R-loops as a source of DNA damage

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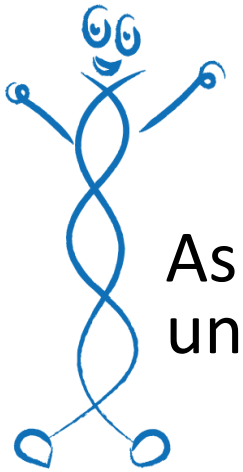
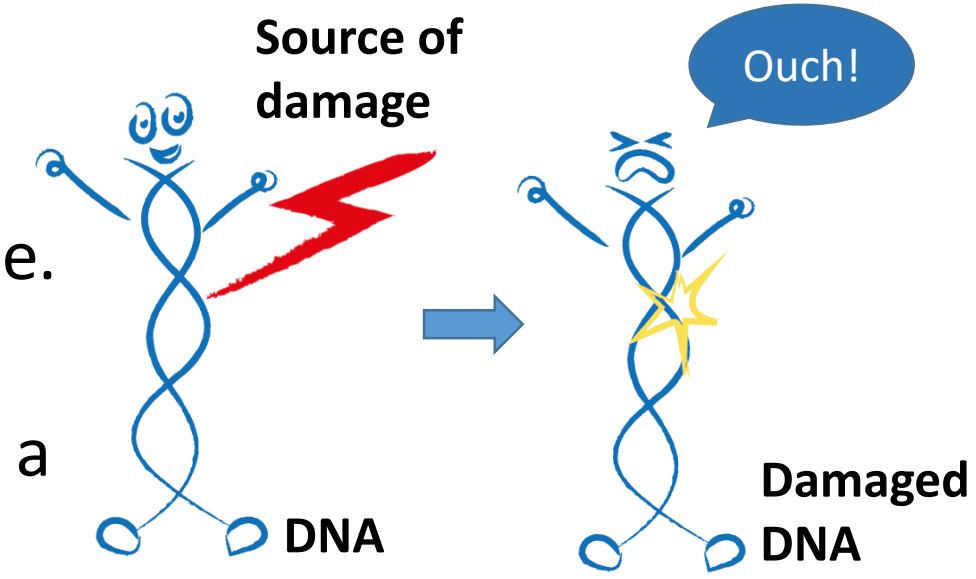
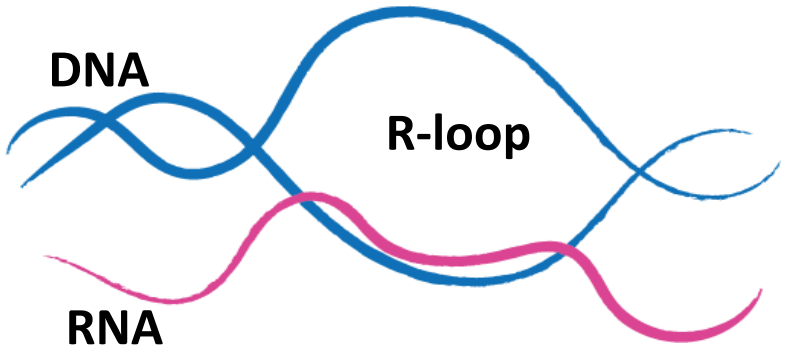


HELLO!

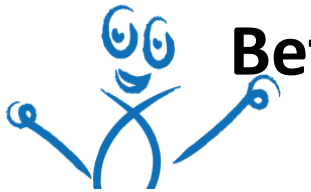
As you now know, our DNA is constantly under attack by different sources of damage.



A special endogenous source is the **R-loop**, a three stranded hybrid, where one RNA strand binds to one of the two DNA strands, and leaves the other one exposed to damage.



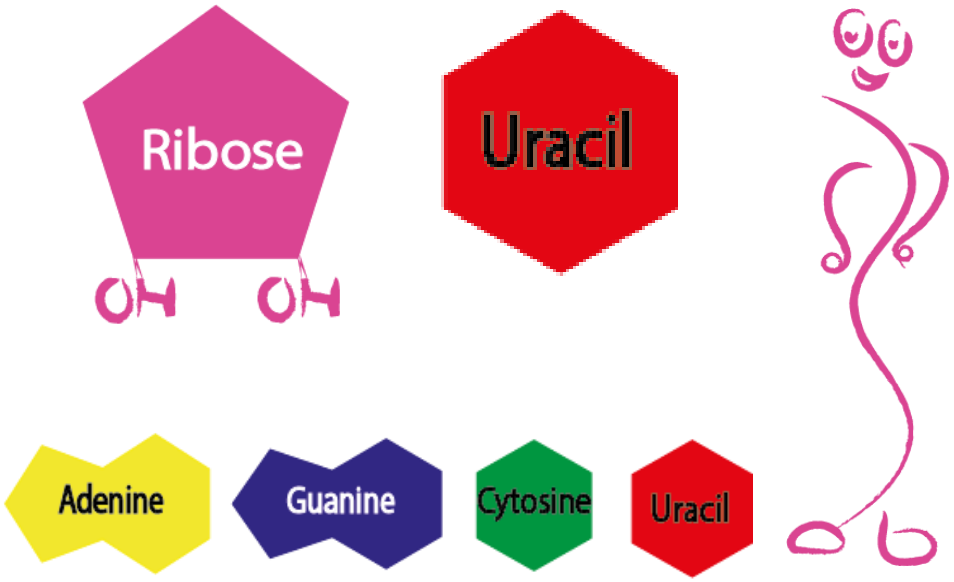
R-loops are interesting because they are needed for several cellular processes, but can be harmful if they come out of balance.



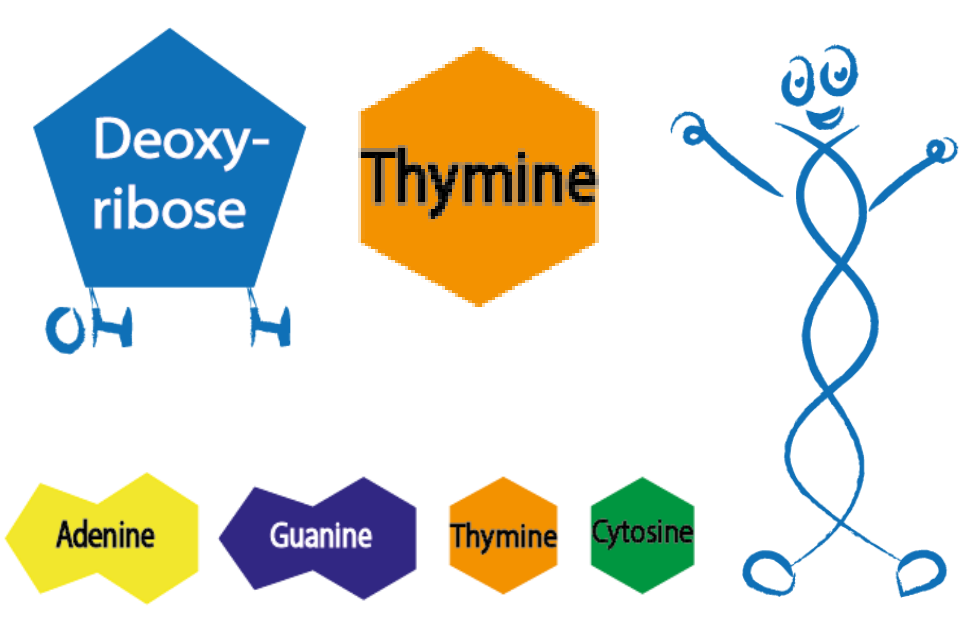
Before we continue let me introduce to you my friend the RNA!

Hi, my name is RNA and I'm very similar to the DNA; however, my backbone is **single stranded**, contains **Ribose** instead of **Deoxyribose**, and in my nucleobases I have **Uracil** instead of **Thymine**.

RNA

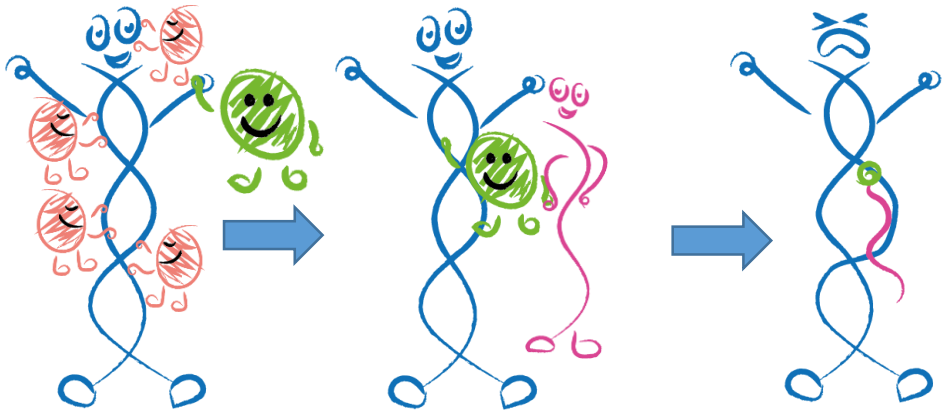


DNA



How R-loops rise?

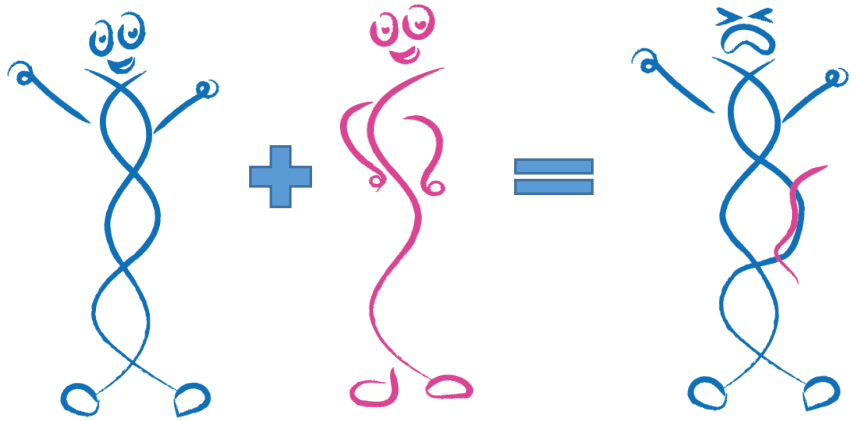
RNA needs enough space between the DNA strands for the invasion to take place.



Transcription

A suitable scenario is during **transcription**, where proteins called **topoisomerases** relax the DNA strands and allow me, the **RNA polymerase**, to bind to one of the DNA strands and make RNA, using the DNA sequence as a template.

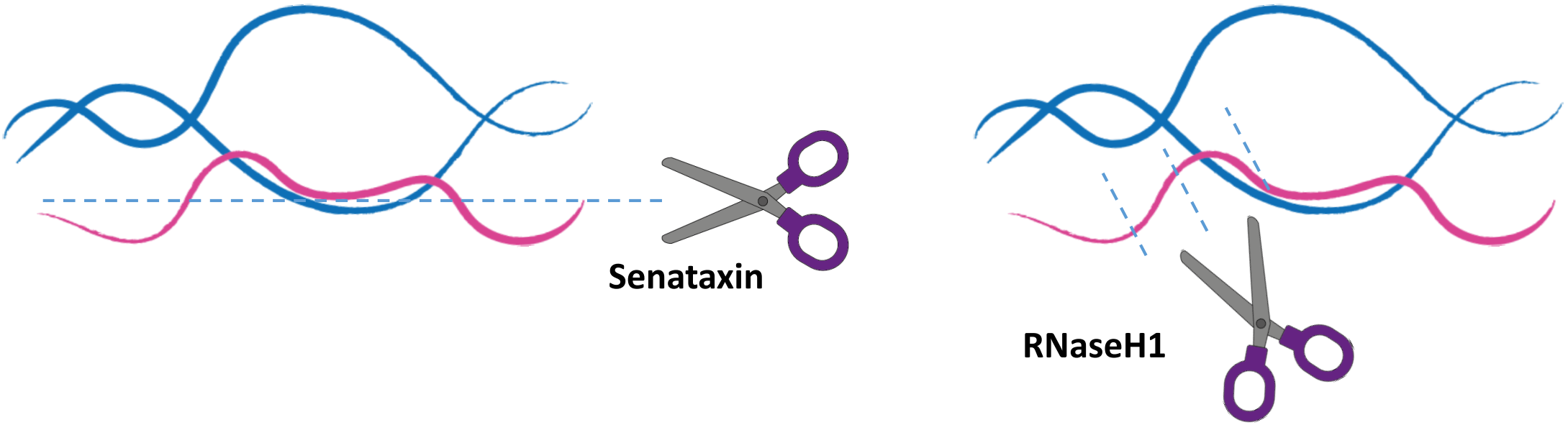
R-loops can also occur when an RNA molecule that **will not turn into a protein** (non-coding RNA), invades a region within the DNA.



Non-coding RNA

What happens after the formation of an R-loop?

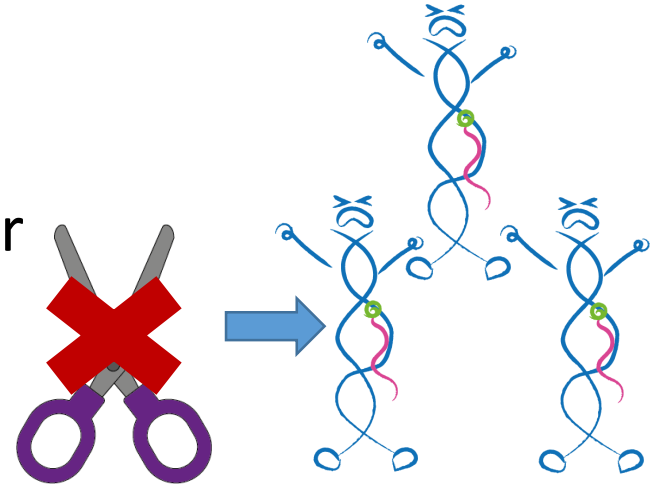
Our body has specialized proteins that detect when RNA binds to DNA and removes the RNA strand. For example: Senataxin (helicase), removes the RNA by cutting the bond between DNA and RNA strand: and RNaseH1 (nuclease) cuts the actual RNA strand.



Once the R-loop is removed, the DNA goes back to its original structure.

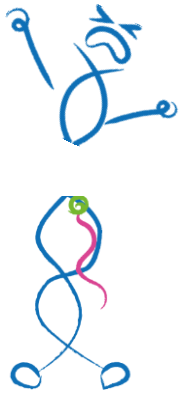
R-loops as source of DNA damage

R-loops can become toxic when they can't be resolved, or when there is not enough of them for a cellular process that requires the formation of this structure.



R-loop accumulation

Accumulation of R-loops can disrupt cellular processes like replication and transcription; also, the exposed DNA strand can be attacked by other agents with the eventual break of one or both strands.



Double strand break

On the other hand, a low presence of these hybrid structures can affect the expression of some genes, antibody production and mitochondrial replication.