

Lecture 24B • 06/21/12

DNA

DNA is the form in which genetic information is encoded and transmitted. In humans, we have [26] chromosomes which are these large molecules of these complexes of DNA. Double helix.

Let's first look at what chemically DNA is. DNA stands for deoxyribonucleic acid. As that name sounds like, there is ribose in it; it is also acidic because DNA is essentially a polymer that incorporates phosphoric acid. Let's look at the components of DNA first. These bases are heterocycles, which means they are rings that contain atoms besides carbon in the rings themselves. The bases are derivatives of two commonly-encountered heterocycles: purine and pyrimidine [cousin to pyridine]. Add just a couple of substituents to these molecules and we get the different nucleic bases. They're called bases because they do contain these nitrogen groups; nitrogens tend to be basic [except in amides or imides]. Add just a methyl group to purine, we get adenine. Make an amide out of purine, we get guanine. From pyrimidine, if we make a urea derivative, we get cytosine. From there, if we put yet another carbonyl on, we get thymine. These are the four bases that are contained in DNA; they're often abbreviated [as] one-letter abbreviations, rather logical ones: AGCT. There is the fifth base, uracil (U). Uracil is very similar to thymine, except that it contains one less methyl group. That one is only found in RNA.

What is made of these bases? They show up in what are known as nucleosides. [glycoside – making some kind of connection through the anomeric position of a sugar to some other kind of substituent] In this case, the nucleoside is a combination of one of these bases with a sugar at the anomeric position. DNA, being deoxyribonucleic acid, the deoxyribo- refers to ribose. Let's draw a furanose form of ribose. [structure] 2'-deoxyribose means leave out the oxygen. It's called the 2' position because technically the oxygen is substituted at the 2-position itself. It'll look like this. No stereocenter, no -OH group whatsoever. Why is there a difference between these two for DNA versus RNA? DNA is the master template of the genetic information; RNA is something that's generated on a more temporary basis in order to replicate DNA itself or to perform one of the actions of DNA, which is to take some of that genetic information and turn it into amino acids. The ribose is much more easily reacted because of the participation of that hydroxy group on the 2 position. [huge number of times difference in hydrolyzability and reactivity between ribose and deoxyribose] If DNA is supposed to be the template, you don't want your template to be able to fall apart; you don't want you, your genetic information to fall apart. The more robust, the more tolerant deoxyribose is used for that. Since RNA is used just on a temporary basis, and it's replicated and destroyed, replicated and destroyed, it doesn't matter so much whether it is as stable as long, nor you need to then expend the energy to make something that would be more stable and then would require a little extra push to break apart. That's why ribose ends up being used in RNA, because it's being formed on just a temporary basis.

If we take one the bases and stick it on to one of the sugars, we get a nucleoside. For example, if we take adenine and combine it with ribose, then we get adenosine. The ending changes to indicate that it has been stuck to the sugar, the nucleic base, that is. If you made the same thing, used the same base, but you used ribose instead, then it is 2'-deoxyadenosine.

These four different bases are used to encode amino acid information. It's going to be in groups of three of these bases that together will code one individual amino acid. We've now made the individual pieces that are going to go into this DNA strand. Each of these is like one of the building blocks in making a DNA strand. How do we then link these individual building blocks together? By making phosphate esters. Here's hydrogen phosphate; it's been monodeprotonated. We react it with two alcohols. We make what looks like an ester, other than the fact that we have phosphorus there, and we can make it in two different directions. This is a phosphate diester. [metabolic pathways – phosphate] If we take a nucleoside and we combine it with a phosphate, then we get a nucleotide. It's a phosphate combined with a sugar combined with one of our bases. Let's take that same adenine; I'll combine it with deoxyribose. On the back carbon, the one that is not itself a stereocenter, that's where we're going to attach the phosphate group.

These have abbreviations as well. Phosphate easily forms a phosphate anhydride. You can stick two phosphorus together to get an ion known as pyrophosphate. You can stick three of them together to get triphosphate. What I've shown you here is 2'-deoxyadenosine monophosphate 5'-monophosphate. The mono refers to the fact that there's only one phosphorus involved, that it's not one of these phosphorus anhydrides [or is it number of deprotonations?] If you look at these abbreviations, it's a close relative of ATP. ATP, without the little d beforehand – the little d refers to deoxy(ribose) – if you don't have the d, it means it's stuck on normal ribose. If you have adenine stuck onto ribose and you have the triphosphate, that's the molecule ATP, which is involved in lots of biological redox reactions.

[Nucleotides are assembled into DNA strands][a small segment of DNA – thymine; adenine] [Thymine and adenine] have the exact complementary structure that there's the perfect distance and orientation of these two to have hydrogen bonding with each other. [critical and sophisticated aspects of DNA] What's in this double helix? It's two strands of DNA that are complementary to each other. On one strand of DNA, for example, if you had the thymine, automatically on the other one, you're going to have adenine. If you have cytosine on one, then you'll automatically have guanine on the other.

There's this relationship: thymine with adenine, guanine to cytosine – or vice versa; whichever strand has one, the other strand has the other. This is because these two pairings of adenine-thymine, guanine-cytosine have this exactly perfect hydrogen bonding between them, which is what keeps the two chains locked together. Otherwise, the chains are separable, which is why DNA is able to be replicated. [finishing structure, extending chain] DNA is a polymer, meaning multiple repeating units, of phosphate, sugar, phosphate, sugar, phosphate, sugar, phosphate, sugar. On every sugar, then, you have one of these bases. Between the two strands of DNA, you have complimentary base pairs. [interaction between cytosine and guanine]

[description of double helix being replicated] [It's called a double helix] because it's got two strands – the two individual polymer strands, that do wrap around with each other. There are two grooves – there's a tight relationship between the strands and then a larger gap between the strands; one of those is called the major groove, one of those is called the minor groove [which one!]? It's just because of having the exact right shape that these automatically end up twisting as you go from one base pair to the next to the next to the next. You can see that everywhere along the chain, where there's a thymine, there's an adenine that's paired with it; wherever there's a cytosine, there's a guanine that is paired with it. At some point, the chain starts to split. [process for creating a new DNA chain – two new sets, each set has one of the original chains of DNA in it][thymine can turn into uracil, but there are enzymes that will convert uracil back into thymine to correct what would be known as a transcription error]

Transcription. Here's a strand of DNA that gets split apart; then there's the initial copying of that chain. Transcription is where you're just making pieces of RNA from DNA. Translation's where you act on the encoded information to make proteins, to make amino acids. When you first copy the DNA, you make an initial run of RNA that actually gets acted upon and split off into different types of RNA. There's messenger RNA, there's ribosomal RNA, and transfer RNA (tRNA). Here's the way that transfer RNA works: at the bottom of the transfer RNA [picture] you can see it's a shorter sequence of bases, and the bottom of which they have something called an anticodon. Codon is the word for [the] three-base sequence that is equivalent to a particular amino acid. You have those along the RNA chain. You have a bunch of these molecules floating around in solution, which have the complementary codon called the anticodon that tries to line up with them. At the top of this molecule [example], the amino acid that corresponds to the codon is attached at the very top of this molecule. Once you pull the chain apart, we have the RNA chain that has the genetic information. You have these transfer RNA bits that line up and fit just exactly right the sequence of the three bases. Once you have all of the amino acids lined up, then, there's an enzyme that can come together to make all the amide linkages that would create the protein. DNA can split up and turn into RNA. RNA can split into different kinds of RNA, one of them transfer RNA, which are like the assembly line approach – they all line up in the correct places along the [RNA] with the amino acids attached to them. As they line up, the amino acids get linked one to another, to another, to another – that's how a protein is generated. [table of codons] A codon does refer to a grouping of three of the nuclear bases. [64 combos; some redundant [did there used to be more?]; three code as stop] meaning it shows where, once you start making that protein, should that whole machinery stop and make the end of the protein. [PCR; solid-support DNA synthesis]

DNA – deoxyribonucleic acid

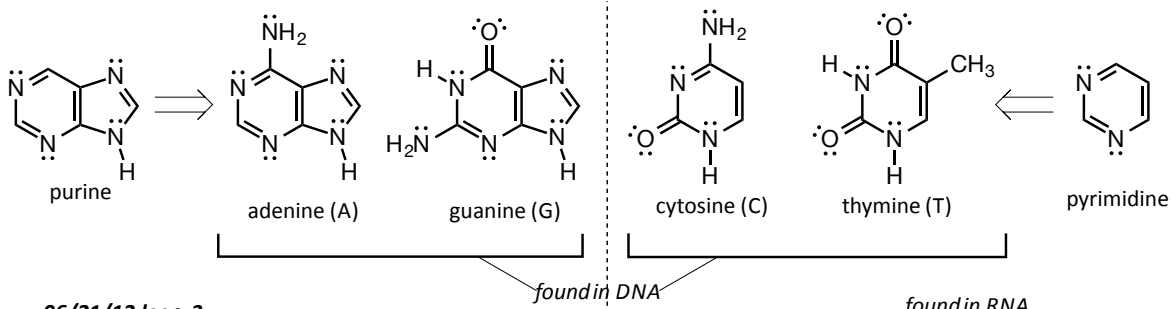
2'-deoxyribose – missing O

nucleoside – combination of a nucleic base with a nucleic sugar

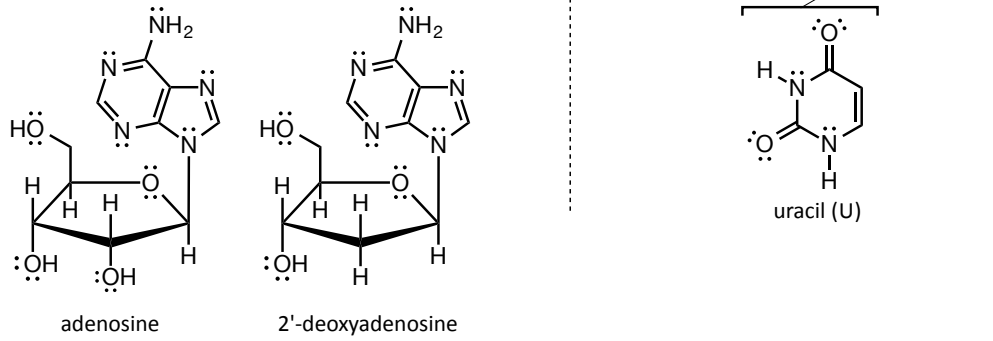
nucleotide – combination of phosphate + sugar + base

Structures

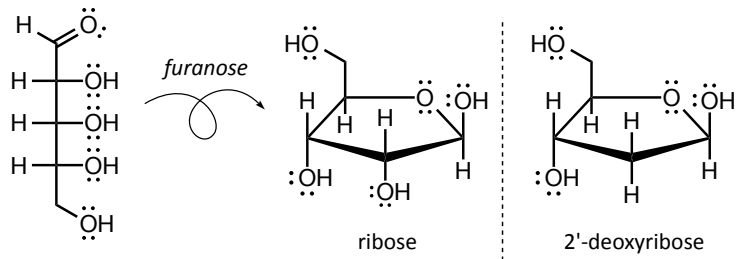
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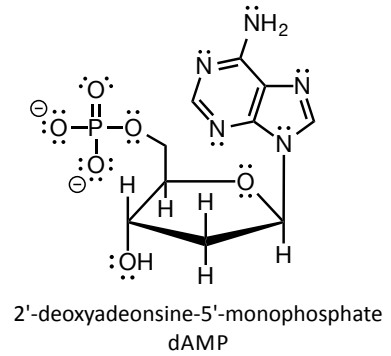
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