere Europe and North America, and Asia.

28. Adaptive changes in freshwater sticklebacks (35:49)

When naturalists first came through the lakes in northern hemisphere they found what they classified as over 40 different species of sticklebacks because they looked so different from each other. So in these fresh water lakes the three spined stickleback can turn into a two spine, a one spine or a no spine stickleback. The teeth in the jaws are extensively modified as the fish adapt to different food sources that are available in particular environments. The armor patterns change a lot. It can be heavily armored and slow or lightly armored and fast. The hind limb of the fish comes and goes. Colors, variety of physiological traits, salinity tolerance, temperature preference, it all depends on what environmental challenges the fish have been trying to reach.

29. Crosses between stickleback forms reveal underlying genes (36:32)

All of this has happened in just the last 10,000 years or so since these environments got created and in fact although many of the fish are reproductively isolated in the wild, the isolating mechanisms turn out to usually be either behavioral or mechanical in compatibilities so you can overcome those by squeezing out eggs and sperm from the fish and you can raise perfectly fertile F1 hybrids that can then be used for exactly the sort of genetic experiment that we've gone through before for teosinte and corn to try to track down the genetic basis now of evolutionary change in natural populations subject to a full range of fitness constraints in the wild. All kinds of interesting traits that are analyzable by this sort of approach and that's because of the incredible diversity of different traits that have evolved in wild sticklebacks. There's actually huge literature on sticklebacks a couple of thousand papers and several full length text books that have been written on the distribution and the ecology and the morphology and the behavior of different fish forms around the world.

30. Important varieties in wild stickleback armor plating (37:36)

So it's possible to take almost any trait that you're interested in and find interesting stickleback populations. We and many other stickleback labs send out students and post docs from the lab each year to go collect from interesting sites where fish have evolved. This is a graduate student in the lab shown collecting sticklebacks in the Northwest Territories. The fish are relatively easy to catch. You throw in these minnow buckets that have conical openings at the end, the fish get funneled in to the trap and then the hole is small enough, or they're not smart enough to swim back out the other side. So if you trap a whole bunch of lakes and streams you can just come back the next day and the traps have typically got lots of sticklebacks in them. The fish are small and relatively easy to move around and work with in different aquatic environments. You can see here buckets of fish that have been brought back to a hotel room in the Northwest Territories. It's actually possible to set up fertilizations and crosses under the microscope right there in the hotel rooms and bring back fertilized egg clutches. We also bring back live fish. We're also collaborating with lots of stickleback investigators that are interested in particular populations and have studied them for years, including a long standing collaboration with Dolph Schluter at the University of British Columbia who raises thousands of sticklebacks every year for ecological studies.

31. Genetic basis for reduction in stickleback armor plating (39:02)

Okay so we've got all sorts of different traits that are segregating in these wild populations. I want to talk about the genetic basis of some of the differences and we'll start by talking about the lateral plates. This is one of the major morphological differences that's evolved repeatedly in different locations. This image is actually taken from an old monograph by the famous French naturalist Cuvier who several decades before *The Origin of Species* gave different species names to marine and fresh water forms of sticklebacks because of the dramatic changes in bony patterns. The marine form is shown on the top with plates from head to tail. Fresh water form is shown on the bottom, many of the fresh water forms have lost a lot of the armor plates retaining them only at the front of having very few plates at all. Again this is thought to be almost a military decision about the best kind of armor to have in particular environments. You can either be heavily armored and slow or lightly armored and fast, so there's a higher burst swimming speed in the low plated sticklebacks, depending on the predators that are chasing you it may be better to have one form or the other.

32. Genetic archaeology locates the plate-number gene (40:07)

Okay now we can do for sticklebacks exactly the sort of genetic archaeology experiment that we described before for maize and teosinte. So take a marine form and a fresh water form that look very different in the number of plates, 35 or 36 plates in the marine fish shown on the left. Only a single plate left in one of these fresh water populations from Paxton Lake near Vancouver. Generate an F1 hybrid generation intercross the F1's to generate the F2 grandchildren that are putting back together in various chromosome combinations all of the marine and the fresh water chromosomes, then go in and count armor plate numbers in all of those F2 offspring, isolate DNA samples, type them with a set of genetic markers that we've developed for genome-wide linkage mapping in sticklebacks and then look to see whether there's particular chromosomes that always go together with particular traits. When you do that what we found is that there's a single major gene on the distal end of linkage group four that controls about 70% of the variation in armor plate number in the cross. So a very large genetic effect.

33. Modifier genes also influence plate number (41:12)

It's not as simple as a Mendelian trait. There's also chromosomes that have smaller quantitative effects on plate number so we call these modifier genes quantitative modifiers, they may each control somewhere between 5% and 10% of the variation in armor plate number in the cross. Okay so in many ways these results are very similar to what I described before for doing this kind of experiment in maize or teosinte. As in maize and teosinte, it's also possible, once you've identified one of these chromosome regions to go into that region, sequence all the DNA in that area and decode the actual genes that are in that region that may be controlling the traits. We've been able to do that for this major gene region that controls armor plate number in sticklebacks and been able to identify a single signaling molecule gene that plays a key role in armor plate formation.

34. Genetic engineering adds armor to a plateless stickleback (42:03)

The easiest way to demonstrate that it plays a key role is to reintroduce that gene into eggs from low armored fish so you can directly inject fertilized eggs from low armored fish with the gene from the chromosome region that controls armor and when you do that you put armor plates back on the sides of the stickleback. So again very like the kinds of single gene experiments that have been done for corn and teosinte and the conclusions are very similar, single genes can control major morphological differences now in these populations that have evolved in natural environments.

35. Genetic control of stickleback hindfins (42:38)

Okay, there's actually... talk about one other trait which is the presence or the absence of the hind fin. Fish are like most land animals, they have four major fins appendages or limbs. Two fore fins, or pectoral fins and two hind fins or pelvic fins. These traits get modified in some of the fish populations

36. Limb reduction has occurred in many vertebrates (42:59)

and we think that the presence or the absence of the hind fin is actually a very interesting sort of trait because it's the same kind of trait that's evolved repeatedly in a whole range of different animals. Of course snakes and some reptiles have evolved major limb reduction, they've lost both their fore limbs and hind limbs. Whales and some aquatic mammals like manatees have evolved hind limb reduction, they still retain fore fins or flippers but they've lost the hind fin. And pelvic or hind fin reduction also occurs both in fossil sticklebacks and in some living populations. Again in those special populations that have decided to lose their hind fin, it's thought to be a likely adaptation to particular predator environments. If you're a fish that's evolving an environment where there aren't any trout trying to eat you so you don't need to erect spines to try and avoid a trout but you are being chased by insects, it may actually be good to lose some of these structures that the predators try to grab onto. So I'll show you a little bit higher resolution look at the hind fin of a stickleback in this short video.

37. Animation: 3-D CT scan of stickleback skeleton (44:05)

This is a three dimensional reconstruction of the stickleback skeleton created by Craig Miller in my lab based on a micro x-ray approach. You can see the armor plates that we talked about before along the sides of this marine fish and then colored in red you can see the pelvic apparatus which consists of this spine that projects from the side of the animal. It articulates in a ball and socket joint with this underlying pelvic structure which is shown in red wrapping around the side and on the ventral surface of the fish. The fish can actually raise and lower those spines so then the pelvic fin consists of this spine and this underlying pelvic bone.

38. Hindfin reduction controlled by major and modifier genes (44:44)

Marine fish always have the pelvis the form shown at the top, pelvis highlighted in red in the middle. But again some of the fresh water populations have evolved the complete elimination of the hind fin like the Paxton Lake shown at the bottom. So what is the genetic basis of completely losing a limb in natural populations? Again we can use exactly the same sort of genetic archaeology approach, measuring now the presence or the absence of the hind fin and these crosses between marine and fresh water fish. When you do that it turns out, and we get a result that should be now sounding familiar. There's a single major gene that maps to the distal end this time of linkage group seven that controls about two thirds of the variation in pelvic size in the F2 progeny from this sort of cross. Once again it's not Mendelian so there are a series of chromosomes that have smaller quantitative effects and control maybe five to ten percent of the variation in pelvic size. So again, more complicated than Mendel, but even the presence or absence of an entire limb or fin here is being controlled by a relatively simple genetic system just as we saw before for major transformations in both corn and in dogs.

39. Artificial and natural selection give rise to variety (46:05)

So I think it is amazing what can be done by simply selecting and accumulating genetic variants. Artificial selection has transformed teosinte into maize and transformed wolves into a diversity of different dog breeds. But natural selection can generate equally large changes in completely wild animals that are adapting to the kinds of environmental changes that occur all the time in the history of the earth. One of the conclusions of this sort of genetic work is that it doesn't take that long to generate really major changes in plants and animals. So all of the changes that we've talked about have been generated in the last 10,000 years or so. That's just a blink of the eye compared to the long geological eras that Sean summarized in the first lecture.

40. Review of how quickly selection can act (46:53)

So how can things go so fast? Part of the answer is that single genes have big effects, right? So we saw that, for the genes that controlled the fruit cases in corn or the branching pattern in corn or the leg length in dogs. Those are all examples of artificial selection. Exactly the same thing we've seen in some of the genetic analysis of natural selection. So major genes that control armor plate numbers or presence or absence of a hind fin or in the case that Sean mentioned this morning, whether you're a black or a light colored rock pocket mouse, another example of natural variation. The other thing that helps the speed is that it doesn't take very long for selective pressures to increase the frequency of an advantageous allele once the mutation has occurred, even at random. Sean showed you this morning that that's true for the case of coat colors in pocket mice, one percent, five percent selective advantage and pretty soon whatever the gene is that controls that trait spreads rapidly through the population. I think that's likely to be true not just for coat colors but for a whole range of different traits. I think one of the striking things about the sticklebacks is that all sorts of things have changed in the last 10,000 years. Skeletal traits, feeding traits, traits related to mating and reproduction and whether fish are even compatible to mate with each other. All sorts of physiological differences and behavioral differences. So I think that the principles that Sean outlined this morning how one gene could sweep to produce a color change in 1000 years or less is actually an example of selection that's occurring for multiple traits simultaneously, even in natural environments. There's all kinds of challenges out there in the changing world and the process of random variation followed by selection for those variants that are best adapted to a given environment can do remarkable things to animals and in a time scale that's completely compatible with the needs of the animals to adapt to different environments.

41. Q&A: Would domesticated dogs go extinct in the wild? (48:52)

So I'll stop there and I'd be happy to take more questions. Yeah.

[STUDENT:] I actually have a question about what you mentioned earlier about the dog breeders.

[DR. KINGSLEY:] Yeah.

[STUDENT:] Well when you're creating dogs for beauty, what would happen if these dogs were not used for domestic purposes anymore and then they were placed out in the wild? Would they go extinct because they had not evolved like the wolf has to adapt to such an environment or how would that work?

[DR. KINGSLEY:] Great question, what would happen if the dog breeds were released in the wild, and this is actually an interesting question because one of the old arguments about whether artificial selection was relevant to the way evolution would work, was a lot of people said "Well, if you released those dogs in the wild "they'd be toast" and therefore the kinds of genetic architectures that underlie the major changes that humans have been able to achieve aren't relevant for the kinds of genetic mechanisms that might underlie a process of natural selection to change an environment. So I think that's one of the things that's so striking about the stickleback result. There's no humans involved in trying to sculpt these organisms to adapt to these new post glacial lakes and yet if you go in and use exactly the same sort of genetic archaeology methods to try to investigate what kinds of genetic changes underlie those differences, in fact the architectures are in many ways surprisingly similar. You can get major genes that have substantial effects on huge structures and I think that that shows the power of what genes can do and the power of what selection can do by acting on those genes.

42. Q&A: Are there inbreeding effects with F1 crosses? (50:28)

[STUDENT:] Isn't it possible with the constant F1 crosses like the dogs, the maize, and the sticklebacks that like the results would be affected by inbreeding? You're breeding the same, the children from the same parents over and over.

[DR. KINGSLEY:] Question is whether you get inbreeding effects when you do these sorts of crosses and you can, so there are recessive mutations that can be present in populations, as Sean said, mutations occur randomly. So during the replication of DNA you'll get errors. Those sometimes are not apparent unless the same mutation is on both chromosomes, so they may have occurred originally on one, but when you start to inbreed you bring those mutations together so that absolutely can be seen. Inbreeding effects that plague breeders because you have to find the stuff that you want amidst the stuff that you might not want and I think what that really serves to emphasize is something that came up also in the questions this morning. The process of mutation itself is random. It's not that the corn or the teosinte knew what corn should look like or that the dog breeders were able to pick preexisting traits that had already varied in the way that somebody wanted to have happen. The mutations occur at random. They can be advantageous, they can be disadvantageous. What selection does is it screens. The ones that are bad are eliminated. The ones that are good can be chosen either by a human breeder or by the process of a mutation having a one or a five or a ten percent advantage in overall survival or reproduction.

43. Q&A: Has artificial selection helped improve other crops? (52:06)

We'll take one in the red shirt.

[STUDENT:] Does the understanding of the evolution of the teosinte to corn, has that played a big role in the genetic enhancement of like common agricultural products like the giant tomatoes or how they're improving the world source of food?

[DR. KINGSLEY:] Very similar experiments have been going on to look at the genetic basis of domestication traits in other animals and plants. So part of the motivation of that research is if we understood the genes that made crops better for humans it might actually be possible to move those genes around in a more designed, targeted approach to improve plants. So there's very similar work that's gone on for tomatoes to try to identify the genes that make tomatoes you know big and juicy. There is similar work that's going on in lots of different organisms. So far I don't know of any examples where one of the domestication genes that has been found in this plant has been moved over into another one, but I do think that the better our understanding is of how you can change plant architecture, the better long term hope there is for achieving real improvements that are based on trying to modify our knowledge of the genetic pathways of how the structures develop. Off by one. OK.

44. Q&A: What fish are used with the stickleback crosses? (53:27)

Yeah, did you have a question?

[STUDENT:] I gathered from the opening video that in your laboratory you do sort of similar ideas with the fish as in the Cornell Anatomy Farm. Do you do this just through breeding or through some sort of other form of manipulation?

[DR. KINGSLEY:] The stickleback project in the lab is very focused on trying to analyze the genetic basis of natural variants that have never been manipulated in humans. So lots of people who work on model organisms may set up mutagenesis experiments to try to identify rare variants that test what is possible to do to an animal in the laboratory. The stickleback project is very geared towards trying to understand how nature has redesigned animals in natural environments so all of the crosses are taking wild caught fish that have adapted in different areas and then trying to carry out these sorts of experiments to identify what genes have made them look the way that they do.

45. Q&A: Are dogs still closely related to wolves? (54:32)

Okay I think we better take one last question. Yeah.

[STUDENT:] Because people who breed the dogs so many times different ways, are they still as close as they were to wolves, like, in their components. Like, could you still breed them with wolves, are they still, like, close in, like, cousins or something like that?

[DR. KINGSLEY:] So one of the most remarkable demonstrations of how closely related dogs and wolves actually still are is the fact that you can breed wolves and dogs they'll make fertile hybrids. The dog genome project just recently been carried out. We've got a lot of sequence information now from dogs and you can ask what other organisms are the most closely related to dogs based on DNA sequence. That confirms the same thing that people knew from breeding experiments that dogs come... are very closely related to wolves, you can see that both by the inner fertility and similarity in DNA sequence. You are the easiest toss of the day. Okay, so thanks very much. We're happy to take more questions at the break. You've asked great questions and I'll give it back to Peter.

46. Closing remarks from HHMI Vice President Dr. Peter Bruns (55:44)

[DR. BRUNS:] Thank you David I'm really glad that we selected you to give that lecture. It's really exciting I think to learn how evolution is working in living populations now and to see the mechanisms behind it. There were all those good questions and there are many more and I know our audience out there in the virtual world couldn't ask their questions anyway. But there is a way you can ask these questions. That web site I mentioned before, BioInteractive.org has a section called "Ask a Scientist." you can go to that section and put in a question and our panel of volunteer scientists will answer it for you. Not only will you get an answer back, but if we think the question is generally interesting and the answer is a good one then we'll put it on the site for others to see and there's an archive of questions and answers and a search function. So it's actually a pretty good resource in a lot of things. So that's "Ask a Scientist" on BioInteractive.org. That was a commercial message. So join us again tomorrow for two more lectures on evolution from our speakers, David will explore the connections between the fossil evidence and molecular evidence for evolution and Sean will move our evolutionary thinking from insect wings to human traits. Thank you.