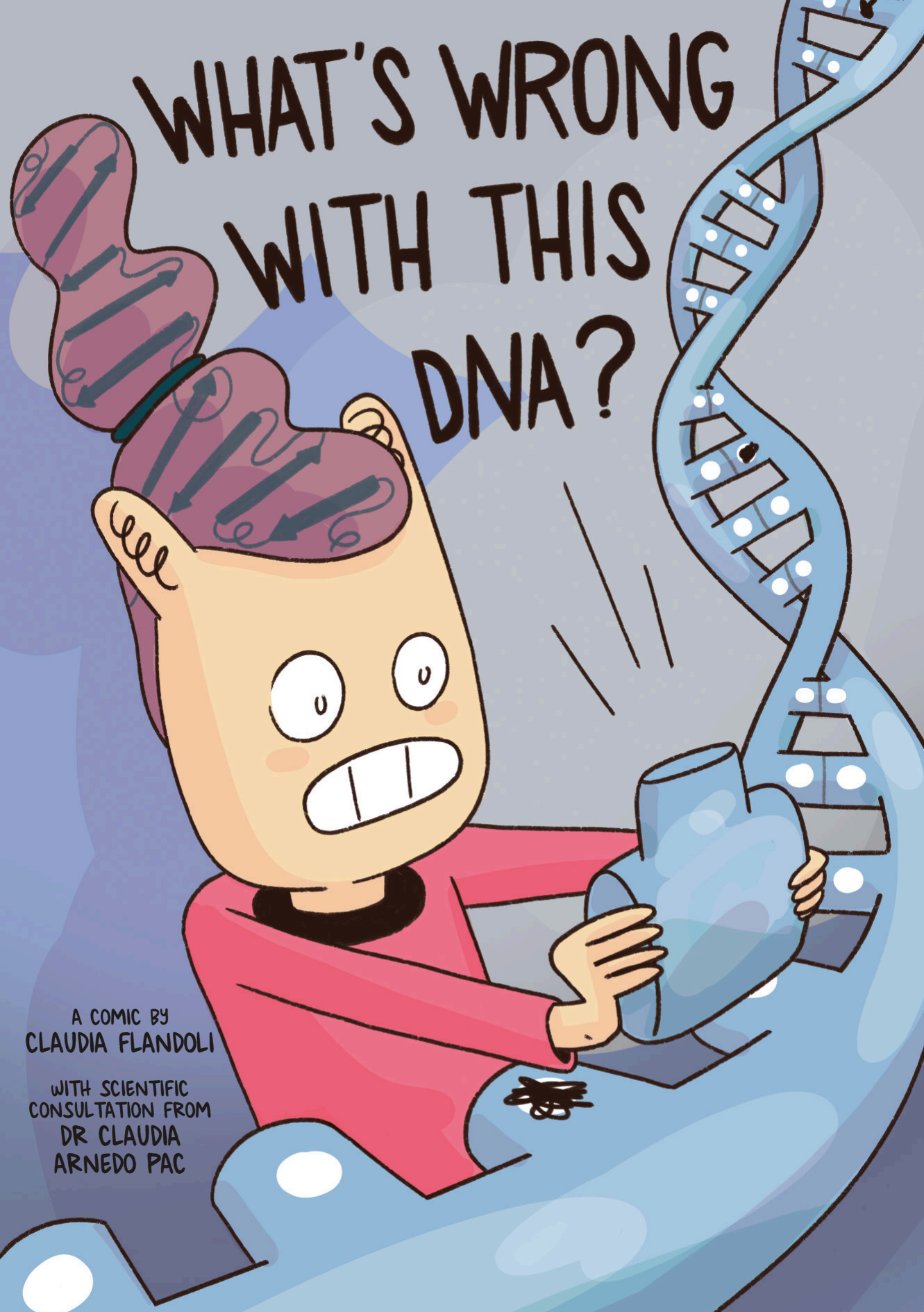


# WHAT'S WRONG WITH THIS DNA?



A COMIC BY  
CLAUDIA FLANDOLI

WITH SCIENTIFIC  
CONSULTATION FROM  
DR CLAUDIA  
ARNEDO PAC

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First Published in April 2024

Published by the Institute of Genetics and Cancer

Edinburgh University

Edinburgh EH4 2XU

United Kingdom

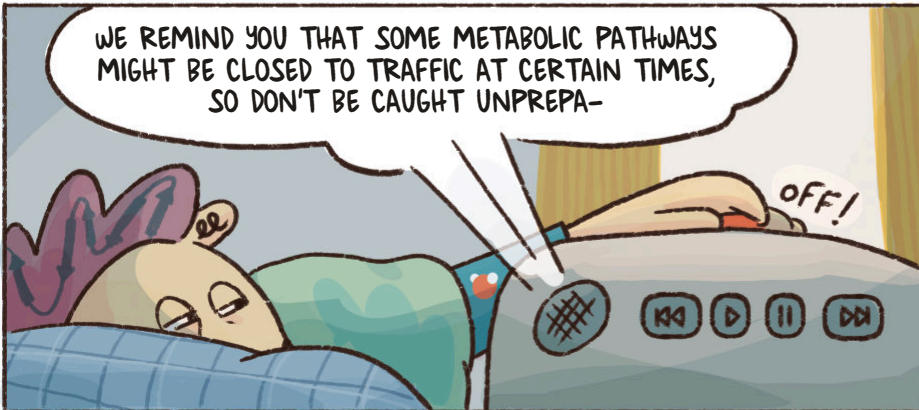
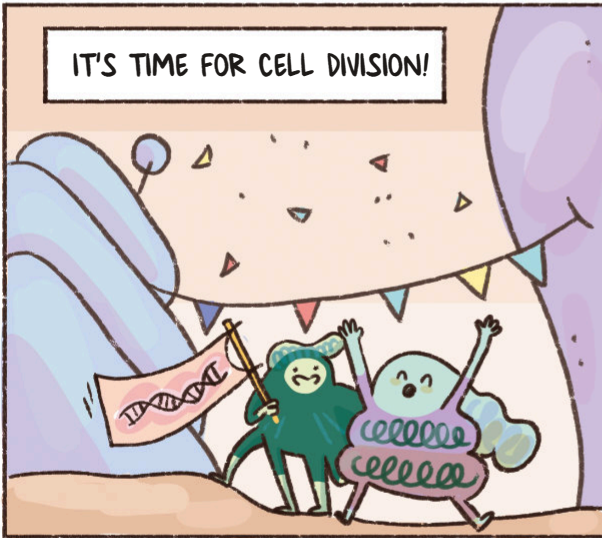
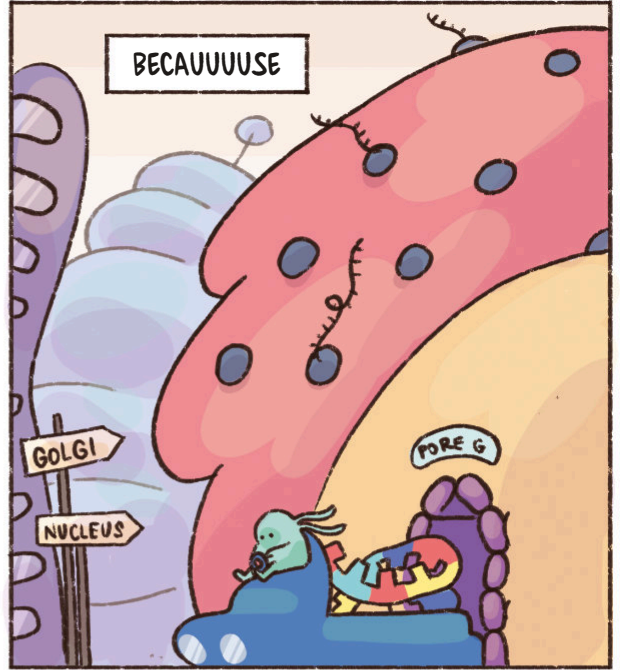
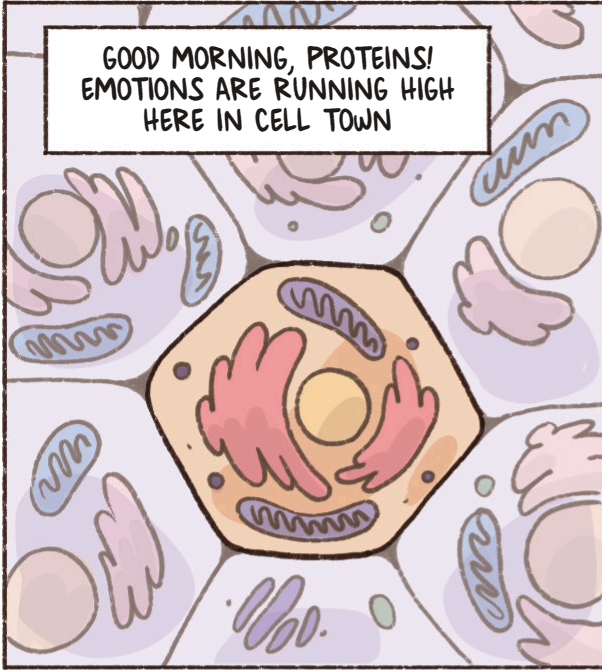
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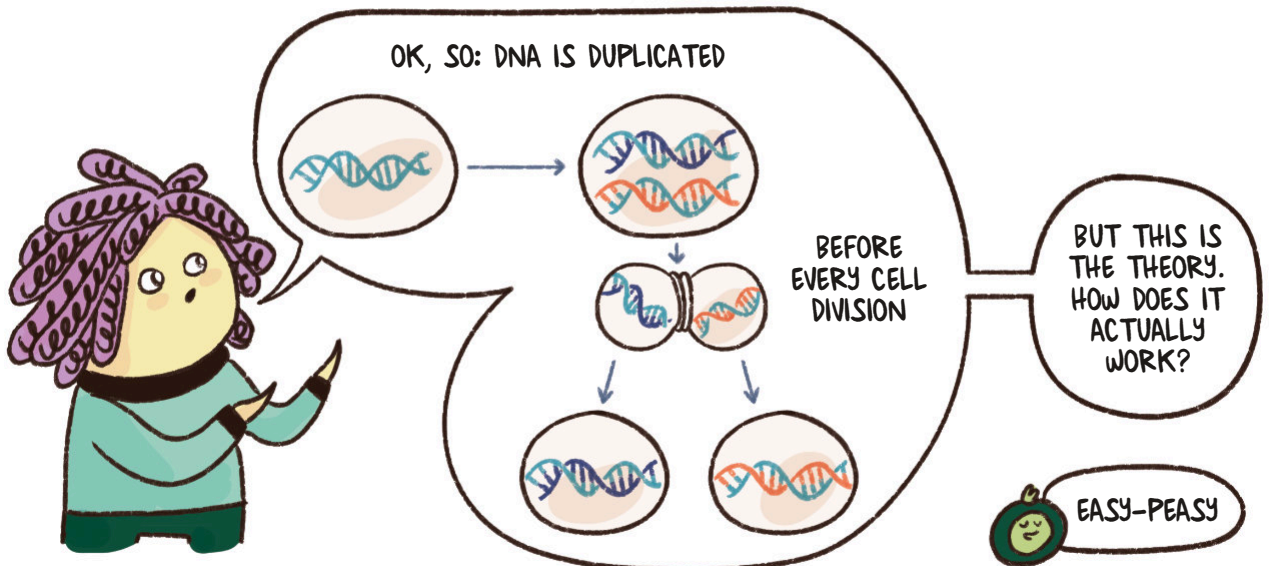
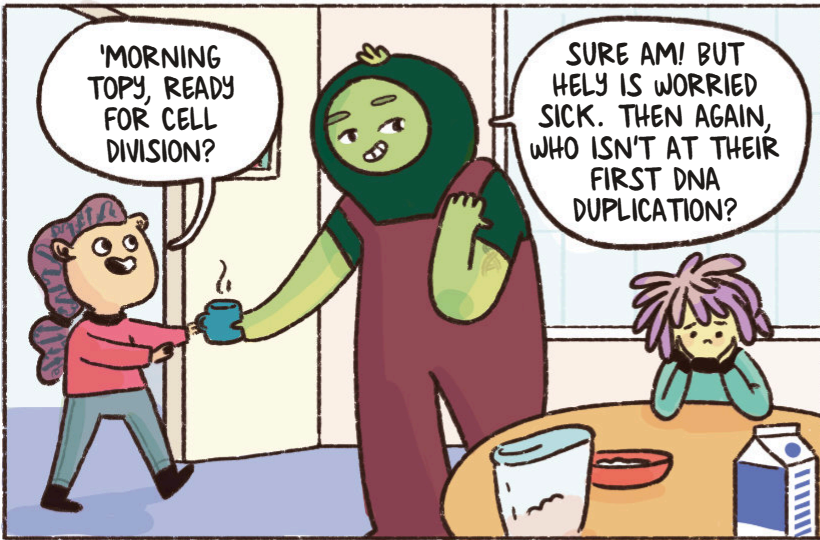
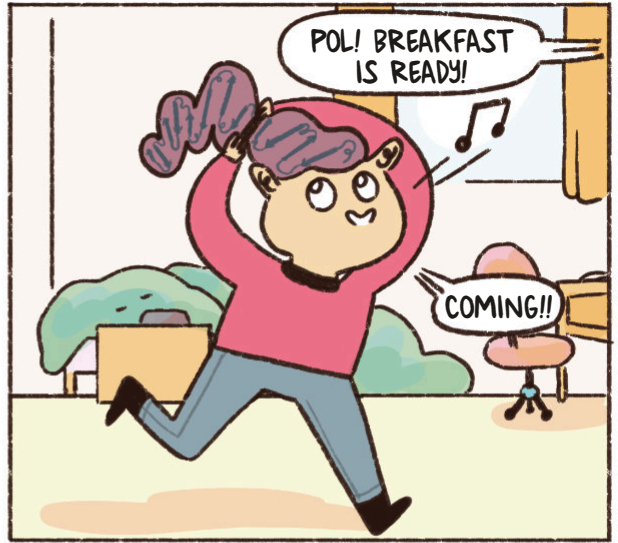
MRC Toxicology Unit

Cambridge CB2 1QR

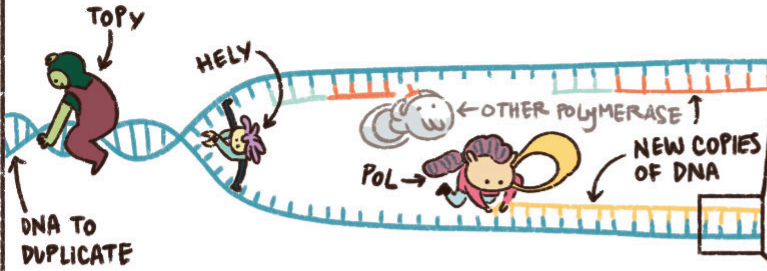
United Kingdom

For more information, contact: [communications@igc.ed.ac.uk](mailto:communications@igc.ed.ac.uk)

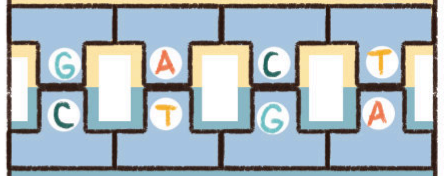




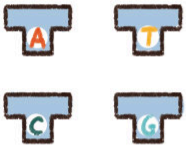
ONCE YOU'VE OPENED THE DNA'S DOUBLE HELIX, POL AND ANOTHER POLYMERASE WILL GET TO WORK DUPLICATING IT



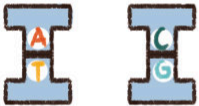
THE INITIAL DNA IS A LONG DOUBLE STRAND OF BASES, HERE'S A LITTLE EXAMPLE:



THERE ARE ONLY 4 DNA BASES



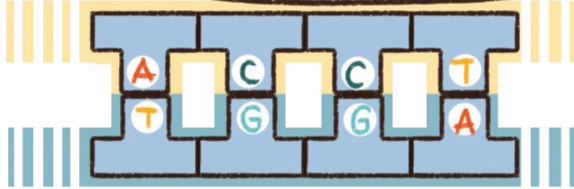
AND THEY ALWAYS FORM THE SAME PAIRS



YOU PASS ME ONE STRAND, GOT IT?



I ADD THE OTHER HALF TO MAKE IT DOUBLE AGAIN. WHEN I SEE AN "A", I ADD A "T", WHEN THERE'S A "G" I ADD A "C". AND VICE VERSA. THIS WAY THE INITIAL DNA AND ITS COPY ARE IDENTICAL.



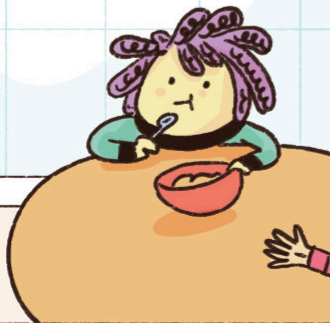
ANOTHER POLYMERASE DOES THE SAME THING WITH THE OTHER STRAND. BUT THERE ARE MULTIPLE TEAMS, IT'S NOT LIKE WE DUPLICATE ALL THE DNA ON OUR OWN!



IT'S MY JOB TO UNWIND THE INITIAL DNA SO KNOTS WON'T FORM

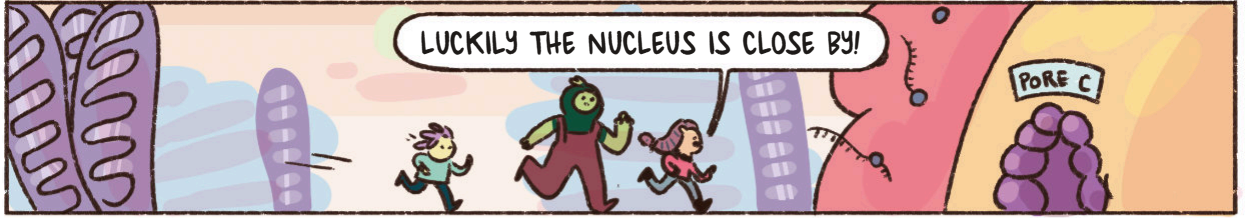


ONCE DUPLICATION IS COMPLETE, THE CELL DIVIDES. ONE COPY OF THE DNA COMES WITH US, ANOTHER GOES WITH THE OTHER CELL



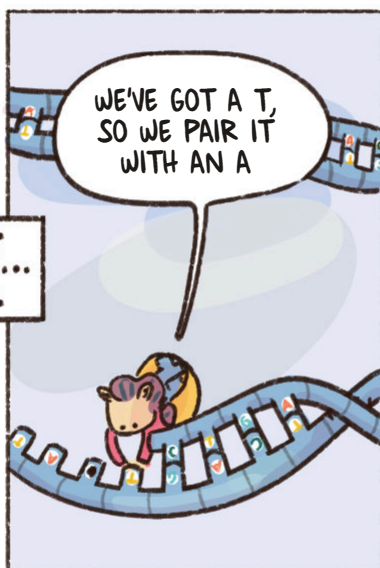
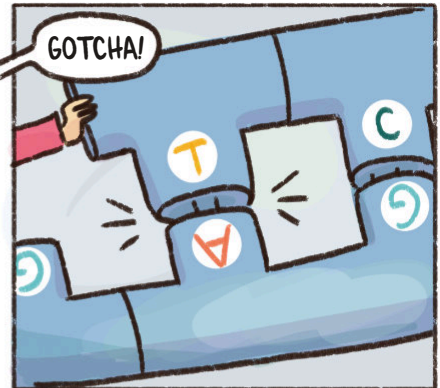
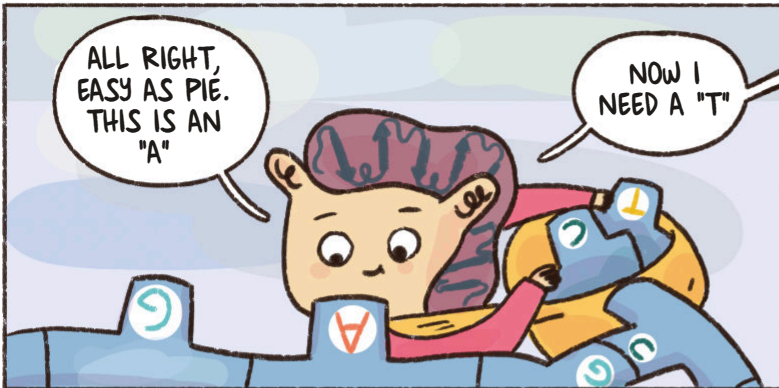
BUT LOOK AT THE TIME, WE NEED TO GO!

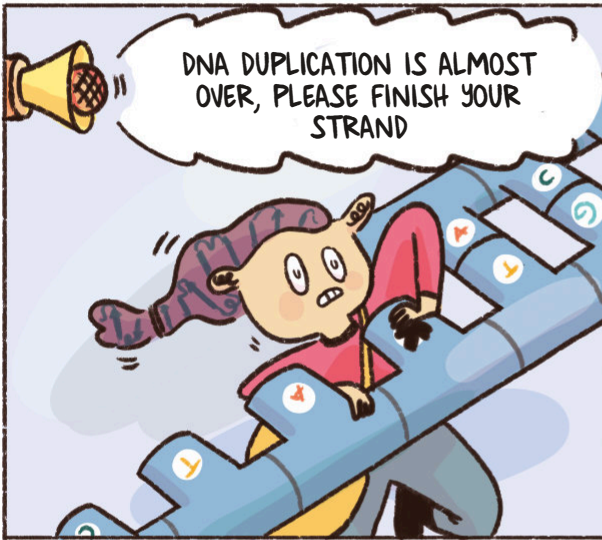
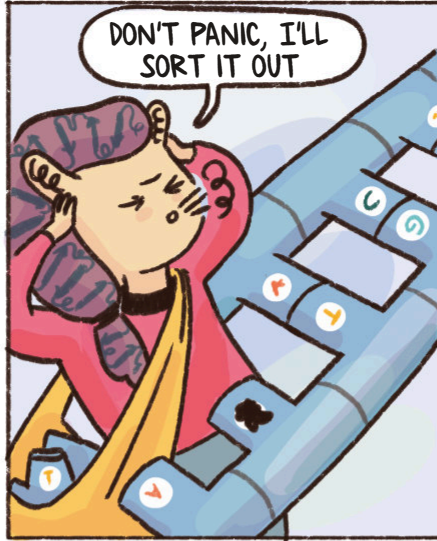




# DRILL!!!

HERE WE GO!





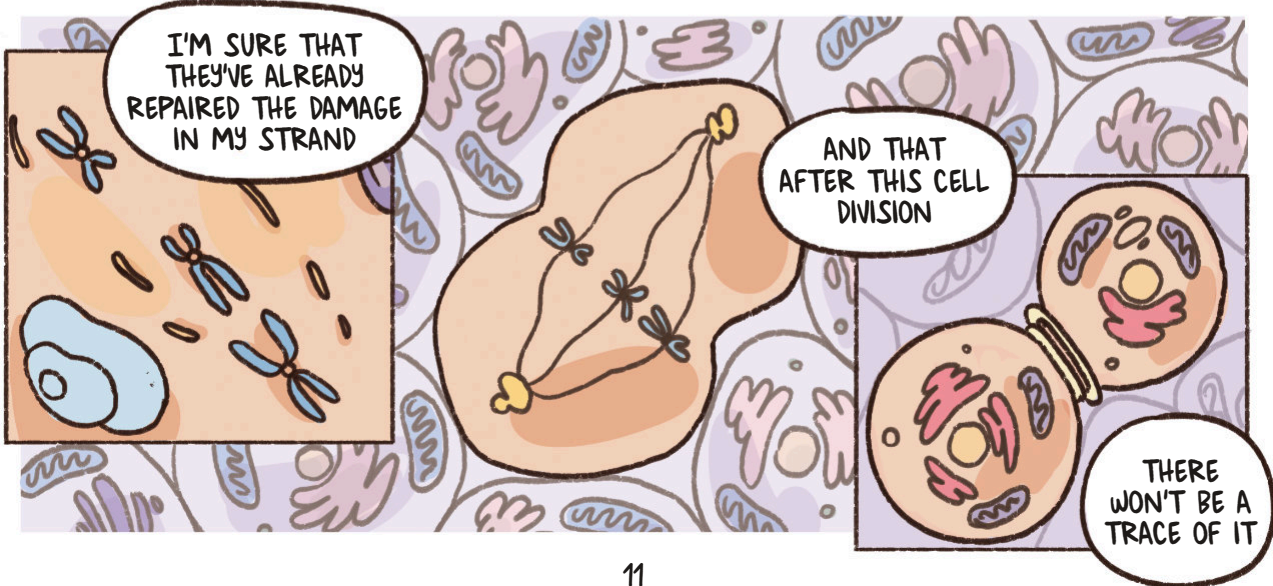
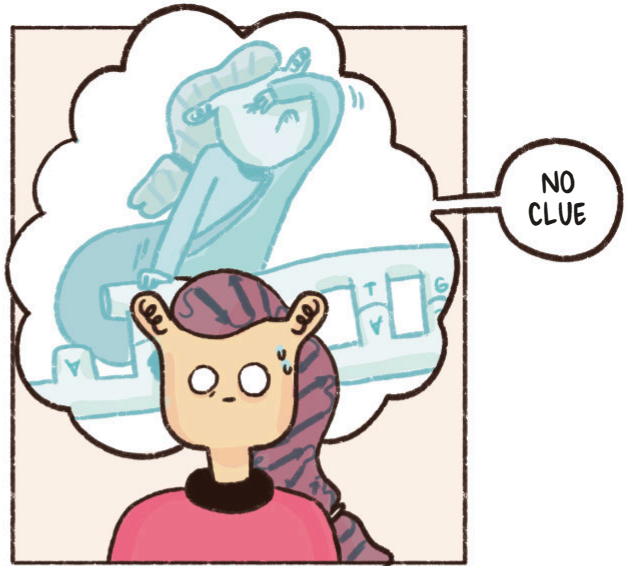


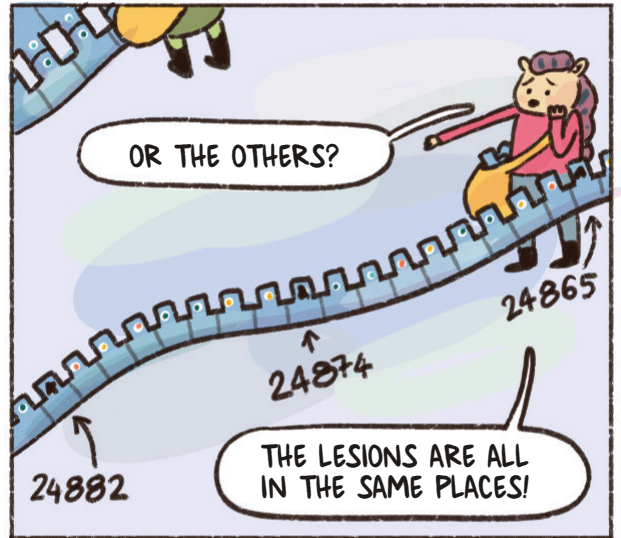
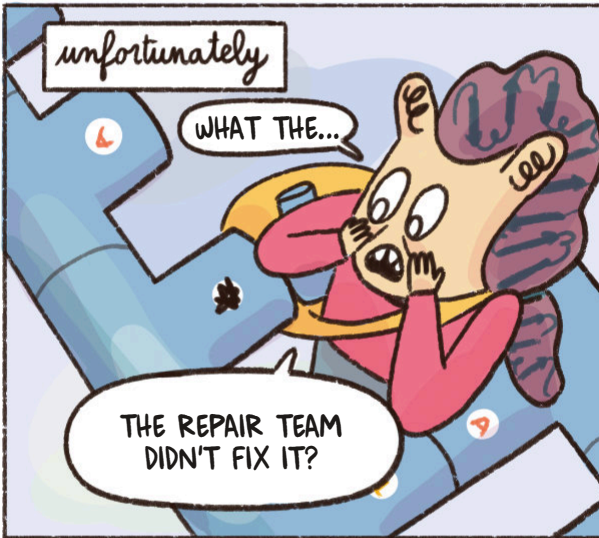
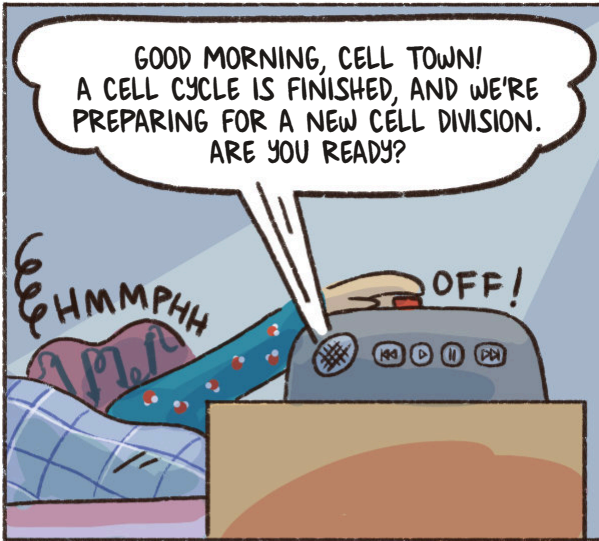


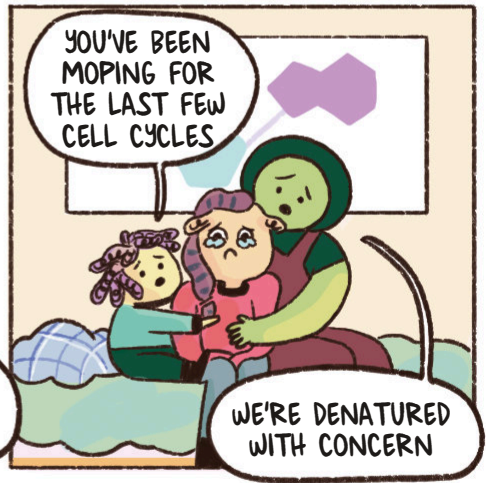
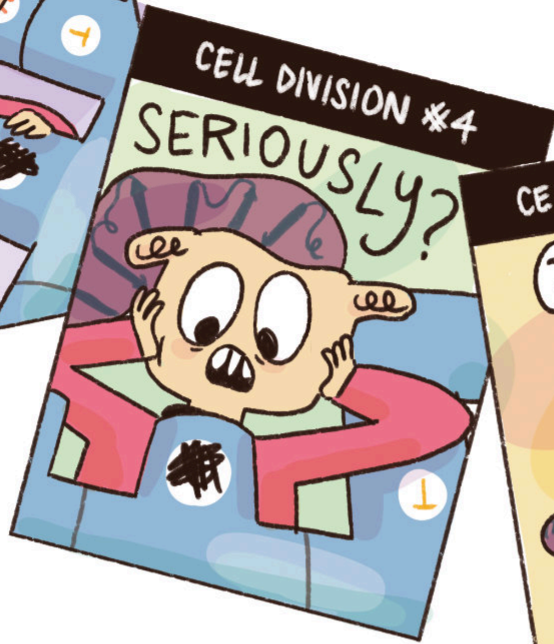
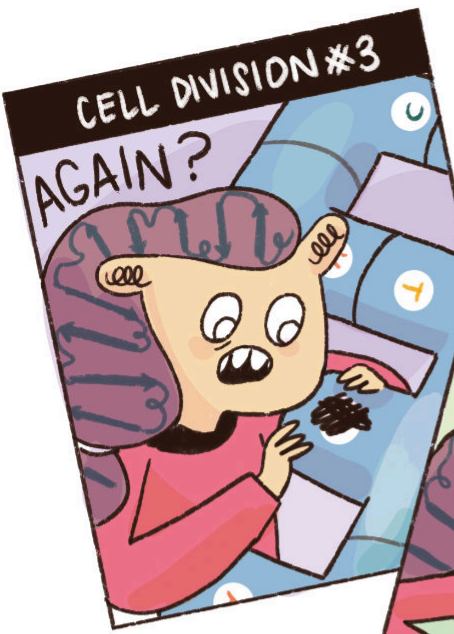
# DONG!

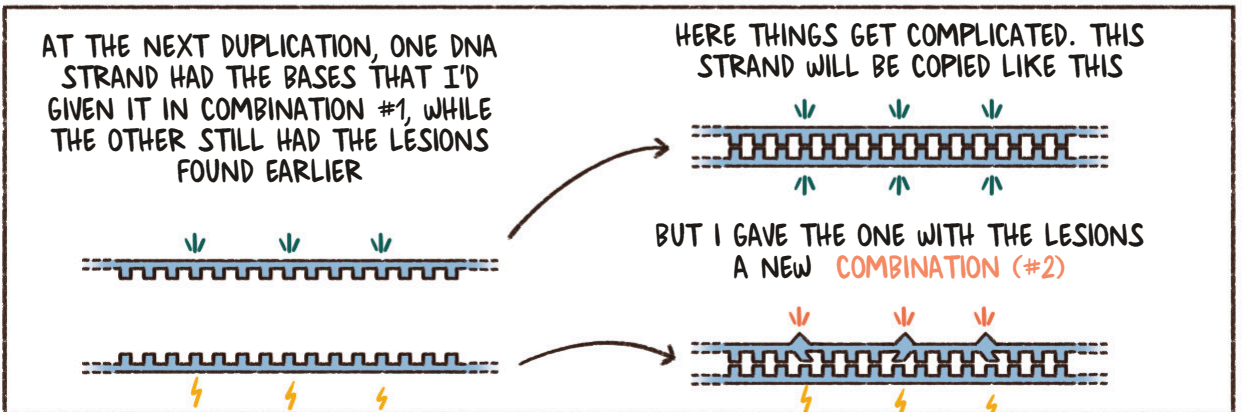
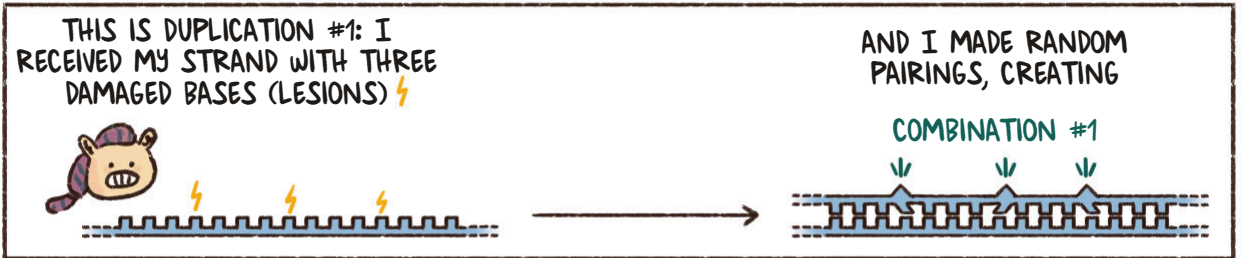




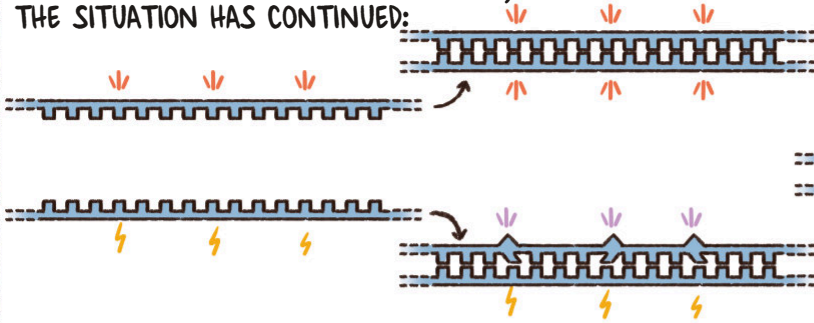






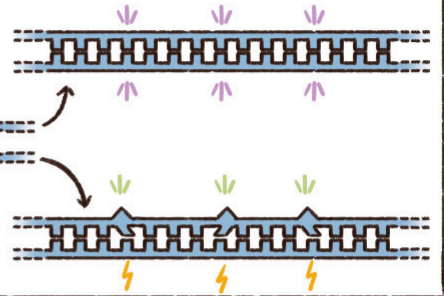


AND SINCE THE LESIONS HAVE CONTINUED TO "SEGREGATE", OR PASS ON TO THE FOLLOWING CYCLES, THE SITUATION HAS CONTINUED:

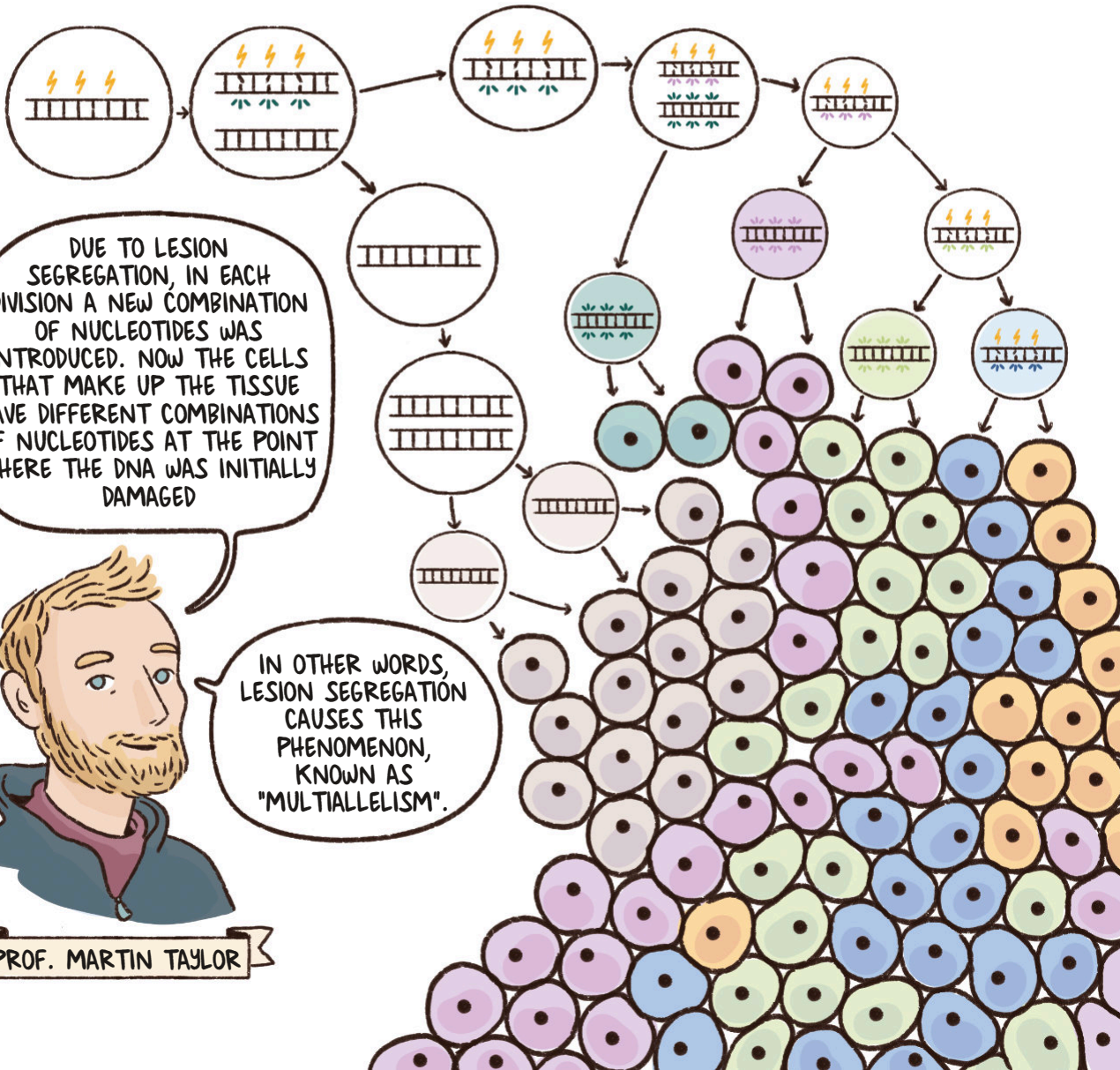


ON THE ONE HAND, A CELL POPULATION WITH THE COMBINATION I'D CREATED IN THE PREVIOUS CYCLE WAS MULTIPLYING

ON THE OTHER, I KEPT MAKING NEW COMBINATIONS BECAUSE I DIDN'T KNOW WHICH BASE PAIRS WERE CORRECT



LET'S LEAVE THE WORLD OF THE CELL AND LOOK AT IT ON A LARGER SCALE: THAT FIRST CELL WITH DAMAGED NUCLEOTIDES CREATED A CELL POPULATION THAT LOOKS LIKE A MOSAIC:

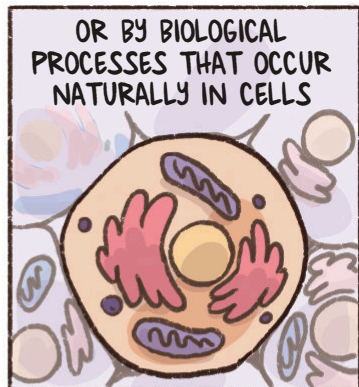
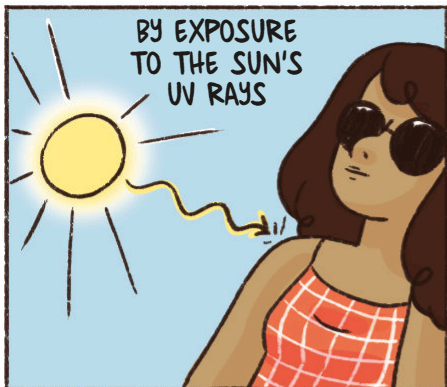


DUE TO LESION SEGREGATION, IN EACH DIVISION A NEW COMBINATION OF NUCLEOTIDES WAS INTRODUCED. NOW THE CELLS THAT MAKE UP THE TISSUE HAVE DIFFERENT COMBINATIONS OF NUCLEOTIDES AT THE POINT WHERE THE DNA WAS INITIALLY DAMAGED

IN OTHER WORDS, LESION SEGREGATION CAUSES THIS PHENOMENON, KNOWN AS "MULTIALLELISM".

PROF. MARTIN TAYLOR

DNA CAN BE DAMAGED IN MANY WAYS

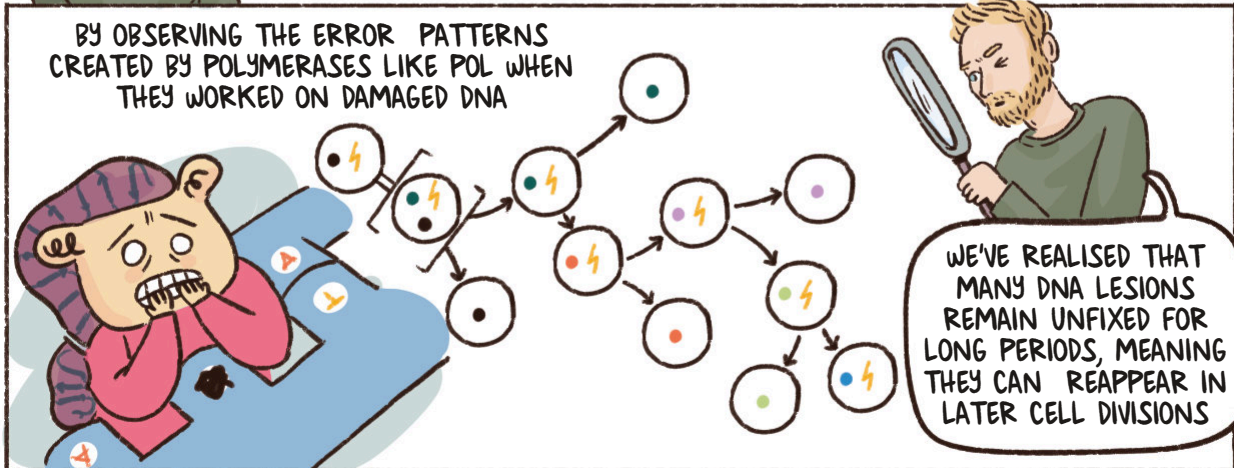


OUR CELLS KNOW HOW TO REPAIR THESE LESIONS, THANKS TO THE WORK OF THE REPAIR TEAM

WE SCIENTISTS USED TO THINK THAT THE REPAIR TEAM REACTED QUITE QUICKLY, WITHIN A FEW HOURS

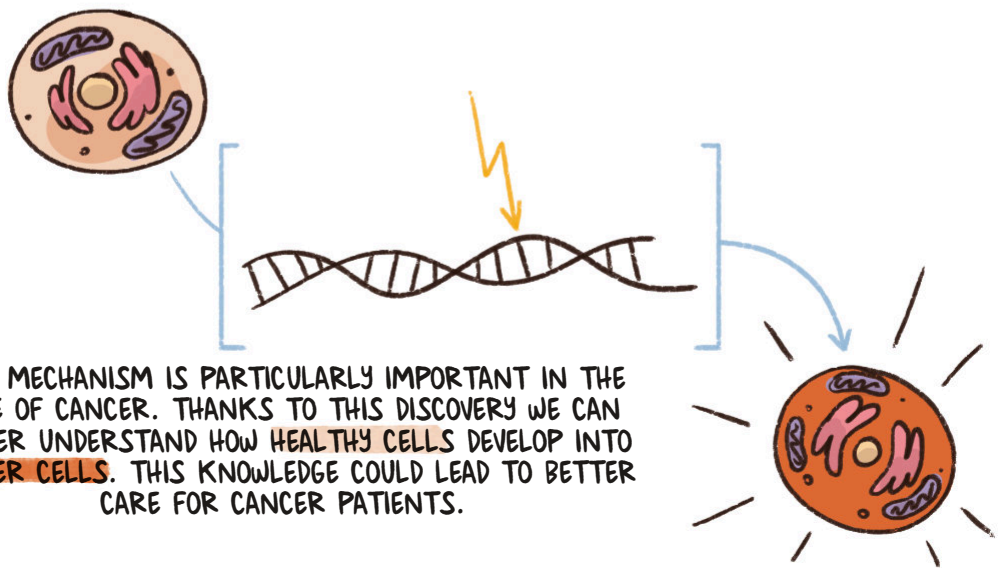
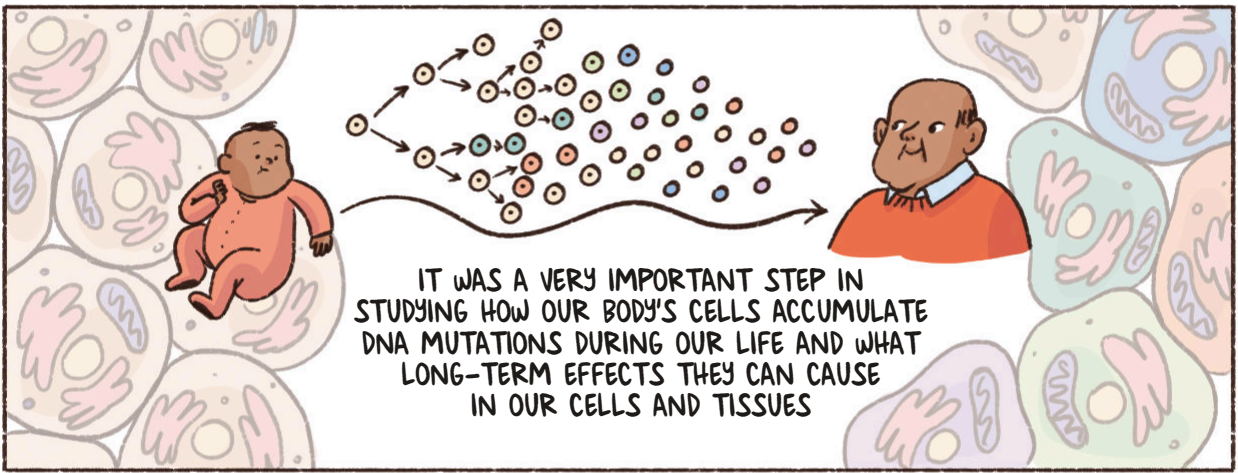
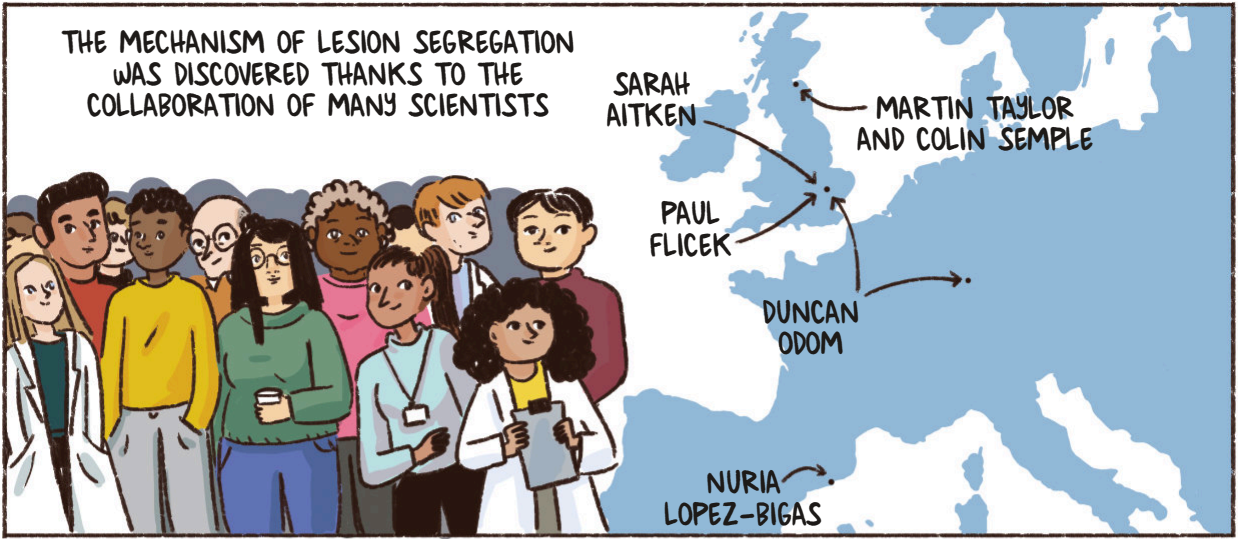


BUT THIS ISN'T ALWAYS TRUE



DEPENDING ON WHERE THESE DNA LESIONS OCCUR, THIS MECHANISM CAN LEAD TO THE CREATION OF A TUMOUR, WHICH WILL HAVE A "MOZAIC" CELL POPULATION LIKE THE ONE WE SAW ON THE LAST PAGE.

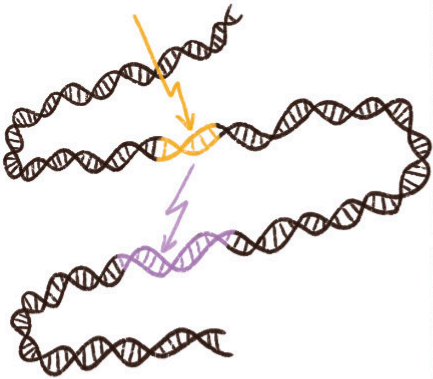




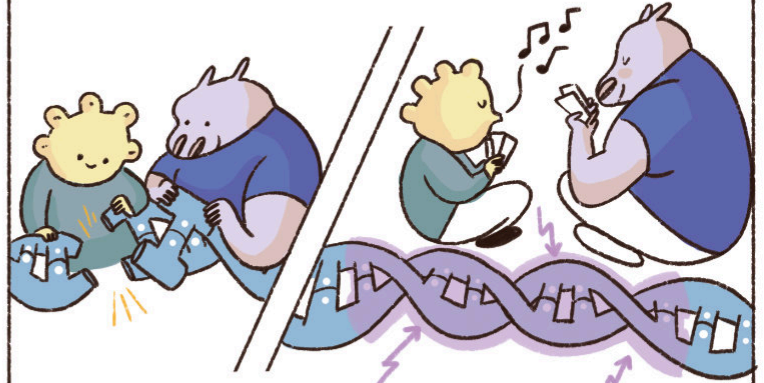
MUTATIONS CAN HAPPEN IN MANY WAYS, NOT ALL CAUSED BY DAMAGE, AND SOME PARTS OF DNA ARE MORE LIKELY THAN OTHERS TO BE AFFECTED. IN MY LAB AT THE INSTITUTE OF GENETICS AND CANCER, UNIVERSITY OF EDINBURGH, UK, WE DECODE THE PATTERNS OF MUTATIONS IN ORDER TO UNDERSTAND HOW OUR DNA IS COPIED, PROTECTED AND REPAIRED



BY COMPARING MUTATIONS ACROSS DIFFERENT CELLS, AND ACROSS DIFFERENT STRETCHES OF DNA

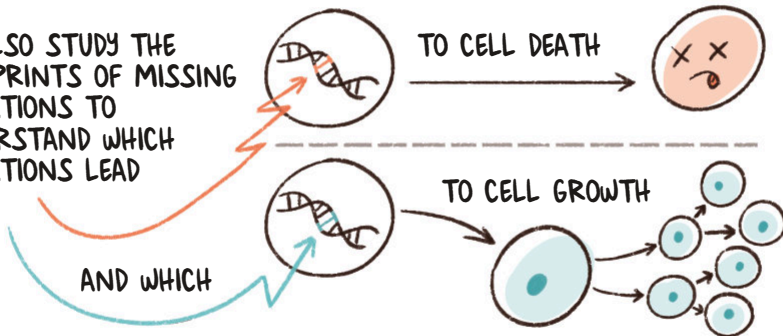


WE CAN ASK WHICH BITS OF DNA ARE BETTER CHECKED FOR ERRORS OR MORE EFFICIENTLY REPAIRED.



IT TELLS US WHERE AND WHEN THIS CHECKING AND REPAIR IS HAPPENING, AND WHEN IT FAILS

WE ALSO STUDY THE FOOTPRINTS OF MISSING MUTATIONS TO UNDERSTAND WHICH MUTATIONS LEAD



BUT ALSO TO UNDERSTAND THE HISTORY OF A PERSON: THEY ARE THE RECORDS OF EVENTS THAT HAPPENED IN PAST CELLS, AND THEY ALSO GIVE US A TOOL TO TRACE THE CELL TYPES AND EVENTS THAT WERE INVOLVED IN THE LEAD UP TO CANCER

OUR WORK HELPS TO SHOW HOW CANCER DEVELOPS AND MAY GUIDE ITS TREATMENT



## **The group**

The Taylor group has been established at the MRC Human Genetics Unit since 2010 where they study why mutations occur where they do and what effect they have when they arise. The group specialises in the large-scale computational analysis of genomic and related data. The MRC Human Genetics Unit is part of the Institute for Genetics and Cancer at the University of Edinburgh.

## **The Liver Cancer Evolution Consortium**

The science presented in this comic was the result of an international collaboration involving the research groups of Dr Sarah Aitken, Dr Paul Flicek, Prof Nuria Lopez-Bigas, Prof Duncan Odom, Prof Colin Semple and Prof Martin Taylor. The original publication describing these discoveries can be found at <https://doi.org/10.1038/s41586-020-2435-1>

## **The project**

Comics are a powerful and appealing tool for storytelling and we, at the Institute of Genetics and Cancer, want to use them to make our research stories accessible to a wide range of audiences.

## **The Institute**

The Institute of Genetics and Cancer is tackling one of the greatest biomedical challenges, determining how mutations – constitutional and acquired – drive the molecular and cellular dysfunction that result in disease. Defining the molecular mechanisms of genetic disease and cancer, and the flow of information from DNA through to the production and regulation of RNAs and proteins is critical to deliver pathways targetable by future therapies.

Everything is going well for Pol the polymerase, living their best life in Cell Town, until the day they find some mysterious bases on the DNA they have to duplicate...

