Discovery: Greatest Discoveries in Genetics, Hosted by Bill Nye

https://www.youtube.com/watch?v=17foW4mLBFk

00:00
Bill Nye: A good priest who left his mark as a great scientist by exploring the miracle of heredity. [Gregor Mendel]

00:15
Bill Nye: A brilliant researcher, her work largely ignored by her male colleagues until a revolutionary breakthrough. [Barbara McClintock]

00:22
Bill Nye: A spellbinding journey to find the common thread of molecules that define the biology of life. [Watson and Crick with help from Wilkins and Franklin]

00:35
Bill Nye: An unprecedented collaboration of scientific minds and willpower to solve the mystery of what makes us human.

00:45
Bill Nye: These are the greatest discoveries in the history of genetics.

01:25
Bill Nye: Nearly 50 years ago. This man discovered that I am his brother.
Darby Nye: Bill, that's not one of the great discoveries, is it?
Bill Nye: No, no, that's a joke.
Darby Nye: Yes, it's a joke, geez.
Bill Nye: No, no, not geez, genes!

01:42
Bill Nye: When we're conceived, we inherit the genetic characteristics of our parents, but how are those characteristics transmitted from one generation to the next? That's our first great discovery.

Laws of Inheritance

02:01
Bill Nye: In the middle of the 19th century an Augustinian monk named Gregor Mendel took up the question of biological inheritance with a series of experiments.

02:12
Bill Nye: Mendel had a naturally inquisitive mind and a profound love of nature. His scientific interests ranged from research on plants to meteorology, and the theories of evolution. Working at a monastery, in what is now the Czech Republic, Mendel started

by crossbreeding different strains of garden peas then observing the characteristics of their offspring. Why choose peas? He did it, he said, for the fun of the thing.

02:40
Bill Nye: Mendel noticed that when he crossed a round pea seed with a wrinkled one, the offspring were round, not a mix of the two characteristics as he had expected. Yet when he bred the round pea offspring, that's where the mix appeared, and the second generation had both round and wrinkled seeds.

03:01
Bill Nye: He continued to experiment trying to understand what kind of biological mechanism would cause certain characteristics to disappear in the first generation, only to reappear in the second. Then one day, Mendel counted the number of peas in the second generation that had the wrinkled characteristic. Exactly one-quarter of the peas were wrinkled.

03:24
Bill Nye: What Mendel observed in his experiments were the biological phenomena we now refer to as dominance and segregation, only Mendel didn't know it yet. Still, his experiments produced a curious set of facts which, as he said, "Forced themselves upon my notice."

03:41
Bill Nye: You see, no matter how he cross bred the various strains of peas, the hidden characteristics showed up, but only in one quarter of the second generation. For Mendel here was the breakthrough: For the first time he could demonstrate that the traits of successive generations were inherited in certain numerical ratios. In other words, there were fixed laws of nature that governed heredity.

04:09
Bill Nye: With this insight Mendel made the first great discovery in the science of genetics: Each inherited characteristic must be decided by a pair of, what he called, factors. Each parent, he said, contributes one factor for each characteristic. Certain factors are dominant, and others recessive, depending on the combination of the factors the offspring inherits, and Mendel's factors are called genes.

04:37
Bill Nye: The term Mendelian trait is used to describe a characteristic caused by a single gene that sometimes reappears in one quarter of the offspring. That characteristic can be innocuous (harmless) such as freckles or the ability to curl your tongue, but it also can lead to serious illnesses like cystic fibrosis or Tay-Sachs disease. Imagine, all that from. one man's work with the humble pea, and it was experiments with another humble species that produced our next great discovery.

Genes are Located on Chromosomes

05:15
Bill Nye: Meet drosophilia melanogaster, the common fruit fly, its role in genetics research is as important today as it was over a century ago. See, in the early 1900s, scientists began to re-examine Mendel's work on inherited traits, and in 1909 a Danish botanist named Wilhelm Johannsen coined the term genes to describe Mendel's factors.

05:40
Bill Nye: Among the researchers in the new field of genetics was Thomas Hunt Morgan an independent-minded Columbia University embryologist. In his early work, Morgan was critical of Mendel's conceptions of heredity, and even skeptical of Darwin's theory of natural selection. That is until Morgan started working with drosophilia.

06:05
Joseph Gall is a cell biologist at the Carnegie Institution in Baltimore Maryland.
Bill Nye: Why did Morgan choose fruit flies? What was going on?
Joseph Gall: Well, I think he chose fruit flies for several reasons. The chief of which for the short generation time, so that's very important. The other important thing is that one female fly can give several hundred offspring, so to do genetics first of all you need a lot of data. You need a lot of flies, a lot of individuals, and you don't want to wait forever to get them. You can have many generations per year, and thousands and thousands of offspring.

06:41
Bill Nye: The story goes that one day, shortly after Morgan started breeding Drosophila for his experiments a striking mutant appeared in his lab, a fly with distinctive white eyes.

06:55
Bill Nye: He decided to breed it with a female fly that had ordinary red eyes curious to see what the offspring would look like. Two weeks later he had his answer. One by one, the first-generation offspring appeared. All of them had red eyes. Thinking that the white eyes might be a hidden characteristic, similar to what Mendel had observed Morgan waited to see what would happen in the second generation. Sure enough, the characteristics skipped a generation. This time some of the flies had red eyes and some had white eyes, but then Morgan saw something else. All of the flies with white eyes were male.

07:40
Bill Nye: At the time it was known that the gender of a species is determined by two of the rod-shaped structures found in the cell nucleus, the chromosomes. For example, human females have two X-chromosomes. Human males have one X-chromosome and one Y-chromosome.

08:01
Bill Nye: Morrigan realized that the gene responsible for the white eyes must somehow be associated with the fact that male flies have only one X-chromosome.

08:12
Bill Nye: This meant that in the females the gene responsible for red eyes on one of the X-chromosomes might be overshadowing the gene for white eyes on the other.

08:24
Bill Nye: To prove his point, Morgan bred thousands of fruit flies and studied their inheritance.

08:32
Joseph Gall: Morgan's observations were absolutely fundamental to everything about genetics because what Morgan and his students showed was that the genes are located in a linear order on the chromosomes.

08:48
Bill Nye: Today geneticists know that diseases like hemophilia and muscular dystrophy are caused by defective genes on the X-chromosome. It's believed that other diseases like cancer may be linked to damaged or defective chromosomes.

09:03
Bill Nye: For his discovery, Morgan was awarded the Nobel Prize for Medicine in 1933, the first scientist to win it in the field of genetics, and Drosophila melanogaster, thanks to the fruit flies' contribution to Morgan's work, drosophila is enshrined as one of the basic animal models in experimental science and its legacy led to our next great discovery.

Genes Control Biochemical Events

09:37
Bill Nye: One of the geneticists who studied fruit flies alongside Morgan was George Beadle. Working in Paris in 1935, Beadle detected evidence that the inherited trait of eye color in drosophila might be the result of genetically based chemical reactions,

09:56
Bill Nye: Beadle pursued his investigations at Stanford University with colleague Edward Tatum. For their experiments, Beadle and Tatum selected another simple organism, neurospora crassa, bread mold. They chose mold because it was easy to grow. With simple nutritional needs, bread, air and water, Neurospora also had a single set of chromosomes which allowed the researchers to observe genetic changes easily. Knowing that x-rays damaged the chromosomes, Beadle and Tatum irradiated the mold which caused mutations in the genes of its spores.

10:37
Bill Nye: These mutant genes were unable to produce the nutrients necessary for the mold to grow, however, when they added the nutrients, some of the spores began to germinate. For Beadle and Tatum, this was a breakthrough moment. They realized that the irradiated spores failed to produce the essential nutrients because their genes were defective. This was significant. It meant that genes were responsible for more than just passing inherited traits from one generation to the next.

11:11
Bill Nye: They [genes] also directed the production of enzymes that the mold depended on for its survival. Beadle and Tatum's breakthrough is known as the one gene one enzyme hypothesis.

11:23
Bill Nye: Lactose intolerance is an example of a human metabolic condition caused by a single missing enzyme, missing because some people have inherited a gene that fails to produce lactase and are unable to digest the sugar in dairy products.

11:38
Bill Nye: This disorder can be easily treated by taking tablets containing the missing enzyme. Thanks to Beadle and Tatum, we gained a fundamental understanding what genes do, and the stage was set for a new generation of remarkable genetic discoveries.

Transposons

12:04
Bill Nye: So far we've seen how genes are transmitted, where they're located, and how they work, but our next great discovery revealed a brand new surprise about what else genes can do, and it came from a surprising source. Meet Barbara McClintock, a woman who became one of the most distinguished scientists of the 20th century. To learn more about McClintock, I paid a visit to David Kirk, professor of biology at Washington University in St. Louis Missouri.

12:38
Bill Nye: There's many, many, things I'd like to ask you, but let me start with Barbara McClintock.
David Kirk: A fabulous scientist, one of the world's best.
Bill Nye: But she faced a lot of challenges.

12:45
David Kirk: Oh, she sure did, partly because she was just too bright for most people, and her mind went too fast, but even though she was a member of the Academy she was never offered an academic position, primarily because she's a woman, also because she was so much brighter than any of her male colleagues that many people were afraid of her, afraid of her brain.

13:10
Bill Nye: In 1942, disenchanted by her lack of career advancement in the male-dominated field of genetics, McClintock went to work at the Cold Spring Harbor lab in New York. It was here that McClintock made history.

13:24
Bill Nye: Working alone, she chose to research the genetics of maize (corn). Of special interest to her was the genetic mechanism underlying the unique mosaic of colored kernels it was while studying these that McClintock began to notice a correlation between the color of a kernel and a break that occurred in one of its chromosomes. The colors of the kernels corresponded to where on the chromosome the breaks occurred. A break in the chromosome occurred, she said, when a gene randomly jumped, or transposed, from one chromosome to another. When this happened, it disrupted the activity of the other genes responsible for producing the pigment of the kernel.

14:10
David Kirk: Everybody at that time thought of chromosomes and genes as being very stable things just transmitted from one generation to another. She found that certain genes she was trying to locate on the chromosomes would be in a different position at different times. In one corn plant it would appear to be in one position in the chromosomes, in another corn plant and be in a different position, and a third corn plant might be in a third position. How could this be, a single gene in different locations in different plants, and she made the intuitive leap that these genes were leaping, going from one place to another, which is totally unheard of at that time. She was the first person who really saw the kind of detail that's present in every chromosome, literally the first person. She could look at a single kernel of corn and see the genes, see the chromosomes. She could look at the chromosomes and see the whole plant. She was incredible.

15:06
Bill Nye: Barbara McClintock's discovery of transposons was as evolutionary as it was revolutionary. While some genetic mutations caused by transposons are linked to cancer and other diseases, transposons may also be a mechanism that causes genes to mutate in response to changes in the environment and spur the evolution of a species. Today we know that transposons exist in the genes of all living things, everything from algae to human beings.

15:40
David Kirk: My postdoctoral fellow, whose name was Steve Miller, came here specifically to try to find a transposon that could do what Barbara McClintock showed the transposons in corn. He finally found one that he could control the jumping of, and it jumped so well when he was interested in it that he named it after his basketball hero, Michael Jordan. So, we always keep a picture of Michael around the laboratory slam

dunking algae.
Bill Nye: Every basketball player's dream, to dunk algae.

16:15
Bill Nye: While Barbara McClintock never gained the fame of Michael Jordan, she did achieve her own notoriety. When she presented the findings of her research in 1951 at a Cold Spring Harbor symposium, her work was ignored and rejected. The experience made her so bitter that she never gave another lecture there, though she continued working at the lab until her death in 1992 at the age of 89. She did live long enough to be vindicated thirty years after her pioneering discovery, McClintock was awarded the 1983 Nobel Prize for Medicine.

DNA Carries Genetic Material

17:02
Bill Nye: The Cold Spring Harbor Laboratory was the site of our next great discovery as well. It happened here in 1952. Biologist Alfred Hershey and Martha Chase were studying bacteriophage, a virus known to infect bacteria. Through a process called transformation, the virus takes over the bacterium's internal machinery and commandeers it to produce more viruses.

17:29
Bill Nye: Bacteriophage consists of two simple components a protein shell and, inside, a mysterious substance [that] scientists had known about for decades called deoxyribonucleic acid, or DNA. Hershey and Chase wanted to know whether it was the protein or the DNA in the virus that carried the genetic information. Using two radioactive chemicals, they labeled the protein in one set of bacteriophages and the DNA in another. Then they exposed a culture of E. coli bacteria to these viruses. After using a kitchen blender to separate the bacteria from the empty viral protein shells, Hershey and Chase saw that the radioactive protein was not penetrating the bacterial wall, but inside the bacterium was the radioactive DNA. It was the DNA, not the protein, that was able to direct the host cell to make new viruses.

18:28
Bill Nye: It was an extraordinary breakthrough. Thanks to Hershey and Chase, and the other scientists who helped pave their way, suddenly we understood the true identity of DNA. It's genetic material, the blueprint of life, and it all came out of a blender like this. Hershey was awarded the Nobel Prize in 1969 for his work, but Hershey and Chase's blender experiments went on to inspire a new era of genetic research beginning with our next great discovery.

The Double Helix

19:07
Bill Nye: As late as 1951, the chemical structure of DNA remained a tantalizing enigma

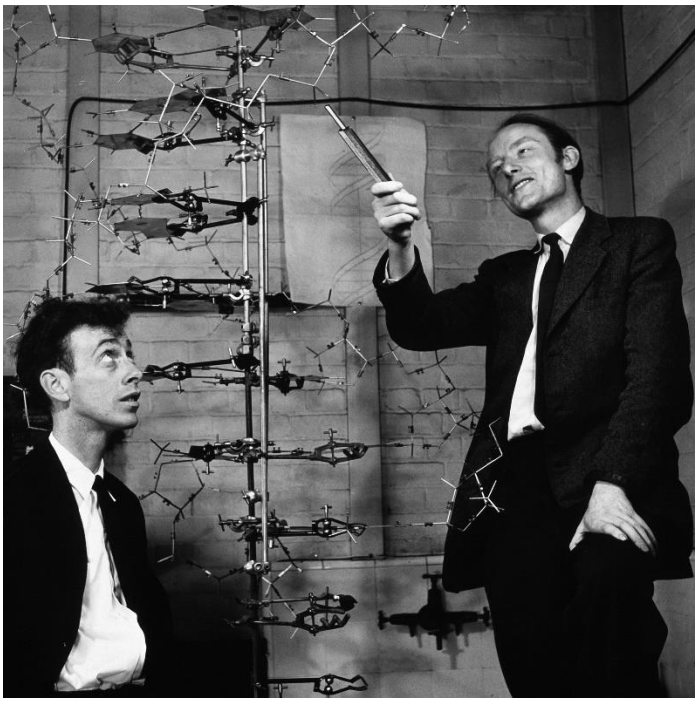
(very challenging puzzle). At Cambridge University in England, biologist James Watson and physicist Francis Crick had been working to unlock the secrets of the DNA molecule, but they weren't alone. Several other groups of competing scientists were hard at work trying to solve the same puzzle.

19:35
Bill Nye: Some important facts about DNA were already known. For instance, scientists knew that DNA was composed of four bases: Adenine, Cytosine, Guanine, and Thymine. They also had been able to infer something about its structure with the help of x-ray crystallography. This technique involved passing an x-ray beam through a crystallized DNA molecule and capturing a vague shadowy image of its internal structure on a photographic plate. Armed with this information, along with their own knowledge of chemical structure, Watson and Crick began building a three-dimensional model of DNA.

20:22
James Watson: I wanted an arrangement, you know, where I had a big and a small molecule (the small had one hexagon, and the larger had two) and somehow you had to form link bonds. Here's A, and here's T, and I wanted this hydrogen to point directly at this nitrogen, so I hit something like this. So, then I went to the pair, and wanted this nitrogen to point to this one like this, whoa!

21:03
Bill Nye: Today you can buy a kit and assemble the structure that Watson and Crick put together, but we're getting ahead of ourselves.

21:10
Bill Nye: Watson Crick needed more data. With the help of physicist Maurice Wilkins, they gained access to an x-ray picture of a DNA molecule that had been taken by his research partner. Her name was Rosalind Franklin.



21:28
Bill Nye: Without her knowledge, Watson and Crick used the data from that x-ray image and successfully completed their model. In a 1953 issue of nature magazine, Watson and Crick revealed their amazing discovery to the world. Their model showed

that the DNA molecule was a double helix. The twin strands were composed of pairs of the four known bases (ACGT) linked together by hydrogen bonds and the whole structure quarks grew like a spiral ladder which could easily pull apart in order to make copies of itself with the same encoded genetic information.

22:10
Bill Nye: Watson and Crick had won in the race the discovery of the structure of DNA sparked a scientific revolution it illuminated the molecular and biochemical foundation of life in a whole new way. It opened doors for areas of research and other great discoveries that few ever imagined possible.

22:29
Bill Nye: As for Watson and Crick, their discovery of the double helix, along with Maurice Wilkins, won them a share of the 1962 Nobel Prize. And what of Wilkins' colleague, Rosalind Franklin? Despite her contribution to the discovery, she wasn't considered for the '62 prize; the rules state that it can only be awarded to a living recipient, Rosalind Franklin died in 1958 of ovarian cancer, most likely caused by exposure to x-rays.

23:14
Bill Nye: Welcome to my world. This is one of the trillions of cells that make up my body. This material in the cell is called the cytoplasm. Over here is the cell nucleus. Inside the fragile nuclear envelope are the long thin strands of DNA. As we've seen, DNA contains the genetic instructions that control the cell's metabolic functions and heredity. Sounds simple enough, but the process by which this genetic transfer occurs is sublime. It's the story of our next great discovery.

24:10
Bill Nye: Years before Watson and Crick had defined the structure of DNA, scientists knew that DNA was responsible for making proteins that resided in the cytoplasm, but they were puzzled by how the DNA managed to transfer its genetic information for making proteins through the nucleus wall. The answer to the puzzle came through the collective work of several different scientists, and like many discoveries, it began with an educated guess.

24:45
Bill Nye: The production of protein in the cell is seen here in red. Scientists found that cells with lots of protein production contained lots of this: RNA, a chemical similar to DNA, but with only one strand, not two. This led scientists to wonder if RNA was somehow involved in running the protein factories in the cytoplasm. To find out, once again researchers turn to the bacteriophage. They detected that soon after the bacteriophage injected its DNA into a bacterium, traces of viral RNA appeared in the host cell, and the production of proteins began to increase. This was the moment of discovery. Here was a special kind of RNA never seen before.

25:40
Bill Nye: As its single strand enters one of the cell's protein factories, it communicates the messages for making new protein scientists called it messenger RNA. Today, many scientists believe that messenger RNA and other RNA molecules are descendants of the Earth's most primitive chemical materials, part of the primordial soup that cooked up the first living organism. [***See Primordeal Soup Hypothesis Worksheet***]

The Genetic Code

26:14
As we've just seen, RNA translates instructions from DNA for making proteins, but what was the genetic code the sequence of instructions that made this process possible? In 1961, molecular biologist Marshall Nirenberg and postdoctoral fellow Heinrich Matthaei, carried out a series of experiments to see if they could synthesize proteins in the laboratory.

26:44
Bill Nye: They already knew that there are 20 amino acids involved in the production of proteins. In their experiment, Nirenberg and Matthaei were working with RNA. Like DNA, RNA is made of four chemical bases in a Eureka moment of discovery they found that when three of the bases align in a specific sequence called a triplet. Two triplets code for a specific amino acid. The order of the triplets is the blueprint for the production of proteins today Marshall Nirenberg is a research scientist at the National Institutes of Health.

27:25
Bill Nye: So what does this mean to me as a citizen, taxpayer, voter?

27:29
Marshall Nirenberg: What it meant is that RNA is transcribed from DNA. DNA is copied into RNA, and RNA contains the information that determines the sequence of amino acids in protein. So that what you inherit from your parents is the sequence of letters in DNA, that determines how you synthesize, how you make all the different kinds of proteins that are needed for life.
Bill Nye: That make me.
Marshall Nirenberg: They make you, they make me, yeah.

28:00
Bill Nye: Nirenberg and Matthaei's discovery was the first crack in the genetic code, a peek at the secret vocabulary encrypted in each DNA molecule enabling it to instruct the synthesis of proteins. Over the next five years, Nirenberg successfully deciphered the 64 triplets that comprised the entire vocabulary of DNA. The genetic code had been broken, and in 1968 the discovery earned Marshall Nirenberg a share of the Nobel Prize for Physiology and Medicine.

28:36
Bill Nye: What was this like, you make this discovery?

28:38
Marshall Nirenberg: Well, it was opening a door to a toy shop. I mean, we could do virtually anything. We could decipher the genetic code.
Bill Nye: Every living thing has the same code.

28:49
Marshall Nirenberg: Yeah, there's one code that's used by every living thing on this planet and it's the same, it's basically the same language that's used, and when we found that out, you know I knew about all about Darwin, I knew all about the evolution, but this brought it home and in such an immediate fashion. All living things on this planet are related, were all derived from a common ancestor, and you know our bodies won't speak the same language it had. It had a very marked effect on me.

29:22
Bill Nye: Where Watson and Crick identified the structure of DNA Nierenberg and Matthaei uncovered the blueprint for how the structure worked.

Restriction Enzymes

29:40
Bill Nye: The breakthroughs that led to some of the discoveries we've seen so far might never have happened if not for this familiar organism, bacteriophage, and our next discovery dependent on it as well. For decades it was believed that bacteria were completely vulnerable to invading bacteriophage, but in the 1950s researchers found a wrinkle in that view. Certain types of bacteria were in fact resistant to being infected by a bacteriophage. How is that possible? The first answer was provided in 1962 by a microbiologist Werner Arber. He found that some bacteria had enzymes that fought back against the virus by cutting its viral DNA into pieces. This restricted the virus from taking over the bacteria, so they were called restriction enzymes, but how exactly did they work? Among those hoping to unlock that secret was microbiologist Hamilton Smith.

30:51
Bill Nye: Working in his lab in 1972, Smith was growing bacteria and bacteriophage together when he noticed that the DNA of the virus was breaking down. Smith acted quickly. He purified the restriction enzyme, then he identified the exact place where the restriction enzyme had severed the DNA. Then came the moment of discovery. Smith found that the enzyme repeatedly cut the viral DNA in the same place. He had discovered the first site-specific restriction enzyme.

31:31

Bill Nye: With restriction enzymes scientists now had a pair of molecular scissors they could use to cut DNA molecules, to virtually recreate nature. This is significant. Today, this ability to manipulate DNA is one of the basic tools in genetic engineering, what's called recombinant DNA research.

31:52
Bill Nye: Since Hamilton Smith's discovery, hundreds of restriction enzymes have been identified and scientists are using recombinant DNA for a world of applications on which we depend—everything from the creation of more effective less expensive drugs, to the production of human insulin for the millions of diabetics worldwide who rely on getting their daily dose.

RNA Alternative Splicing

32:26
Bill Nye: With the discovery of messenger RNA scientists had found the process by which DNA communicates instructions for making proteins in the cytoplasm. For decades, they believed this process operated by one simple rule: instructions were coded from one gene in the DNA to one type of messenger RNA which then produced one protein, but in the 1980s this theory was challenged when scientists began detecting something new: genes that coded multiple messenger RNAs, which then produced multiple proteins. It would take the combined efforts of several scientists to find out how this was possible, but finally they had their answer.

33:15
Bill Nye: Through a process called alternative splicing, some genes are able to code for more than one protein. The discovery of alternative splicing was important because it gave scientists valuable new insight into the role that RNA plays in the production of proteins, and that insight helped researchers make advances in a whole range of biomedical applications.

33:43
Bill Nye: For example, scientists have used their knowledge of alternative splicing to create more effective painkillers. Some medicines are designed to block the production of specific alternatively spliced proteins and enzymes which regulate pain in the nervous system.

Minisatellite DNA

34:08
Bill Nye: London, 1985. A boy arrives by plane from the African nation of Ghana. The purpose of his visit? To be reunited with his mother, but custom inspectors are suspicious. The boy's passport appears to be a forgery and there's no proof that the woman he's meeting is really his mother. The British government decides to deport the boy. Desperate, the woman turns to a detective for help.

34:39
Bill Nye: His name? Alec Jeffreys. Not a real detective but a geneticist at Leicester University. Before we learn the rest of the story, a little background: By the 1980s, scientists had become aware that genetic variation among individuals is very common, and they had begun to link the presence of these so-called DNA variants to the presence of disease-causing genes in large families.

35:07
Bill Nye: For example, Huntington's disease and that brings us back to Alec Jeffreys. In 1984, Jeffreys found something never seen before. It was a DNA variant formed by short identical sequences of DNA that were repeated, over and over. Jeffreys called these repeated sequences mini-satellite DNA. Then came the breakthrough discovery.

Sir Alec Jeffreys: What we're detecting, lots of bits of DNA, and in the humans at least are clearly variable, very variable. In fact, what we've got was our first very, very, murky DNA fingerprint and at that point the penny dropped.

35:50
Bill Nye: Jeffreys' discovery made history when he was asked to help solve the mystery of the boy from Ghana. For the first time, DNA fingerprinting was put to the test. Jeffreys compared the DNA of the boy with the DNA of his supposed mother. The results showed a striking similarity in the mini satellite DNA, proving beyond a doubt that the boy was her son.

36:16
Sir Alec Jeffreys: So I was there when she was told, "We got the DNA evidence, it's been accepted your boy is coming back and he's permanently with you." The look in that lady's eyes was magic. This was, really, I mean the first time DNA had ever done this. It was the first time that DNA always modern arcane science of molecular genetics had actually being used to go out in a non-clinical context and actually directly help someone.

36:47
Bill Nye: It's been over 50 years since Watson Crick's great discovery of DNA's double helix structure. Since then, scientists have probed and revealed many of the genome secrets, but not without some surprises.

37:07
Bill Nye: In 1997, scientists Andrew Fire and Craig Mello were conducting a series of experiments to better understand the function of specific genes. They injected synthetic RNA made up of two strands into the cell of a roundworm, then watched. What happened next was astonishing. A mechanism within the worm cell destroyed the double-stranded RNA, as well as some of its own messenger RNA. In effect the gene responsible for coding the production of proteins in the cell was turned off. Fire and

Mello had discovered what came to be known as RNA interference. Today, Andrew Fire is a geneticist at Stanford University.

Andrew Fire: We sort of came upon this in experiments where we were injecting RNA and hoping that things would happen that were very specific things and as everything

Bill Nye: Injecting with a little?

Andrew Fire: With a little glass needle, right, into the into a worm in our case, although similar experiments were done in a bunch of other systems, and if you see a situation where the RNA goes in there, and not only is it shut off, which is not too surprising, you don't know what happened then, but it's also shutting off one of the cells own genes, then you have a surprising situation. That was really the surprise that came up in the early 90s.

37:57
Bill Nye: The discovery of RNA interference was a milestone it gave scientists a potentially powerful new technology.

38:37
Bill Nye: What is RNA interference you're going to mean for the future? What are their applications for this?

38:42
Andrew Fire: The first one is really understanding this new biological mechanism.
Bill Nye: Whatever makes genes silenced.
Andrew Fire: Whatever makes gene silenced, turn on or off.

38:49
Andrew Fire: The second is being able to do these general screens of what genes do, being able to look at gene function, just using this mechanism as a tool, and the third thing is sort of, I would say, a Holy Grail in the field, is can we use RNAi as a therapeutic,

Bill Nye: To cure disease.

Andrew Fire: RNA interference as a therapeutic, can we cure disease with it, and the model there, the idea is, you take a disease where the people are sick because there's a gene there that's out of control.

Bill Nye: This is a genetic disease.
Andrew Fire: A genetic disease, which includes viruses, it includes tumors, it includes certain genetic diseases as well, and the question is, can we shut that gene off?

Bill Nye: This holy grail of therapeutic use in humans is still just out of reach, but Fire's discovery of RNA interference opens the door to a new generation of life-saving breakthroughs.

[There are an estimated] 25,000 [human protein-coding] Genes

39:50
Bill Nye: The mystery of what makes us human was partially solved with a cracking of the genetic code, but the rest of the answer lay in our next great discovery, the sequencing of our complete genetic blueprint, called the genome. The effort has been called the largest scientific collaboration in history, but it began as a race between two teams vying to be the first to sequence the human genome.

40:21
Bill Nye: By 1990 the teams had joined forces. Craig Venter was one of the team leaders.
Bill Nye: How did you get started on this thing? What made you want to sequence the human genome?

40:33
Craig Venter: Well, I started my career looking for one gene, the gene for the adrenaline receptor in the brain, and the heart, and it took 10 years to get one, and the choice was trying to look at the entire human genome which we had essentially no knowledge of, only a few hundred genes at the time, and there was speculation maybe there were 300,000 genes. So, here's the most important information to our own humanity, and we knew essentially nothing about it.

41:05
Bill Nye: By June 2000 the two teams were ready to make history.
Press Announcement: Today marks a historic point in the 100,000 year record of humanity. We are announcing today for the first time our species can read the chemical letters of its genetic code

41:24
Bill Nye: So, what did you find?

41:28
Craig Venter: Well, first, the simplest thing we found is that we had only a tiny fraction of the genes that some people are predicting. Instead of 300,000, we found 26,000, so then we found that the variation between any two humans is remarkably low, we're almost virtually identical to each other, and then by sequencing the genomes of other mammals we sequenced my standard poodle, Shadow, so we have the dog genome, the mouse genome, the rat genome, we're now doing the rhesus monkey genome here.

42:00
Craig Venter: We find that all mammals share most of the genes in the same order, the

same sets of genes, and they just move around from one chromosome to another.

42:12
Bill Nye: So where is all this sequencing taking us?

42:15
Craig Venter: Well what I've argued from the beginning is that this lays a whole new foundation for science. People were expecting miracle cures, I think, there was a lot of overhype on things, but what took me a decade to do with the adrenaline receptor,

42:28
Bill Nye: This one you first started out
Craig Venter: That's right. Now any scientist, any student in the world that has access to the internet, can make that same decade-long discovery in five seconds, or a few seconds, and most human genes we don't know yet even any functions about them, so we're starting at a new foundation of having this information. They have the structures of actual genes, they can study their function, and it's changing our view already of evolution, our similarity with other mammalian genomes, even with plant and bacterial genomes. It's impacting medicine already with new diagnostics, understanding the complexity of genes associated with human traits and disease, and that's going to be a huge challenge for the future.

43:10
Bill Nye: So how did you feel when your group sequenced finished, did it, pulled it off?
Craig Venter: When we finished it and finished writing the paper describing it for the first time, it was probably one of the most fulfilling moments I've ever had in my life, and it was a fantastic period of satisfaction with what our team did in trying to contribute to the history of humanity.

43:37
Bill Nye: It's hard to believe, but from Gregor Mendel's discovery of the laws of heredity, to the complete sequencing of the human genome, has been a mere hundred and fifty years, but thanks to some of the greatest discoveries in the history of science, it's been time enough for us to understand some of life's deepest secrets, and to understand the genetic ties that bind all living organisms.

43:59
Bill Nye: That includes you, brother.
Darby Nye: Thanks Bill.
Bill Nye: Oh no, no, it is I who must thank you, for taking the time to come here and do a little Discovery.