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Transcript – Lecture 12

By the time that Watson and Crick figured out the structure of DNA, you know, it was sort of obvious that since the two strands were complimentary you could see how it replicated. And they also could see that somehow the information must be encoded in the sequence of letters down the strands of the DNA. But it wasn't obvious what the code was and how it was arranged, how it worked. And in principle it was anything you could do with four-letters.

And so I pointed out the other day this was sort of a four-letter alphabet. And I think it's useful to think of it this way with A, G, C and T, and RNA as also being a four-letter alphabet. But proteins are actually a 20-letter alphabet because there are 20 different amino acids. And so somehow, since one of the key things that the DNA had to do, it somehow had to encode the information for making the proteins.

And there was a lot of work on protein biosynthesis at the time. And it looked pretty complicated. People had found that RNA seemed to be important. Cells that were making lots of protein had lots of RNA in them. And another thing they noticed was that if you looked in eukaryotic cells the DNA stayed in the nucleus. The proteins, most of them, were out in the cytoplasm.

And the evidence was that they were made out in the cytoplasm. So somehow the information had to get out of the nucleus where the DNA was and into the cytoplasm. And biochemists were breaking cells open and trying to make cellular extracts that would synthesize proteins. And I think it's fair to say at the time that it looked extremely complicated. And so thinking about how DNA encoded information and got translated into proteins was a very complex issue.

But then actually there was a very interesting development that had a strong influence on Watson and Crick and led to them, Crick in particular, getting a key insight into the nature of this coding problem. There's a physicist, George Gamow, who some of you know. He proposed the "Big Bang Theory". A very strong theoretical physicist. And he wrote a letter to Watson and Crick. He thought he'd figured out the basis of the genetic code.

And his idea was you had these sequences of A, G, C and Ts. And so everywhere the two bases came together there was sort of like a little different shaped hole. So his idea was the amino acids would stick into these little holes. And he had a theory showing that you could encode the sequence of proteins by having the side chains in the amino acids stick into these little holes along the DNA.

Now, there turned out to be a number of problems with that. It didn't take into account the involvement of RNA, which there sort of was quite of bit of evidence for. And more importantly it didn't take into account the structure of the side chains of the amino acids, which you guys have been exposed to. But it had a very profound influence on Watson and Crick. They read this letter.

They immediately realized the idea was wrong and went out and had a lunch at a pub, decided again how they actually thought there were 25 amino acids, but they realized some of them were just sort of special ones that were modified only in particular proteins and there were really 20 amino acids that were found universally in nature and amino acids. And what they, Crick in particular, realized was that maybe instead of having to think about protein synthesis through this very complex set of extracts and mixtures a biochemist would work on, that he could think about it at a purely theoretical level, which basically is up at this kind of level.

But if you have a molecule that has four letters and it's going to be encoding proteins how does it do it? Can I work out sort of the basis or a possible theory for how that could happen without actually knowing all of the biochemical details? So Crick made a couple of simplifying assumptions. One was that the DNA only determined -- -- the linear sequence of amino acids and protein.

That all this information about the 3-dimensional stuff came from the properties of the linear sequence once it was made. And I think you hopefully have enough understanding of hydrophobic and other sorts of interactions that would cause a linear sequence amino acid to take a particular confirmation. And the other assumption he made was that it must be universal. And it would be hard to see how life could have started if there wasn't some kind of code that was universal between organisms.

And if you start from those kinds of considerations then what you can see is you cannot just have a one-to-one correspondence between a letter in the nucleic acid alphabet and a letter down here. If A stood for valine that would be fine, but you could only have code for four amino acids that way. So if you had one-letter words in DNA there are four possibilities.

And so it could only make four. If you had two two-letter words then you'd have 16 possibilities, still not enough for all the amino acids. If you had a three-letter word -- -- then you could do 64, and in principle that would be all you'd need. It doesn't rule out there couldn't be five or six or seven-letter words. Or if you think about this as they were thinking about it at the time, even if it were let's say a three-letter word, is it a code where you have one word, then the next word, then the next word? Or could it be an overlapping word? And what about punctuation? And maybe another thing, you can see if it's AG, CT, etc.

, there's a frame of reference problem, because if I'm going to read them in groups of three, if I start here I'll get one word, but if I start one letter over the next group of three won't be the same. So somehow there would have to be a starting point. And so these are the sort of considerations that they had to take into account. And, in fact, Watson, excuse me. Francis Crick and another scientist Sydney Brenner and some other scientists worked out a very elegant genetic experiment that demonstrated that it was a three-letter code.

And I don't have the time to go into it in this course. If you take a genetics course it's a very beautiful experiment. The principle of the thing, which I could show you rather easily, is if you're writing a thing where you're reading in three-letter words, something like this. The cat ran out and, I don't know, ate the rat or something like that. And these were all just continuously run together, not separated out, but I've put them out here.

As you can see they're three-letter words. If you lost one letter then it would change to sort of gibberish. You'd get stuff that looked like this. And if you put one in you'd have the same problem, but if you were to either take out three letters or put in three letters then, even though there'd be a little mess in here somewhere, say I took out two more of these, what we would now have from then is the rest of it would now make sense again.

And they did this sort of experiment genetically. They managed to figure out there were two kinds of mutations they could get in a particular way. Some were putting in a letter. Some were taking out a letter. And they didn't know at the time whether they were adding or deleting, but they could tell they were in the opposite directions. And then they found if they took three of one class, like three that would delete a letter and put them all together then things would more or less work.

Or if they put three that stuck in an extra letter then everything would more or less work. So there was a genetic proof of the three-letter part of the code before it was figured out exactly how the code itself worked. And so going from this sort of theoretical insight into the code to actually figuring out how proteins were made there was still quite a lot of stuff that had to happen. And one was the concept of messenger RNA.

As I said, there'd been quite a lot of evidence that RNA was somehow involved in protein synthesis because cells that made a lot of protein made a lot of RNA. And it seemed to be in the right sort of place in the cell for the proteins to be made. So the idea merged that RNA was somehow a carrier of information from the DNA to the cytoplasm. So it could serve as a template for making proteins. So the idea that the cell copied the sequence of a portion -- -- of the DNA.

And we'd probably think of this as a gene right now. Into RNA. And the RNA would go into the cytoplasm. That's the part outside the nucleus. And then it would serve as a template -- -- for protein synthesis. Because of this thought that if you had a cell like this with a nucleus and the DNA in here, that if a piece of RNA were to go out into the cytoplasm and have those properties it would be functioning more or less as a messenger.

It would be carrying the genetic information from inside the nucleus out into the cytoplasm. And so the term began to be used of a messenger RNA. And so over here I'll put an mRNA to indicate that. Now, one thing you can also see is we've talked about the structure of DNA and RNA. And it's essentially the same with one. This is the nucleotide, which is the fundamental building block of DNA.

And if you recall, in DNA there's a hydroxyl, excuse me, a hydrogen there, but in RNA there is this extra hydroxyl. This is 1 prime, 2 prime, 3 prime, 4 prime, excuse me. Let's just leave it like for the moment, 1, 2, 3, 4, 5. And so the DNA was deoxyribonucleic acid because it's missing this. But other than that the backbones are similar and the letters are almost the same.

The A, the G and the C are exactly the same bases in DNA and RNA. The only difference is with the T and the uracil. So this is thymine which is found in DNA. And this is uracil -- -- which is found in -- -- RNA. So the base pairing is over on this part of the molecule. So whether or not you have a methyl group doesn't really change the base pairing. And so this process of copying information in DNA to information

that's in RNA was seen as essentially the same kind of language, but it's just sort of like taking somebody's word processor file and writing out longhand.

You'd be transcribing the information but it would be essentially the same kind of information in essentially the same form. So this is known as transcription. I'll take just one very brief thing. Some of you may wonder why did nature do it this way? Why didn't it just use uracil in DNA? So as a very brief aside, I think we understand pretty much why it does it.

And that is cytidine has this structure. So this is C which is found in DNA but it undergoes, all of your DNA is a chemical and it's able to undergo spontaneous kinds of damage. In fact, in every one of our human cells every day, 10,000 times in any given cell a base falls off totally just leaving the deoxyribose sitting there. And the cells have to fix it up. And we have DNA repair systems that do that.

But another very common kind of thing that happens is that this NH2 group deaminates. And if you do that, if a C happens to deaminate in DNA it gives you a uracil. And if that ever happens, the cell is actually able to tell that something went wrong because uracil is not supposed to be in DNA and there are repair systems that constantly scan the DNA and take out any uracils that are in there. And the reason, if instead of using thymine it used uracil then the cell wouldn't know whether the uracil got there because it was supposed to be there as part of the sequence or whether it had arisen by deamination of a cytidine.

It's a minor point but I think we do have an understanding as to why there's thymine in DNA and uracil in RNA. This isn't such a worry in RNA. OK. But anyway. So there's still a really big problem here, though, that Watson and Crick and others were grappling with. And it has to do, as I say, with this fact that the information up here is the first in DNA and RNA.

It's written as a sequence of letters, if you will, chemical letters, but there are only four letters in the DNA alphabet and essentially the same four letters in the RNA alphabet. However, the protein language has got a totally different alphabet so it's somehow like sort of translating now from English to Japanese or something like that. Some really fundamental change had to happen because there was a real conversion from one kind of language to another.

And so this process is known as translation, as going from information that's written using a four-letter nucleic acid alphabet to information that's written using a 20-letter amino acid alphabet. And Crick on purely theoretical grounds figured, well, if you're going from one language to another what do you need? You need a translator? And what's a translator? A translator is someone who speaks both languages.

So his idea was that if there was -- I'm going to just separate out, let's say this is the messenger RNA. And I, just for clarity here, have spaced out the three-letter words so we can see them. These would be three like G-A-C or something like that in the RNA. That there would be some kind of translator. And his idea was that it would be something that had a particular amino acid at one end and it had the complimentary nucleotides at the other end.

So it could, if you will, read the genetic code that was written in the RNA using the nucleic acid alphabet, but it would also be speaking the amino acid language. Got the

idea? So the idea was that this would be, they used the words adaptor or a translator. So that was on basically theoretical grounds. If you had to go from a four-letter language to a 20-letter language you needed some kind of translator or adapter.

Now, at that same time that these considerations were going on, biochemists began to find a class of small RNAs -- -- that had an amino acid -- -- attached. And so there were entities that had just the sort of properties that Crick had envisioned you'd need from theoretical considerations. These were given the name transfer RNAs or tRNAs as they're usually referred to now.

And I've told you that RNA has, since it's got nucleic acid bases, if you have a single strand of either an RNA or a DNA and you don't have a complimentary double-strand, then if there are complimentary sequences they can come together and pair just the same way that complimentary sequences can come together in DNA. And in the case of tRNAs, once the sequence of these was determined, oops.

There we go. They folded up into a clover leaf shape. And the amino acid is attached up at the 3 prime end of the chain up here in what's known as the acceptor part of the molecule. And so that corresponds to this part up here. And here is what's known as the anticodon. Each of these three-letter words -- -- in nucleic acid language is called codon. And so something that had a complimentary sequence to a codon was called an anticodon.

So if G-G-G is the codon then C-C-C would be the anticodon. Now, this is just a schematic, as you can see. It shows where the hydrogen bonds are that form this stuff. When the crystal structures were done, the first crystal structure of tRNA was actually done by Alex Rich. He's in the Biology Department at MIT. And he was in this picture I showed you talking to Matt Meselson.

And although we cannot see this terribly well, maybe you could hit the lights here, the crystal structure showed that the molecule didn't look like a clover leaf as in there. It had more this shape. And I'll show you this more clearly in this picture. I showed you this little part of the thing when I was showing you how an RNA could form. For example, if you copy the gene encoding a tRNA and, for example, the sequence here in green is complimentary to the sequence here, or the sequence here in sort of blue or purple was complimentary to the sequence here.

That what can happen then, if you allow a single strand RNA like this to fold up, thermodynamically it will then go to the lower energy state which involves being able to make these hydrogen bonds. And I think you can sort of see the clover leaf. Here's one of the leaves. The other is down here and the others. It's a little bit distorted here. And the reason is, because I'm going to continue now to show you how this structure, once you get to the clover leaf, then it folds up to make other kinds of interactions and it takes that shape with the tRNA going on at this end and the anticodon being down here.

And what's happening now is they've morphed on the van der Waals surfaces so you can see what this would look like, 3-dimensional shape. The amino acid would be attached at that end and there is the anticodon that we'd be able to recognize, the codon in the RNA. I mean the physical reality is pretty close to this simple little depiction here. OK. So once this basic paradigm had been straightened out that gave

rise to this idea then, putting it all together, that the information in DNA, that a portion of it would be copied into RNA and that would go out into the cytoplasm.

And then in the cytoplasm these translators, the tRNAs would be able to decode, read the nucleic acid information and use that to determine the linear order of amino acids in a protein. Crick, when he came up with this, gave this the term "the central dogma". And people still use this term to apply this idea of information flow going from DNA to RNA in protein. And it's still used to this day. There's actually sort of a little twist to that, because at the time that Crick proposed the term he actually thought that the word dogma meant "an idea for which there is not reasonable evidence".

But he was sort of amused years later to realize that a more reasonable definition of dogma is it is something that a true believer cannot doubt. So he kind of accidentally made an assertion that he was right, but fortunately he was right. Now -- -- the next big job, though, in working this out was to crack the code. And it's fine to know that it's a 3-letter code and it's fine to know it goes into RNA and then the tRNAs translate it, but if you cannot crack the code then you have no idea what any of the information means.

It was sort of like before the Rosetta Stone they could look at the hieroglyphics in the Egyptian tombs and they could see that it was a lot of information and there were symbols and so on, but they didn't know what it meant until finally they got something that allowed them to relate it to a language they did know and they were able to work out the principles.

So somehow scientists had then to crack the code. And there were two scientists who played a really big role. One was Marshall Nirenberg who was at NIH and is, in fact, still at NIH. And the other was a scientist who's on the same floor as me at MIT, Gobin Khorana. And they used two different approaches, but between these two approaches the genetic code was cracked. And what Nirenberg did was to take a protein synthesizing -- -- extract that he knew needed RNA in order to work.

So that wasn't a surprise at this point because people were thinking the RNA would be the message. And at that point the ability to make synthesized nucleic acids was quite limited compared to what we do now. And so there were different ways of making them. Sometimes you could do it enzymaticly. But what Nirenberg, for example, was able to make was poly-U. So this was an RNA that was just UUUUUUU.

And then what he did was he set up 20 reactions, and in every reaction he put some of this extract, he put poly-U and he put 19 of the amino acids that were unlabeled. And then only one amino acid that had radiolabel in it. So he ran these 20 reactions and waited to see in any of these did he get protein made that would have been coded by the poly-U. And what he ended up with was polyphenylalanine.

Which you may recall when we were talking about structures of amino acids, there's the basic backbone. And the polyphenylalanine is the one that has, if you will, a benzene ring hanging off the end. And so what that meant was that UUU must code for a Phe or phenylalanine. And if it's UUU in the RNA that must mean that the DNA that encodes this must have that sequence AAA and TTT. And you can see that one of the two strands of the DNA, since T base pairs the same as uridine, but one of the strands in the DNA is going to have the same sequence as one of the strands in the RNA.

Now, I'll just tell you one brief little anecdote. I heard Marshall Nirenberg at this meeting they had to celebrate the 50th anniversary of the discovery of DNA. And he posed something that I'd never thought about in my years of teaching this but might occur to you guys if we put it on a problem set. You all know something that benzene is nothing but sort of these, this as I call it, we even referred to it as a benzene ring, which is a very organic kind of solvent.

So if we put a problem set, if you've made polyphenylalanine would you expect this to be soluble in water? Well, this is very, very hydrophobic, very, very water-hating. And your answer would be correct. If you said no, I wouldn't expect polyphenylalanine to be soluble in water. In fact, if it were in a protein you'd expect it to probably be in the core where all the hydrophobic interactions, the water-hating parts would go.

So Marshall Nirenberg said in his talk, well, he had shown that he had radioactive phenylalanine, and he still had to prove chemically that he had polyphenylalanine. But he wasn't much of a biochemist so he walked down to the lab just below NIH and walked in the door and saw the first person he saw and said how do you solubilize polyphenylalanine? Just to make sure I got this right. And the guy said, oh, you just take 33% hydrobromic acid and glacial acetic acid and it works.

So he went back upstairs and dissolved it. It turned out it dissolved in that. And he went on and characterized it. And he said it didn't occur to him or he didn't learn until about 15 or 20 years later that he just walked up to the only person in the world who knew how to solubilize polyphenylalanine. By total coincidence this guy who had talked to had been working away trying to figure out a way and had come up with this odd mix of hydro- bromic acid and glacial acetic acid.

And he just said of all the places in the world, he walked up to the one person who knew and got the answer. So the other part of the story then involves Gobin Khorana who I mentioned when I was telling you initially about the Nobel Laureates at MIT. And Gobin is a brilliant organic chemist. He synthesized DNA. You know, it was a point where a whole issue of a journal came out and there was nothing but his labs work and synthesizing DNA.

Well, he was good at nucleic acids. And one of the strategies that they could use chemically was they would make something like a dye nucleotide like CA. And then they were able to polymerize that to make a piece of RNA. So they could make an RNA that had the sequence CA, CA, CA, CA and so on. And what you can see from that is that there are two different codons in that.

One is CAC and the other is ACA. And the reason he made it was he was synthesizing it by polymerizing nucleotides. So in these same kinds of experiments I was describing before, what they found this synthesized was alternating histidine and threonine. And you cannot tell from that experiment alone. One of those must be histidine and one of them must be threonine, but you cannot tell from that experiment so more experiments were needed.

And what was learned from that experiment in that case was that CAC corresponded to histidine and ACA corresponded to threonine. So these kind of experiments were then put together to give what's known as the genetic code which is the three-letter words encoded in DNA that encode the sequence amino acids and proteins. And it's

usually displayed as a table and you read it in this way. That this thing over here is the first base in the codon, across the top is the second base in the codon, and down over here is the third base.

So if we go to C as the first, say the one for histidine we were just showing you. C is the first letter. A is the second letter, so this is the box that we're going to be looking at. And if C is the third letter we can see it encoded histidine or AC come back to A. Then the A is certainly threonine. But you can also see something else here. And that is because there were 64 possibilities with this three-letter word the code is what's known as degenerate.

That is there are more words in the genetic code than are needed to specify the number of amino acids that have to be coded. So I just want to make a couple of points about this. So the genetic code -- It's degenerate. There are 61 codons that correspond to an amino acid. And that means that some, and I think threonine is a good example, there's more than one word in the genetic code that means threonine. There were three codons for which there was no corresponding amino acid.

And those mean stop. And that would make sense because if you're reading down a nucleic acid piece of RNA, at some point you'd have to end the protein. And so there are actually three that are used for that purpose. And although there's some small variation on this in nature there's usually one amino acid that's used for starting a protein, and that's methionine. And it's AUG right there. Now, some of this stuff probably sounds like it's been around forever, and that's certainly true of some of the stuff you hear in your chemistry, math and physics courses.

I just want to drive this home. When I was an undergrad Watson's first book called Molecular Biology of the Gene had come out, so when I was your age, and I realize that I look ancient but, you know, at least I'm still here. When I was an undergrad I had Watson's book. This was the genetic code that was in the book, the genetic code as of May 1965. And you'll notice there are gaps in here. And all the things that are underlined were things for which there was a tentative assignment.

So although you may take this and think that it's been knowledge that's been around forever, it wasn't even complete in the textbook when I was an undergrad. OK. So one of the things then that's important to think about the nucleic acid stuff, this is the basis of how proteins are encoded in the DNA. But everything else has to be there, too.

And the genetic code, that's what we've been talking about, is universal. But there are other languages -- -- written in the DNA that are not universal. And one of them was that little example I gave you with an origin of replication. E. coli only starts DNA replication at one very particular point in its chromosome, so it is a particular sequence of DNA. It's actually about 250 nucleotides long.

So you could think of that as a language. It's like starting a chromosome replication language. It's only got one word in it, and the word is 250 nucleotides long. Another place that's very important, and that is if you're going to make an RNA copy, if you're going to do transcription of a piece of DNA -- And I'll call this the coding sequence. This would be the sequence of three-letter words that we'd specify the amino acid of the protein.

If you were going to make an RNA copy of that, you would have to somewhere have something here that's a sequence up here that means start transcription. And one at the end, some other sequence of letters in the nucleic acid that would mean stop transcription. This is given the technical term that's referred to as a promoter. The stop one is referred to as a terminator.

And these, we'll say more about this. Because the beauty of having this system of making an RNA copy is it provides a beautiful point of regulation. Because the cell can determine whether or not it's going to make a particular protein by whether or not it chooses to make the protein or not. And so having this RNA intermediate and being able to control transcription is a really important part of the whole regulation that makes life possible.

The transcription is carried out by an enzyme that's known as RNA polymerase. And let me make one more point. These promoters and terminators are not universal. So when we talk about recombinant DNA a little bit in the course, if I take a mouse gene and I put it in E. coli. Even though the genetic code is the same, we might have all the same sequence of amino acids specified, you won't get the RNA made because the sequences that say start transcription and stop transcription are different between a mouse and a bacterium even though the genetic code is the same.

So you can kind of see from first principles. If you're doing recombinant DNA and you wanted to express the mouse protein in E. coli, you would have to fiddle around with the sequences up here and the sequences down there, the parts that are not universal. You guys with me? OK. So what does an RNA polymerase do? It recognizes this sequence, and then it teases the strands apart to make a little bubble like this.

So let's say ATAGCTA. So the other strand then would be TATCGTA. And then RNA polymerase, unlike a DNA polymerase, can begin a chain de novo. Remember an important thing about DNA polymerases was they had to have a primer terminus to get started. That was they had to use the Okazaki fragments. So this is DNA. This would be 5 prime, 3 prime, 3 prime and 5 prime. And what an RNA polymerase can do, it uses DATP, DGTP, DCTP and DUTP.

It uses triphosphates, excuse me. Get rid of these. Excuse me. My mistake. No deoxies here. Of course this is RNA. It uses ATP, GTP, CTP and UTP as the substrates. So it uses triphosphates just the same way DNA polymerases do. And then it's able to start a chain de novo. And it synthesizes the RNA in a 5 prime to 3 prime direction, the same direction that a strand of DNA is made by DNA polymerase.

So it would copy here. And so it would put in an A opposite a T. And then because it's RNA it will put in a U opposite an A, and then an AGCAU and so on. So this right here is the beginning of the RNA that's being synthesized by the RNA polymerase. This strand is known as the transcribed strand. And by default then that one is the non-transcribed strand. And what you can see by doing this, it's making an RNA the same sequences up here, except that everywhere there's a T there's now a U in the RNA.

So the final thing then is how this information gets all put together to make proteins. And protein synthesis is done by an machine known as the ribosome. It's made up of some special large RNAs -- -- called rRNAs, some proteins as well. These make up

the ribosome. And then it needs a mRNA and then it needs the various tRNAs, each of which carries an amino acid that's appropriate to its anticodon.

And in a very briefly sort of way this is -- And you can see this in your textbook, what the ribosome does is it takes, let's consider this is the mRNA. I'm just going to take three codons here. And this mRNA treads into the ribosome. And I'll sort of show it's able to recognize the first codon and the second codon. Remember, of course, there's no spacing like this in the RNA.

And then in the context of this large factory it's able to find the tRNA that has amino acid one and the anticodon that would correspond to this. The tRNA that has the next amino acid attached and its anticodon. So you can see what's happened. It's been able to order the first amino acid encoded by that codon and put it physically right next to the next amino acid that's coded here.

And then it catalyzes -- -- the formation of a peptide bond. And what happens when that does is the way this amino acid is joined to the tRNA there's energy stored in that bond. And so thermodynamically that allows this bond formation to go. And now you end up essentially with this. And what happens now is everything clicks over one. So you could think of it as this whole RNA shifts over one so the one that used to be here is now sticking outside.

Here's part of the ribosome. Here's the next codon. What we have here is the tRNA that's got amino acid two joined to amino acid one. The next codon specifies the next amino acid which is three. And the process is then able to go on like that. Now, the structure of the ribosome, the crystal structure of the ribosome was just finished. And I guess we've got as many lights out as we can do right now.

It's absolutely remarkable. It's mostly RNA. The gray stuff and the blue stuff are two huge RNAs that are all folded up in 3-dimensional space. And these things that are sort of stuck on the outside, these purple things here or the dark blue things here that sort of look like cherries stuck on the outside of a cake, those are proteins. So most of this is RNA, big balls of RNA with proteins kind of decorating the outside.

The mRNA is a green thing that snakes through. There's the mRNA. See it snaking through? And maybe you can recognize in the middle this tRNA. There's an orange one and a yellow one. Those correspond to the two tRNAs I depicted here. And I'm just going to see if I can stop this. There's a viewpoint I'd like you to see when it comes around again here in just a second.

I'll see if I can catch it there. Right there. Here's one of the tRNAs in yellow. And its end is right there. And there's the other tRNA. And its end is right there. So this corresponds to the point at which there's going to be an amino acid formed. And something is going to catalyze the formation of that bond. Well, the next picture sort of shows what happens if you pull that apart.

And what you'll see is that here's the end of one end of the tRNA, there's the other end, and there's nothing near it except for RNA. So RNA is actually catalyzing the formation of the peptide bond. Another way to say that would be that the ribosome, which is the protein synthesizing factory, is a ribozyme. Remember I said most of the chemical reactions that need catalysts are carried out by proteins but there are a few that are carried out by RNA where RNA is the catalyst? And remarkably the

formation of the bond, which is at the heart of proteins which are so important for all life, is catalyzed by RNA.

If you look at what makes proteins, what do you see? You see huge balls of RNA, a mRNA threading through two tRNAs, and the enzyme activity or the catalytic activity is encoded by the RNA as well. As I said, people think possibly there was an RNA world that preceded our present-day world with DNA, RNA and protein. And who knows? But this sort of look at a ribosome could at least make you see that that's a plausible explanation that RNA might have been running the show for a while before anything else got involved.

Anyway, we'll see you on Friday then.