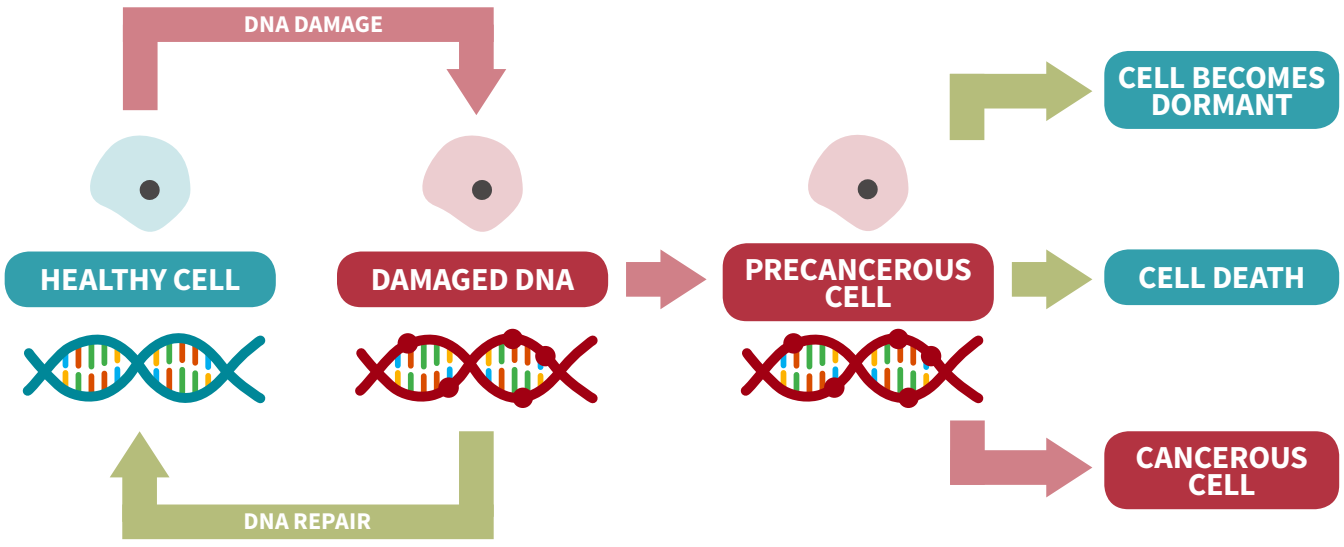
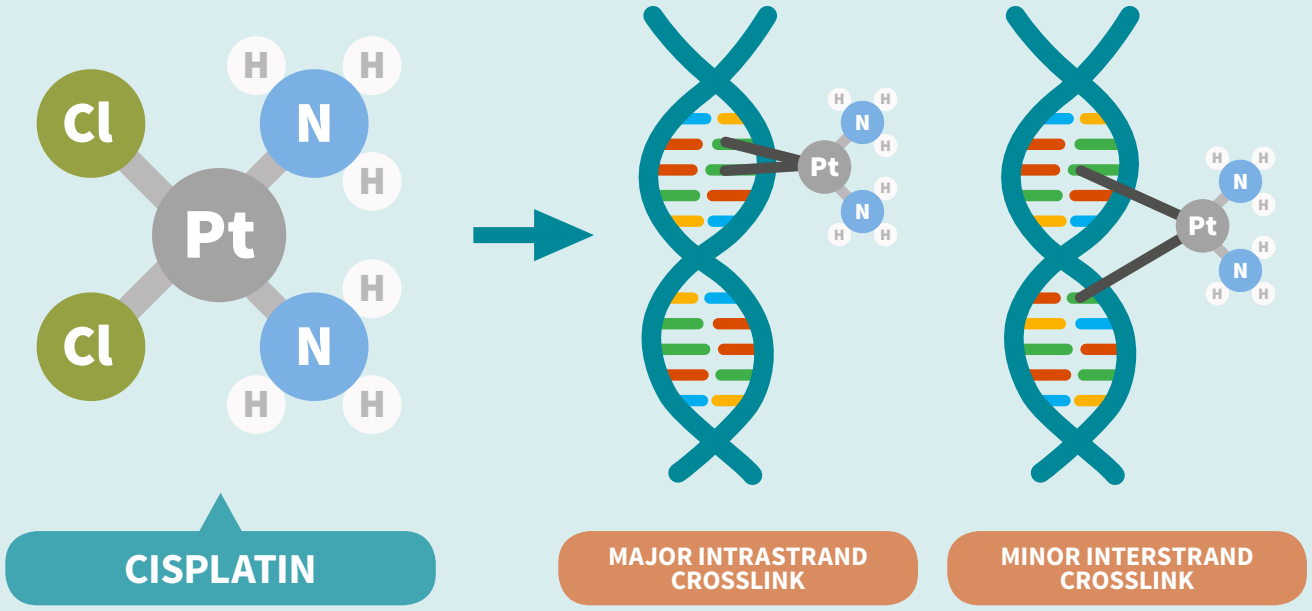
TARGETING DNA REPAIR TO COMBAT CANCER CHEMORESISTANCE

WHAT IS A CANCER CELL?

The cells in our body are continually dividing; when they do, their DNA unzips and replicates, producing two copies. The copy isn't perfect so small changes can accumulate.

In cancer, these changes have broken the control over cell division, meaning they divide constantly and uncontrollably, causing problems.





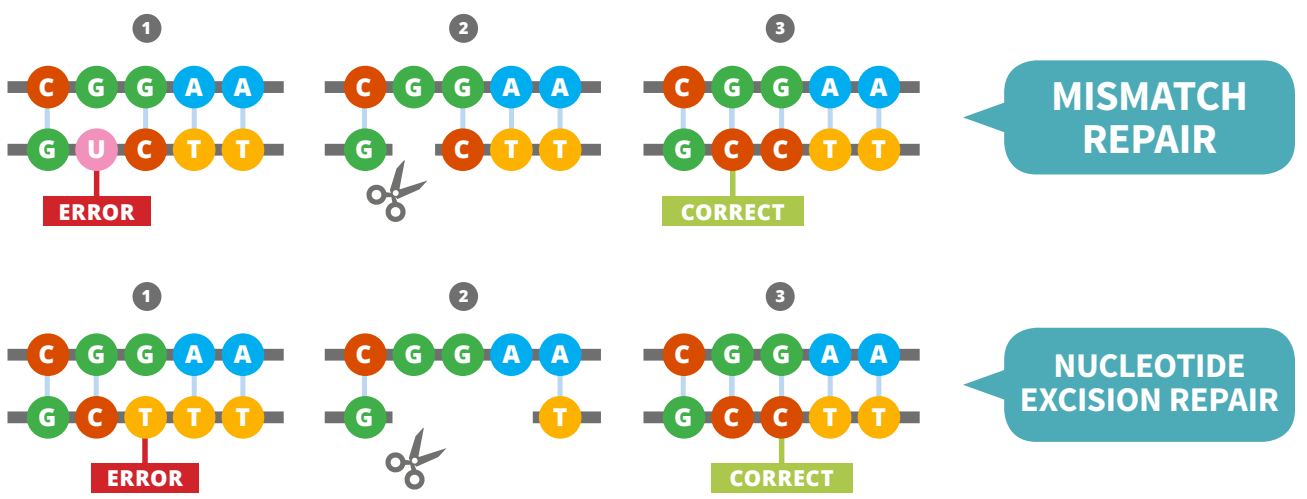
TARGETING CANCER'S DNA

Most cancer treatments target cancer cell DNA. They include radiotherapy (beams of high energy) and chemotherapy (anti-cancer drugs).

Cisplatin is one of the most common chemotherapy drugs; it reacts with DNA, forming a platinum bridge between the strands. This prevents the DNA from unzipping and replicating, and in turn prevents the cancer cell from making new copies of itself.

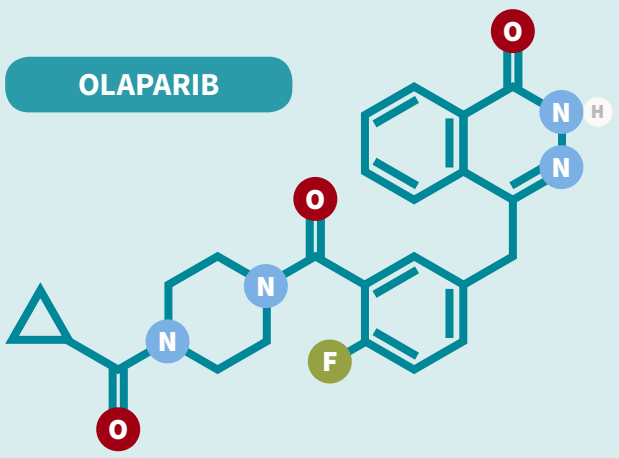
DNA AND CHEMORESISTANCE

Our DNA has a number of repair mechanisms that remove damaged sections of DNA. Cancer cells exploit these repair mechanisms to remove replication blocks created by chemotherapy. This means increasingly high doses of the drugs are needed to destroy the cancer, and sometimes even this is not enough.



COMBATING CHEMORESISTANCE

Our understanding of DNA repair can help us to combat cancer. Scientists have found that cancer cells often become dependant on a particular repair mechanism, and this is an Achilles' heel that can be targeted to kill the cancer. One example is Olaparib, an inhibitor of the DNA repair protein called PARP.



OLAPARIB AND FUTURE DRUGS

Olaparib works by trapping PARP onto DNA, preventing it from completing its repair. There is a good chance that cancers that are PARP-dependent can be treated with Olaparib. Scientists are now developing new drugs to block more DNA repair processes to treat a wider range of cancers.

Based on materials provided by Tom Fleming, ***www.browngroupnucleicacidsresearch.org.uk.*** *Synthesis for Biology and Medicine CDT,* ***www.oxfordsynthesiscdt.ox.ac.uk****, University of Oxford. This work was supported by The Royal Commission of 1851.*

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