**Evolution: Constant Change and Common Threads**
**Lecture One—Endless Forms Most Beautiful**
**Sean B. Carroll, Ph.D.**

**1. Start of Lecture One** (00:17)

*From the Howard Hughes Medical Institute. The 2005 Holiday Lectures on Science. This years 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 first lecture is titled "Endless Forms Most Beautiful." And now to introduce our program, the president of the Howard Hughes Medical Institute Dr. Thomas Cech.*

**2. Introduction by HHMI President Dr. Thomas Cech** (01:07)

Welcome to the Howard Hughes Medical Institute and to our 2005 Holiday Lectures on Science, the 13th in our annual series. We're web casting here live from our HHMI headquarters in Chevy Chase Maryland and with us in the audience are 200 high school students from throughout the greater Washington, DC area. The mission of HHMI is to make discoveries in biomedical sciences and to foster vibrant science education and nothing brings these two activities together as well as having our Hughes investigators speaking to local high school students. To learn more about the Institute go to our web site HHMI.org. Our important topic for these lectures is evolution. It's safe to say that all of HHMI's research activities depend on the central unifying concept of evolution. Evolution is as fundamental and as central to modern biology as the law of gravity or the law of conservation of energy is to physics. In the year 2000 I had the opportunity to travel through the Galapagos Islands and to see the sparse landscape and the exotic plants and animals that inspired Charles Darwin's great idea and similarly a lot of researchers who are particularly drawn to evolution tend to enjoy natural history and field biology. Our lecturers for this series, Sean Carroll and David Kingsley are no exception. Although they earn their bread and butter in the research laboratory, they also spend time in the field hunting fossils, chasing animals, studying habitats. Our first speaker, Sean Carroll, is an HHMI investigator at the University of Wisconsin in Madison. Sean trained in molecular biology and became interested in how genes control embryonic development. As Sean's work in developmental genetics progressed, he began to appreciate the key role that these same genes played in the evolution of species and he became one of the main contributors to a new field called evo-devo, which stands for evolutionary developmental biology. His passion for evo-devo led him recently to write a popular book, "Endless Forms Most Beautiful" and in fact this is the title that he's chosen for his first lecture. Here to introduce our speaker is a short video.

**3. Introductory interview with Dr. Sean Carroll** (04:13)

I think my interest in science started as a little kid when I would like to stroll out into the back yard and flip over logs and I just liked looking for critters and I loved the visceral thrill you got from flipping over a log or turning over a rock and seeing an animal you'd never seen before and appreciating how they live, their patterns their body forms, et cetera. I always had the sense that I was going to be interested in biology and as I started to learn about how biologists worked, and then as I entered college and had the opportunity to work in labs and all that I knew I was on the right path. I was clearly interested in understanding the machinery of how nature works. How cells work, how genes work, and so the first phase of my career was devoted towards understanding some of the mysteries ongoing and the field called developmental biology which is the study of how adults develop from eggs. But I understood also there was a deep connection between that area and the evolution of form because all form evolves by changes in development and so by understanding development you're understanding something about evolution and I've been working at that interface for a

long time. All of the ideas about evolution are important to human health because we are a living species we are variable, we have been and are subject to forces like natural selection and so part of our genetic makeup has been sculpted by battles in the past with the pathogens that we've encountered as humans spread across the globe. So we are an evolved and still evolving species. In the most practical aspects, our medical lives are intertwined with evolution because we're in a constant arms race with the pathogens that affect us. My goal for the Holiday Lectures is to arouse interest in natural history and enrich student's appreciation for the process of evolution. Evolution is the big idea in biology and life is of course the big experiment on earth so there's really no bigger idea to get your head around and for those of us who spent a couple of decades trying to understand what individual organisms do, what species are how they change, what are their relationships to each other, it's a very large and still expanding subject.

**4. The young Charles Darwin** (06:51)

Good morning. You're going to hear a lot about evolution over the next two days. I think you're going to hear a lot of new things about evolution over the next two days. I think Dr. Kingsley and I have agreed that perhaps the vast majority of what you'll hear is not even in textbooks yet and it's a sign of the vigor of evolutionary science in 2005. But all of this science has deep roots. Deep roots that started in a very dramatic way in the 19th century. And so our discussion of evolution today is going to begin with Charles Darwin. For as we'll see his contributions were immense and they have endured and been expanded upon now for 150 years. I think his contributions, even scientists don't realize the scope of his work until you actually dig into the many books, the many contributions that he made over a life's work. So in this first lecture I'm going to tell you about Darwin's key ideas and how he arrived at them, and in the final lectures Dr. Kingsley and I are going to focus on the expanding understanding of how evolution works. So let's start with Charles Darwin. I'll say perhaps one of the most misunderstood characters in the history of science and I hope in the next 15 or 20 minutes you're going to gain a better appreciation of just who this person was.

**5. Darwin's early career choices** (08:14)

Was this greatest of all naturalists always destined for greatness? Hardly. Now among the high school students here in the audience how many of you are pondering a medical career of some sort? Show with your hands. A very high percentage, okay. So was Charles Darwin, until he saw surgery for the first time. And surgery in the early 19th century was not the very sterile process that you see on television in 2005. It was a very rapid process because without anesthesia the idea was to get it over with quickly before the patient objected too strenuously. So Darwin not only wasn't comfortable with surgery he wasn't comfortable with the sight of blood, he had a fairly queasy stomach. So after two years of medical school that he started at age 16, he washed out and it was clearly not going to be the thing for him and he changed colleges and he moved to the University of Cambridge and he took up some of his passions which were natural history, beetle collecting, running around the countryside, he was a good shot, he was a good horseman. He enjoyed a lot of hobbies. He was brought up in a fairly wealthy household the son of a physician. He enjoyed certain advantages. He liked reading, and he read about a particular earlier British naturalist who had explored the tropics and being in dank, gray, dreary, cold, windy, unheated England he wanted to go to some warmer, more vibrant places. Now his wealthy father fearing that his son was amounting to nothing, just enjoying himself and not setting his talents to anything serious, his options were relatively limited in that day and age since he wasn't going to be a physician and the more respectable option would be, for example, for Charles to join the clergy. So that's what Darwin's father chose for him, that he would enter divinity school at Cambridge. Study divinity and become, for example a country parson and he would be able to then take his natural history pursuits living out in the country sort of as a hobby.

**6. Darwin offered job on exploration ship HMS Beagle** (10:28)

So that was the plan, yes, the clergy. That's where Darwin was headed. But fate intervened and Darwin while he was preparing to study divinity was unexpectedly offered the chance to voyage as a ship's naturalist with the British navy. Now being only 22, financially dependent, fresh out of college, he had to ask his dad's permission, and he was turned down. His father had many reasons and Darwin jotted these reasons down, and this is a copy of that original document of Darwin's notes of his father's objections to this voyage, little easier to read in this version. So what were his father's objections? Well that this voyage would be disreputable to his character as a clergyman hereafter. That it was a wild scheme. That they, the navy, must have offered the job to many others before him, the place of naturalist. This was true—Darwin was not the first choice. Because it was not accepted there must be something wrong with the vessel or the expedition. That he would never settle down to a steady life hereafter. That his accommodations would be most uncomfortable. This was definitely true. That he, Dr. Darwin, would consider it as again changing his profession, he'd switched once from medicine to the clergy, and that it would be an utterly useless undertaking. And Darwin, in a systematic manner that would sort of be his whole approach to life, as well as science but even marriage. He worked on a rebuttal, a point-by-point rebuttal of each of these objections, consulted with his uncle and was able to finally persuade his father to let him go. So at just age 22 he set off on a voyage that was planned to be a two year voyage around the world. It wound up taking five. So he left England and never saw his family for five full years most of that time spent on a rickety wooden boat called the HMS *Beagle* in cramped quarters experiencing storms at sea, earthquakes in ports and for Darwin, seasickness for the entire voyage. That queasy stomach haunted him not only from medical school through this voyage, but his entire adult life. So off they went and onboard, with his relatively limited amount of space, Darwin had to figure carefully what was he going to take on this voyage? Well he brought supplies that a naturalist would need. He brought pickling jars and he brought notebooks and he brought all sorts of pens and pencils and things to draw specimens and other supplies he needed to ship specimens home because he wasn't going to carry all this stuff for this multi-year voyage with him, he was going to ship some of it back on British ships that were going home that they passed on the sea routes. Well among the things he had, one of the most important were a couple of books. One book was Charles Lyell's *Principles of Geology*, a brand new book at the time that offered a pretty dramatically new vision of geology from the wisdom of the recent decades and Darwin was very keen on geology. He had a lot of experience while at Cambridge of going across the English countryside which has lots of interesting geological formations and Darwin took extra care to learn about them. Second book he had with him was the Holy Bible. Darwin, who was going to study for the clergy considered this book his authoritative reference on all matters of morality and he would quote onboard ship, literally directly from the bible and read to some of the sailors.

**7. Geology spurred Darwin’s evolution thinking** (14:04)

Now the geological background Darwin had and his grasp of geology was absolutely critical to his future success as a naturalist. This is one element that he had running through his brain that other naturalists of the time perhaps did not. What Darwin understood from reading Lyell and from some of his personal experiences was that land forms change. That was a relatively new idea at the time. Secondly he began to understand the immensity of time, that the earth was much older than he had been first led to think. So just those ideas were percolating in his mind as he started to voyage around the world. One of the topics he first started to think about prompted by seeing interesting landforms as they passed by on the HMS *Beagle* was how do some of these forms actually develop and I'm showing you here a picture from the Pacific Ocean of a series of islands. The few in the background are atolls, so they are just little lagoons surrounded by rings of coral and in the foreground you see a pretty familiar looking island again surrounded by a coral ring.

**8. Darwin’s model of coral reef formation** (15:17)

Now at the time, and reading Lyell the thought on how coral reefs formed was that every coral reef, when you saw an atoll like that, that was coral that had been built on the edge of a volcanic crater. But Darwin thought this was really unlikely. He thought, you know underneath the sea are you telling me there's just

volcano after volcano after volcano just packed right up against each other? He just didn't think that was right. And so he thought about this more and he knew that major landforms would sink under their weight, that land forms would change over time. He thought, no, I don't think that coral reefs are all built on the ridges of volcanic craters, in fact when I look at the different types of coral reefs that exist in the world, I see this as all different stages of the same process and Darwin's first great theory wasn't about animals and organisms at all. It was about the formation of coral reefs. And this was his model. His idea was that when, for example, a volcanic island was tossed up out of the ocean and the corals would grow around the shallow waters surrounding that island. That would form what would be called a fringing reef. And then as the land mass started to sink, shown here in the center of the slide, a lagoon would form between the outside reef and the land and that outside reef would be a barrier reef and then as the land sank completely out of sight, that's when you have these atolls formed. So different stages of the same process. So long before the book for which he's most famous, Darwin wrote an entire book on the structure and distribution of coral reefs, putting forth his first great theory and this turned out, while it was very contentious for decades to be right. And what this demonstrated was Darwin's ability to theorize on a grand scale, to take a few observations ruminate on them, stretch his mind a little bit more, go out of the boundaries of conventional thinking, and come up with a grand explanation, in this case, for the entire range of coral reefs that we see in the world.

**9. Unusual plants and animals intrigued Darwin** (17:22)

Now what did he see in terms of living forms? Well Darwin's voyage took him to lots of interesting places and as soon as he got the opportunity to get off that boat, he went. He got on horseback, by whatever way necessary he probed the deep jungles of South America, and in these jungles he was absolutely delighted, absolutely in heaven to be studying all these vibrantly colored and diverse forms. But there were some strange things things that started to make him think about nature in a different way. What did he see? He saw flightless birds. Now that's peculiar. Every bird he had seen in England could fly, had good fully functional wings. But he saw flightless birds. He also found in the rocks as he looked very carefully at the geology of every area, he found fossils. In this case for example a giant fossil ground sloth. Now he knew there were sloths in South America and he saw these sloths, but these fossil sloths, they were huge they were cow sized, much bigger, and as Darwin started to appreciate, older than anything he saw around in South America at the time. So this is starting to plant some seeds. Then of course he continued on around the west coast of South America to the Galapagos Islands and he saw some very unusual creatures there that prompted a lot of his thinking and we have a little video about those animals.

**10. Video: Galapagos animals challenged Darwin’s thinking** (18:47)

Swimming lizards, the famous marine iguanas. Giant tortoises, large enough for Darwin to ride. They were also a good source of meat. Seals, seals that were so tame the sailors could walk right up to them. They had no predators, so they had no fear of man. And of course the finches.

**11. Darwin begins to form his theory of life evolving** (19:10)

So as Darwin started to piece this together he started to develop the notion that maybe contrary to what he had been taught, not just landforms change but species change. And so as he returned home to England with thoughts of flightless birds and giant ancient ground sloths and strange lizards, he started to connect the dots of what he had seen over the course of five years and really from that voyage of five years he had enough questions to last him five decades and it was five incredible decades of work that followed. Darwin when he returned to England started a phase that he refers to in his own autobiography as mental rioting. What was the meaning of all these things he had seen? He had seen many more things than any naturalist before him. He had studied these things very carefully and had five years to think about them, all that time on the ship for example.

**12. Dangerous ideas and secret notebooks** (20:04)

But he knew that this idea about species changing was dangerous. It was heresy, it was absolutely contrary to the doctrine of the Anglican church at the time. So Darwin knew he theorized at great risk. So he kept his thoughts private and he started writing in secret notebooks. He lettered these notebooks, as he finished one he went onto the next, so these are actual specimens of Darwin's original notebooks with some of his writing shown below and in these secret notebooks he was developing a theory of species formation. It would be a long time before anyone read these theories. Why? Why secret notebooks? Why was he suppressing this? Well as I told you, that the immutability of species was the doctrine of the time. Darwin at that time was getting tremendous praise and attention from the scientific community in England. He had been shipping these specimens back and the paleontologists were studying the fossils and the ornithologists were studying the birds and the mammalogists were studying the mammals, they were having a fantastic time and Darwin was a hero and he was getting all sorts of honors, all sorts of invitations. And he knew that if he set forth his ideas he'd lose all these privileges that he was enjoying. He worried about dishonor to his family, the good Darwin name if he spoke this heresy and eventually he also had another reason which was he married Emma, his first cousin and he was very sensitive to her religious devotion. So he knew he would need more evidence, much more evidence and so once he settled down he set up really one of the most fantastic home natural history stores you could ever imagine all sorts of experiments going on, all based on his work at home.

**13. Pigeon breeding and the Galapagos finches** (21:58)

He became a pigeon breeder. It was a rage at the time in England and he actually frequented various pubs where pigeon breeders hung out and talked about their secrets. Darwin mixed very, very well. Five years onboard ship with sailors taught him a good amount of social lubrication so he did very well and what Darwin understood from the pigeon breeders is that fantastic variety could be derived just with the art of the breeder deciding which animals to breed and he correctly inferred that all these wild varieties carrier pigeons and this old Dutch variety and many more that were in England at the time were all descended from a fairly plain-looking wild rock pigeon shown here at the top. And Darwin started to think, well if the pigeons can be so different descended from an ancestral stock why not natural species? And he thinks back to the Galapagos finches and he learned that the finches he collected were actually very different from each other, each a unique species from different islands that had different beak shape that affected what sort of diet they had, whether they ate nuts or fruits, et cetera. He thought that maybe finches are all descended from some common ancestral stock and a key idea enters his mind and this is a page out of one of those secret notebooks.

**14. “Life as a Tree” and natural selection** (23:13)

He conceives of the idea that life--species—are connected as in a family tree. That ancestors give rise to descendent species a little bit different from each other and this notion of life as a tree no one had had before. And if that's the right description he still wanted to understand why. Why would life branch out from the tree and he was reading a much older essay from 40 years earlier, this is a quote from his autobiography. In 1838, 15 months after he started this inquiry upon his return to England he happened to read for amusement Malthus *On Populations.* Now Malthus had put forth this idea that there would be tremendous competition for resources and that would be an ultimate limit to human growth. Well, Darwin said "Being well prepared to appreciate the "struggle for existence which everywhere goes on, from long "continued observation of the habits of animals and plants "it once struck me under these circumstances that favorable "variations would tend to be preserved and unfavorable ones "to be destroyed." When there's competition, there will be winners and losers and that process would give him a mechanism that would drive species to be different.

**15. Darwin “forced” to go public with his theory** (24:21)

So he says, "ah ha, at last I have a "theory with which to work" but no one would hear about this theory for 20 more years. Why? Well the stakes as I told you must be very high. He had lots of reasons. He was still a young man. He was only roughly 30 when he had conceived this. He saw that his scientific fate would be ruined. So he kept working and he kept working and he kept working but eventually various events in life intervened that prompted him to go public. Let me tell you about two of those events. Darwin fathered 10 children. He was very much a family man, he based all his work at home because of his illnesses he had this queasy stomach all the time, he really was a homebody working all day among this menagerie of animals plants, and children. Well his first born daughter, he was very, very attached to Annie Darwin was very, very attached to her father, they had a sweet relationship, she was a very loving child. But she developed an illness and despite all the interventions that her mother and father took she gradually declined and died before Darwin's very eyes. This shattered him, absolutely shattered him. Now he was more of a middle-aged man and I think this experience made him think, well, what could be worse than losing his daughter? He was fearing the repercussions of his scientific work less. And then a few years later, again as he kept working in this massive development of this species theory, a package arrived in the mail and it was from a naturalist working in the Malay Archipelago, Alfred Russell Wallace. Wallace had gone into the tropics almost a dozen years earlier. He had developed a theory of species formation and knowing Darwin's eminence as a naturalist had sent it to Darwin to see, for Darwin's approval and for Darwin's recommendation on how to publish it. Oh goodness, there's Darwin looking at, in short form his life's work, penned by another scientist. So he was afraid he was going to be scooped. It was terrible timing, he had a two year old son, Charles Jr. who was dying of scarlet fever at the time.

**16. Darwin and Wallace publish the theory of natural selection** (26:38)

But Darwin's friends, his allies which included the great geologist Charles Lyell and many others, made sure that both Wallace's theory and Darwin's theory were presented together to the Linnean Society in 1858 and this was the first public airing of this idea that species change and that natural selection is a force. So that's why we talk about Darwin and Wallace, but Wallace always deferred to Darwin as having done the greater, larger, and more original earlier work on species formation. Wallace was always humble about that. So after the appearance of these papers, Darwin pushed on and in the next year working at a feverish pitch he finally completed his work that everyone is most familiar with, *The Origin of Species.* it is an amazing book, still very readable today. It's a masterpiece of evidence and argument. He not only puts forth all of the evidence he sees in natural history for evolution and for its mechanisms but he puts forth all of the arguments against and dissects that. It's that old thinking from arguing with his father at work evidence and argument. These lectures are largely going to focus on two main ideas in *The Origin of Species* and our understanding today of how evolution works. But Darwin understood that to make these new ideas attractive and inspiring to a new generation, he had to do more than just put forth the raw facts. *The Origin of Species* contains all sorts of poetic passages and he closes with these words. "From so simple a beginning endless forms most beautiful "and most wonderful have been, and are being evolved." and I'm going to talk about, after we take a little time for questions, those two main ideas in this book and eventually how we've learned how the process of endless forms evolving actually occurs.

**17. Q&A: Did Wallace publish anything else?** (28:37)

So let's take a little break and open up the room to some questions. Yes, in the back. Did Wallace publish anything else or did he just kind of fall into not really prevalence? Wallace did not become anywhere near as prominent as Darwin. Wallace published lots and lots of papers, he wrote a great deal, but his writings never captured the popular audience that Darwin did and Darwin's books themselves inspired a lot more writers, so there were more people in the decade following Darwin who took up the pen and wrote their accounts of

evolution or their accounts of geology inspired by the theory set forth by Darwin. So we really don't have a literature from Wallace to read anywhere near as extensive as from Darwin.

**18. Q&A: How did Darwin's family react to his theory** (29:24)

Yeah, right here. How about his family? Like you said he was afraid of saying something because of what he believed, I don't know what religion but did his family ever find out when he got into that one book with Wallace? Excellent question, so what about Darwin's family? Darwin was very tender, he was very careful because he and his wife were so close. I mean they were so close, they played backgammon every night for their entire lives and Darwin, being somewhat compulsive, kept track of the lifelong score. I don't remember what it was. But they had 10 children 7 of whom survived to adulthood. They raised this menagerie together. He was always very careful of her feelings. And she, he would let her read these things. Now in the early 1840s when he first put this theory together in sort of outline form, he let her read it and then asked her to put it in a drawer and publish it after he died. He changed his mind when he lived a lot longer than he expected. So she was well aware of his thoughts and all she hoped for is that it would not, his theories would not disqualify them for time in heaven together and there's a lot of very tender correspondence between them that's on the record, little notes that she would scrawl to him, little notes that he would scrawl back to her. So it was understood and he did not pay the price that he feared with his family whatsoever. We're going to have to wrap up and save some of those questions. We're going to have another question/answer session after I finish the talk here about what was in *The Origin of Species.* So thank you for those questions and I owe you a t-shirt.

**19. Darwin's first big idea: Descent with modification** (31:07)

So let's move on to what's really in *The Origin of Species.* There's two main ideas, I don't know, 600 pages, it's great reading, I really encourage you to sometime take the time to read the real thing but I'm going to just focus on two ideas. Here's the first. Descent with modification. Darwin said, and we'll just take it right out of *The Origin of Species*: "Several classes of facts seem to me to "proclaim so plainly that the innumerable species, genera, and "families of organic beings, with which this world is "peopled, have all descended, each within its own class "or group, from common parents, and have all been modified "in the course of descent." This was a huge idea. This idea that all life is connected through ancestors back further and further and further and further into time. It was a bold idea, very, very bold and really built on at the time, a modicum of evidence, but nonetheless a grand theory. Darwin represents this idea really with his tree of life. This is the only figure in *The Origin of Species,* not a very heavily illustrated book, one figure. And Darwin points out that "This great tree of life fills "with its dead and broken branches the crust of the "earth and covers its surface with ever branching and "beautiful ramifications." Now if I wrote like this today, all of my peers would just wipe me out, okay. You're just not allowed this kind of poetry in scientific journals, all right, but Darwin was trying to get people to understand the inspirational view the grandeur of his view of life and that's why he talked about filling the crust of the earth and covering the earth with its beautiful ramifications.

**20. Fossil evidence for common ancestry** (32:47)

Well what did he mean by filling the dead and broken branches of the crust of the earth? He was talking about fossils. He had good first hand experience with fossils and of course the fossil record was one of the best sources of evidence of the fact of evolution. Darwin, as he explored South America for example, he was exploring the mountain ranges and the sea coasts and to show you here are a couple of paintings that depict explorers from the *Beagle* going across South American mountain ranges and in the bottom is a drawing by Darwin mapping out some of the mountain ranges. Well he was up on a road in the mountains at 13,000 feet and he sees fossil oyster beds, at 13,000 feet above sea level. Of course the land forms have changed, of course the species have changed. He understood that the surface of the earth was far more dynamic than he was first taught and that most of the world believed at the time. So the fossil record is a tremendous source

of insight into the actual history of the earth and from about 1860 to about 1920, after the publication of *The Origin of Species*, there was a golden era in paleontology when some spectacular deposits were discovered that hold key insights into life's history and I'm going to highlight four locations in North America each of which can be visited that hold some of the oldest, youngest, and most dramatic episodes in the fossil record. So in a map I'm going to show you some. They're all west of here, but as I said some are more easily accessible than others as you'll see from some of the pictures of these locations. So I'm going to start with one of the oldest fossil deposits

**21. Burgess Shale fossils** (34:23)

and I'm going to talk about the Burgess Shale. Now this is in British Columbia. It was discovered by Charles Wolcott in the early 20th century. That's Wolcott on the right at the quarry that he was working on. And what came out of these quarries were these little animals, some somewhat familiar to you as trilobites, others might look a little more foreign, *Aysheaia* is an example. These are some of the earliest complex animals in the fossil record. They're over 500 million years old and the original specimens can be seen right at the Smithsonian Institution in Washington. Just step right inside the Hall of Dinosaurs and in some glass cases right there you'll see pieces of the Burgess Shale with these very animals that you're seeing pictures of inside them. So over 500 million years old.

**22. Dinosaur National Monument fossils** (35:05)

Now let's go a little bit younger to Dinosaur National Monument, on the border of Colorado and Utah, fantastic place both in terms of scenery as well as fossils. This is Jurassic Age deposits, of course Jurassic should probably ring a bell, golden age of the dinosaurs and in Dinosaur National Monument in the earliest 20th century, huge bone quarries were found. The main quarry that you can see at the visitor's center at Dinosaur National Monument contains I think somewhere over 2,000 exposed dinosaur bones and you see these things exposed like skulls and major pieces of backbones and huge dinosaur legs all together. This is probably somewhere, this was formed by some river washing lots of bones down and all getting covered up in river sediment and so you have just sort of this hodgepodge of dinosaur pieces, but many full intact skeletons came out of this quarry and they have been assembled and exhibited in all sorts of natural history museums all over the world.

**23. Fossil Butte fossils** (36:05)

Fossil Butte, this is a national monument, this is administered by the National Park Service, Fossil Butte is in southwestern Wyoming. Now what you can see at Fossil Butte are these rock formations. This is a very arid area and in these layers that you can see here as sort of the horizontal layers or what they refer to as horizons, some of these horizons are extremely rich in fossil deposits, amazingly rich. And when the transcontinental railroad was going through this region and they were dynamiting their way through the rock, the workers were just stunned to find rocks everywhere full of fossil fish and the reason why they were full of fossil fish is that Fossil Butte is part of an ancient lake bed, about 50 million years old, an enormous lake that covered that region of the United States and in these lakes there would be some annual die offs, maybe as water levels became low or oxygen levels became low there'd be massive die offs and as those fish became covered in silt, and then protected from further decay they became fossilized and what you can find in layers of this rock, almost like the pages in a book as you crack them open and open them up, you find these mass fish kills. In this slab alone, somewhere perhaps 80 fish in a piece of rock that's maybe six feet long. There are other fantastic fossils at Fossil Butte that tell us something about what the area was like. This is not the sort of fossil, if you look at the current landscape of Wyoming, this is not the sort of thing you'd expect to see perhaps, but yes, 50 million year old palm trees. Beautiful fossils, this one's probably about eight feet tall of palm trees. Palm trees are telling us this was a tropical area or semi-tropical area, probably

had a climate a lot like south Florida 50 million years ago. Very different, of course, today. So again, the environments have changed, the animal forms have changed, the plant forms have changed.

**24. La Brea Tar Pits fossils** (38:10)

Now moving to even very recent deposits, here's a picture from about 1910 of an area known as the La Brea tar pits and you may see in the back those oil derricks. And what those oil derricks are doing is they're extracting the petroleum products out of this bed. This bed is full of this thick, gooey stinky petroleum mess, very tarry sort of substance but it had use as a petroleum derivative and these tar pits are now in the dead center of Los Angeles. So there you are surrounded by Los Angeles skyscrapers but these tar pits have been set aside and preserved as a park and as a museum because they contain the most spectacular deposits of ice age mammals from 12,000 to 14,000 years ago in these bone beds which as you look down at them, and there's lots of open bone beds that you can view as you walk through the park, as you look in there you see just piles of bones and what happened was as animals became trapped in this tarry goo, let's say something like a mammoth, scavengers would come along to feed on it and become trapped in the tarry goo and scavengers would come by to feed on them and become trapped in the tarry goo. So you just have this you know the equivalent of an early L.A. traffic jam, just a pile up of dead animals forming in these tar pits. Well the other great benefit is this tar is an incredible preservative. So while it takes a lot of work to clean it off the bones underneath are exquisitely preserved. So there's hundreds of beautiful skulls of saber toothed cats and of dire wolves and full skeletons of mammoths and mastodons. So unlike what happens when say a dinosaur gets washed down a river and gets broken to pieces these things were preserved as they fell, so spectacular intact fossils. So on the next visit to L.A. I highly recommend a visit to La Brea tar pits.

**25. Key facts from the fossil record** (40:00)

So what are these specimens from the fossil record tell us? Well they tell us four main ideas. First of all undoubtedly that animal and plant forms have changed over time. Secondly the time span of evolution is immense. I've shown you just the animal record spanning more than 500 million years, but also most of this stuff that I'm showing you is not around at all, not around anymore. So extinction is the fate of most species that have ever existed. Biologists estimate perhaps 99.9% of all species that ever existed are extinct. And environments in every locale have changed often drastically so. Those Burgess Shale creatures I showed you, those were marine animals now found above the tree line in British Columbia. Those palm trees of course look nothing like the current landscape, so environments change and one of the main messages, the reason I want to tell you so much about Darwin's geological observations and of the fossil record is that living things are occupying a planet whose surface is always changing. Hurricanes, earthquakes, volcanoes, tectonic movement ice ages, climate changes, whether local or global all of these keep changing the environments that species are in. They are running to keep up and most of the time they fail. So we have to think about earth history to understand life's history. We have to understand what's going on in any particular place to appreciate what's going with any particular species.

**26. Darwin’s second big idea: Natural selection** (41:34)

So the record tells us that evolution has happened but the main question Darwin wanted to address was how and this is the second big idea. The second big idea is natural selection. And I'm going to tell you a whole chunk of code here from *The Origin of Species* contains every element every ingredient necessary for natural selection to work as well as the clearest definition of the process. Darwin says: "Can it then be thought improbable that other "variations useful in some way to each being in the great and "complex battle of life should sometimes occur in the course "of thousands of generations? "If such do occur can we doubt, remembering that many more "individuals are born than can possibly survive "that individuals having any advantage "however slight over others, would have the best "chance of surviving and procreating their kind? "On the other hand we may feel sure that any variation in the "least degree injurious would be rigidly

destroyed. "This preservation of favorable variations and the rejection "of injurious variations I call natural selection." Two sides to the coin. Rejection of things that are less favorable and the preservation of those things that are more favorable. So

**27. Evolution's ingredients: Variation, selection, and time** (42:44)

what are these ingredients? Well if we look at Darwin's quote, he's saying variation there in red, thousands of generations, time and advantage. He means selective advantage. So these are the three ingredients, this is the fuel of evolution: variation, selection, and time. If you want to think of it, think of any process that produces a product. You usually have raw material, some work, over time. The raw material is variation, selection does the work and time, it takes various amounts of time for the process to happen.

**28. Evolution in action: The rock pocket mouse** (43:19)

So to illustrate this process of natural selection I want to give you just one example, sort of a modern example but it illustrates all the features that I want to tell you about of seeing these ingredients of evolution and we're going to think about the adaptation of a really modest humble species, to a changing landscape. What I'm showing you here is a lava flow across part of the desert in the American southwest. Over the last couple of million years there've been eruptions that have led to lava flows. When that lava cools it forms these black rock formations on this general background of sort of sandy dry soil. In this habitat lives the humble rock pocket mouse. And that rock pocket mouse occurs in two varieties. A sandy colored mouse, and a dark colored mouse, and I'm showing you these animals on different colored backgrounds. The sandy mouse that matches well to the sandy colored rock the dark mouse that matches well to the dark color rock and then you can see the mismatch when either the dark mouse is on light rock or the light colored version is on dark rock. And it matters, this color matching really matter with respect to predators. Let me just explain to you a little bit about color matching in mice with a short video.

**29. Animation: Pocket mouse predation** (44:34)

So when that dark mouse finds itself on light colored habitat... it can be in big trouble. Its natural predators are owls but of course if we change the backdrop the dark mouse blends in well but the light colored mouse is in trouble.

**30. Coat color determined by forms of a single gene** (44:53)

so we now know a lot about the ecology, about the genetics and about the evolution of this pattern and this is what I wanted to tell you. The rock pocket mouse inhabits these lava flows in the surrounding rocks and this color matching is important to its survival. Well, there's two forms of the mouse, it's all the same species and those two forms are determined by genetic variation. There's a single gene that we'll abbreviate here called *MC1R* that comes in two alternative versions or alleles. And sandy colored mice have two copies of the light allele for this gene and the dark mice have either one copy or two copies of the dark allele. So scientists in the University of Arizona have pinpointed the exact genetic basis for the fur color difference between the two populations of mice. Now

**31. The odds of a mutation producing a black-coated mouse** (45:49)

let's consider how long might it take for a black mouse to arise in a sandy colored population. That lava flow has happened. How long would it take? Can natural selection really do the job to allow a population of mice to adapt to a new landform in this case lava rock? Well the ingredients there have to do with the interplay between variation and time. What I'm going to do is I'm going to walk you through the variables; I'm going to walk you through crunching a little bit of the numbers and rather than take notes I'm going to urge you to

just follow along or look up watch the board, whatever. Don't worry about the numbers, we can always go over them again later, but just follow along the logic of crunching the numbers of how these ingredients of evolution interact. So to know how often a black coat mutation can arise that's going to depend upon three things, the mutation rate the reproduction rate in these mice and the population size. How many mice are there? How often are they reproducing? Well we know a lot about the mutation rate from decades of study and the mutation rate in mice is about two mutations per billion sites in DNA. So DNA copying is highly accurate, but not perfect and if it was perfect there'd be no evolution. We need variation for the fuel of evolution to work. There are about 10 sites in the *MC1R* gene that can be mutated to cause this black type of appearance and there are two copies of the *MC1R gene in every mouse.* If we multiply all those together

**32. Time and selection** (47:14)

what we come up with is one in 25 million mice, baby mice, will have a black coat mutation. One in 25 million. Well geez, you know, does that mean, one in 25 million is that a long shot, does that mean that I can't see how this evolution would work? Not at all because now we have to introduce some other factors. Those other factors are the reproductive rate and the population size. So each female in this population is having at least five babies, at least five babies a year and an average population is about 5,000 females. So there are about 25,000 pocket mice being born a year in this population. Now if we multiply 25,000 babies times one in 25 million that means every 1000 years there will be spontaneously a black mouse born to sandy colored parents. One in 1000 years. Now let's put it in a geological framework. Those lava flows I'm showing you, some are 1.7 million years old. So this mutation could have arisen 1700 times independently, plenty of time for the raw material to arise 1700 times over.

**33. Selection provides force for a new variant to spread** (48:32)

Okay, so how does this black coloration actually spread through the population? Well that's selection's job. How long does it take for every mouse to become black? Now we have to figure some other variables. It depends on population size, how many mice are there in the population, and it depends on something called the selection coefficient. We denote that as a little *s* and that is the advantage that a mouse carrying the black gene has over mice without it. That's a relative measure of fitness and that measure is a product of reproduction and survival, okay. So if we put this in terms, if black mice, in general produce 101 survivors for every 100 mice produced by sandy colored mice, that's a 1% advantage and we would write *s* as .01. You're about to see that 1% is plenty of advantage for evolution to work, for natural selection to work, and if there was a 5% advantage, okay we'd write that as .05. Remember, just 101 to 100 compounded over time, you're going to see how this works. Okay. So let's show this in this animation.

**34. Animation: Simulation of pocket mouse evolution** (49:41)

Consider the southwestern United States, sandy colored landscape until some lava flows happen. That lava cools and now that black rock is going to be invaded by the sandy colored mice. Once every 1000 years or so a black mouse is going to pop up, the owls are going to be there circling overhead for eons and if we start with a population where just one mouse is black and it has just a 1% advantage, watch what happens over the generations then in about 1000 generations 95% of the mice will be black. That's just natural selection doing the work. One mutation, one founding mutation can spread to 95% of the population in 1000 generations. Now what happens if there's a 10% advantage of being black? Very quick. In 100 generations 95% of the mice will be black. It turns out from measurements in the wild, there's an even greater than 10% advantage of mice being black on the black lava flows.

**35. Evolution works faster than you might think** (50:46)

So natural selection is very swift indeed and the amount of time that we have when we're speaking on the geological time scale for evolution to work is ample time for mutations to arise and for selection to spread favorable mutations throughout populations. So what's the bottom line? The bottom line is that how long it takes for these traits to spread it's a lot faster than most people realize. On the order for these things of maybe a century or millennia and you're going to hear a lot more examples about this in Dr. Kingsley's talk this morning. So you're going to understand more about the power of selection. It's so powerful that our civilization depends upon it and you'll see more about that from Dr. Kingsley. So it's raw material plus selection over time. That's the formula and we see vivid evidence of natural selection working in all sorts of cases both natural and artificial.

**36. Q&A: How does the mutation arise?** (51:43)

So let's stop there and I'll take some questions. In the back right. You're saying like, how over time for a mutation like, how does the mutation even get there? So the question is how does the mutation arise? Mutation is a completely random process. So as sperm and egg are produced for reproduction there are errors made in the copying of DNA at random. These errors change the DNA code at random and that creates random variation in genes. Some of those genes control fur color, I told you the example of one of those, so at a low rate, one in 25 million there are mice born that look different than their parents in terms of fur coloration. But that is entirely a product of just the chemical nature of mutation that happens as the billions of sites in DNA are copied. In every generation of us there is about 100 new mutations in you that were not in your parents, for example.

**37. Q&A: What about black mice on a light background?** (52:44)

Yeah? The way you said the white mice they're recessive to black mice but what if it had been the other way around? For the color of the mice? Great question. That's an overhand shot there for you. The question is if the black mice need to invade a sandy habitat, it's actually very easy to inactivate this gene so it doesn't work and that the mice are lightly pigmented. There's actually lots of ways you can mutate that gene so the frequency of actually going black to white is even higher than it is from going white to black. And there are examples in nature of where this has happened. For example there are some bears on the northwest coast of Canada that are all white fur and they have mutations in this gene that have inactivated it rather than make it form the black form. So both directions are happening in the wild and I can tell you that this same gene I'm telling you about is responsible for the black color phase of jaguars, for the black phase of snow geese, for the black phase of certain other types of cats and for some black phases in domestic dogs. So this is a gene that has been called upon repeatedly to endow mammals with dark fur coloration.

**38. Q&A: Selective difference for hetero- vs. homozygotes?** (53:55)

Yeah. You said with the homozygous, I mean with the black mouse they could be homozygous dominant or heterozygous. Will the homozygous dominant ones be more prevalent just because the heterozygous ones could produce the sandy colored offspring? That's a great question. So the question is about whether it matters whether you carry one or two copies of the gene, is there any selective difference? It turns out there's a bit of an additive effect of the alleles so that the mice carrying two copies are a bit darker than those carrying one copy. That may be a selective advantage. So you may be still favoring the homozygote more than the heterozygote, but still in order to really know that we'd have to do pretty large population studies and genotype a whole lot of mice to understand the relative contribution of those two genotypes in the wild.

**39. Q&A: Black mice on black background: coincidence?** (54:48)

Yeah, right there, right in front of the camera... Sorry, I'll go with him in the front first. Yeah. The way you make it seem is that evolution happens as a coincidence. Is there only black and white choice between the

mice and say the environment had changed to like an orange color is it just these two types or is it just a coincidence that environment had turned black and there was a black mutation for the mice. I don't want to make it sound that there's a coincidence at all. The change in the environment of course is outside of the animal's control, okay. But there are mutations that occur in populations and if you look through this room at 200 humans and you consider our features that are visible, hair color, eye color skin coloration, facial features, et cetera you see tremendous variation. If you had that sort of acuity in a mouse population you'd also, if you were looking at other mice, you'd say, there's a little bit of small variation here, you know. Fred's got a little bigger head, little longer whiskers little taller ears, et cetera. So there's tremendous variation in populations. Now the environment here, the selective pressure is on fur coloration because of the set up between predator and background color. But if you want to say well, look, what if the rocks were a little different color like say tan or something like that and the sandy soil was pure white, would there be advantage for being tan coloration and could the mice evolve that color? And I'd say absolutely. Different sets of mutations, different selective process but eventually as this competition runs, if there is an advantage to a particular fur color scheme, this process will repeat itself again and again and again. So the coincidence, really, the mutations arise at random but there's nothing random about selection. Selection is the conditions that the animal is living in and that either predators or for example mates impose upon it. So I'm going to wrap up but I'm happy to take some questions while we have a break and we'll have many more opportunities to talk about evolution and the process of natural selection over the next three lectures.

**40. Closing remarks from HHMI President Dr. Thomas Cech** (56:58)

Thank you, Sean Carroll for getting our lectures on evolution off to a really great start. It's amazing to see how Darwin's insights continue to inform today's research. And thank you, students, for some really great questions. Now we're going to take a 30 minute break. When we resume David Kingsley will focus in on this idea of the role of selection and how it plays into evolution.