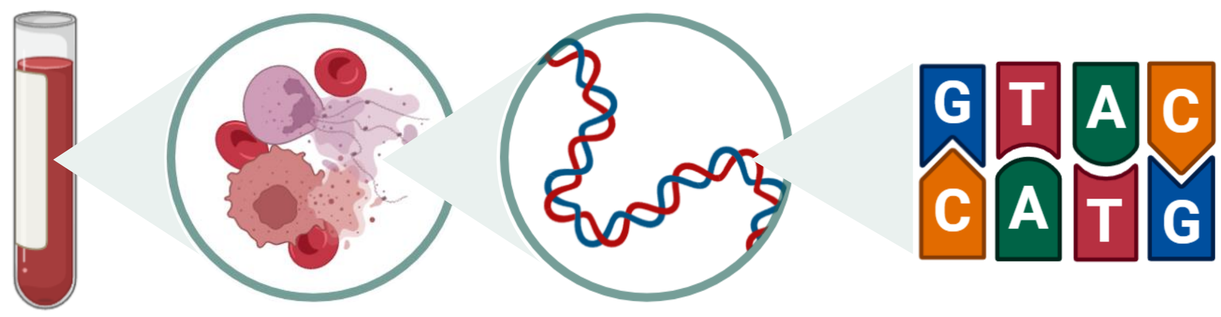
What goes on in a Molecular Lab?

A walk through the MPN service

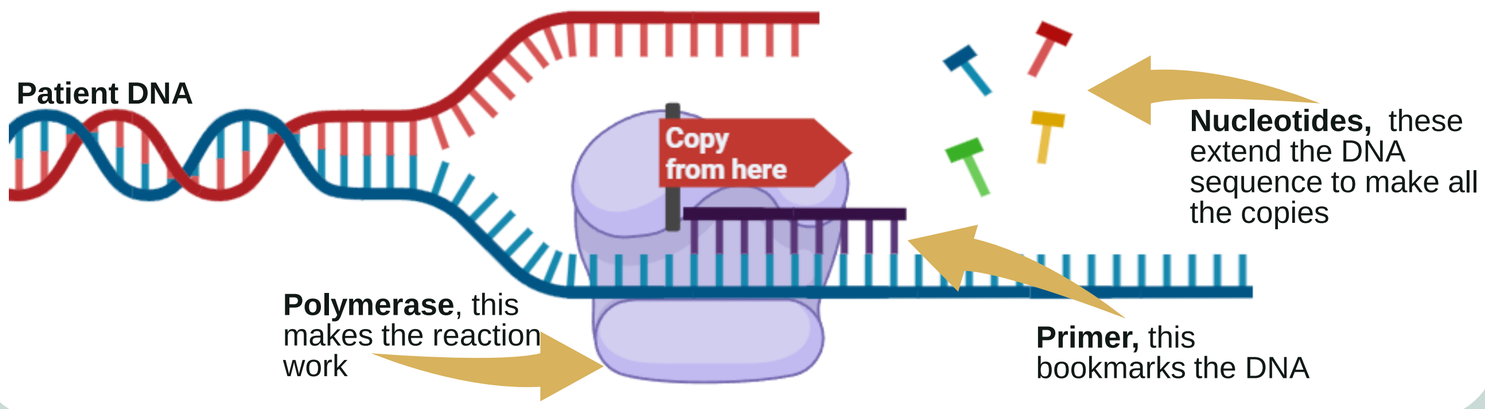
The MPN service looks for genetic variants that cause **M**yelo**P**roliferative **N**eoplasms, a group of rare blood cancers.

The variants we look for are known to cause disease and can help the doctor determine a diagnosis.

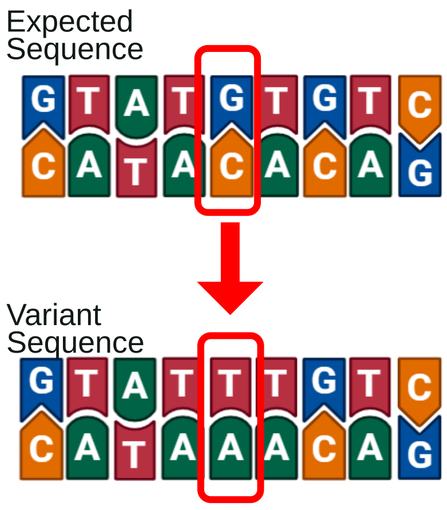
Extracting the DNA
When the blood sample arrives in the molecular lab, the first thing we need to do is extract the DNA. Blood cells are burst open to release the contents and then, using some fancy chemistry, the DNA is separated out from everything else.



Amplifying the DNA
To look at the DNA closely, we have to make lots of copies. This method is called PCR [Polymerase Chain Reaction] and is done on a thermocycler. We add little sections of DNA called primers, which bookmark the bit of sequence we want to copy.

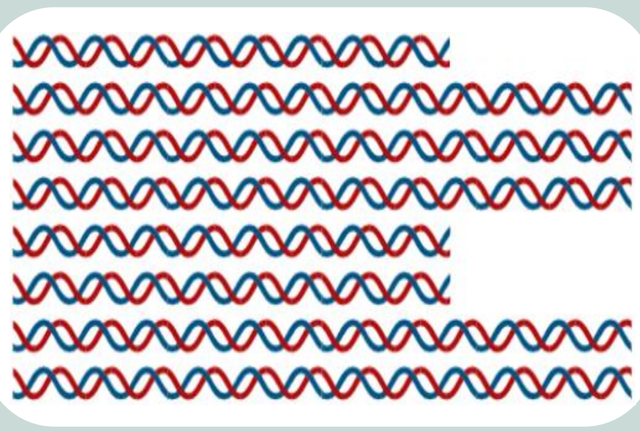


Looking for a specific variant
Sometimes we are looking for a specific mistake in the DNA sequence. We can perform a PCR using probes with different colours attached. One colour is detected for the expected sequence and one colour for the variant sequence.



This is REAL TIME PCR

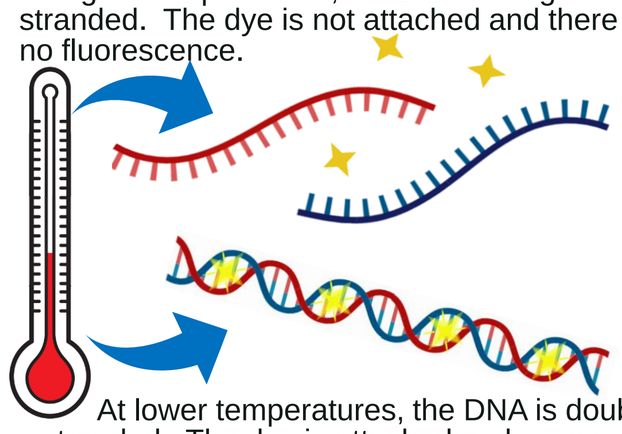
Looking for INDELS
INDELS describes when there are extra bits of DNA [**IN**sertions] or bits are missing [**DEL**etions]. When we amplify the DNA, we end up with bits that are not the expected length. In the example below, some are the right length, some are too short!



This is FRAGMENT ANALYSIS

Looking for any variants
If we don't quite know what we are looking for, we can look at how DNA separates at high temperatures. By including a special fluorescent dye, DNA that contains a mistake pulls apart differently, so the pattern of fluorescence is a bit different to what we would expect.

At higher temperatures, the DNA is single stranded. The dye is not attached and there is no fluorescence.



At lower temperatures, the DNA is double stranded. The dye is attached and we can detect the fluorescence.

This is HIGH RESOLUTION MELT ANALYSIS

All the results get collated into a single report to help the doctor see the whole picture.

The MPN service is brought to you by a small team of Biomedical Scientists, Healthcare Science Associates and Healthcare Science Practitioners. With extra support from Clinical Scientists, this service is part of Molecular Pathology at the Royal Infirmary of Edinburgh.

I.Henderson Hunt
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NHS Lothian

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