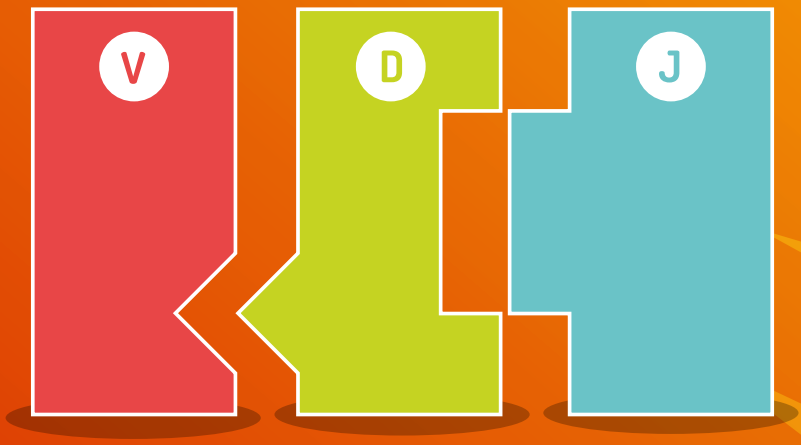
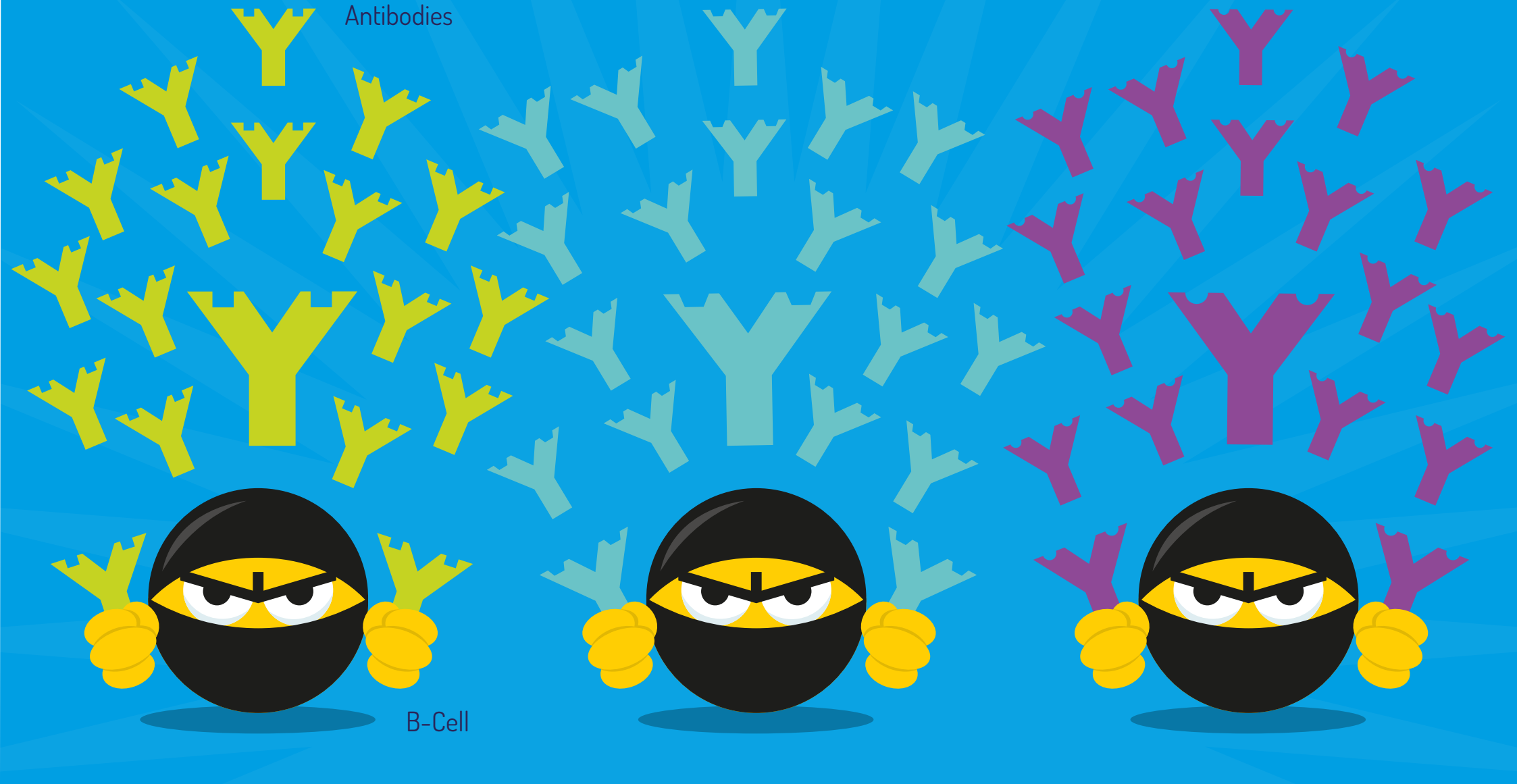
Missing Antibody Puzzle Pieces – Danger to Older People



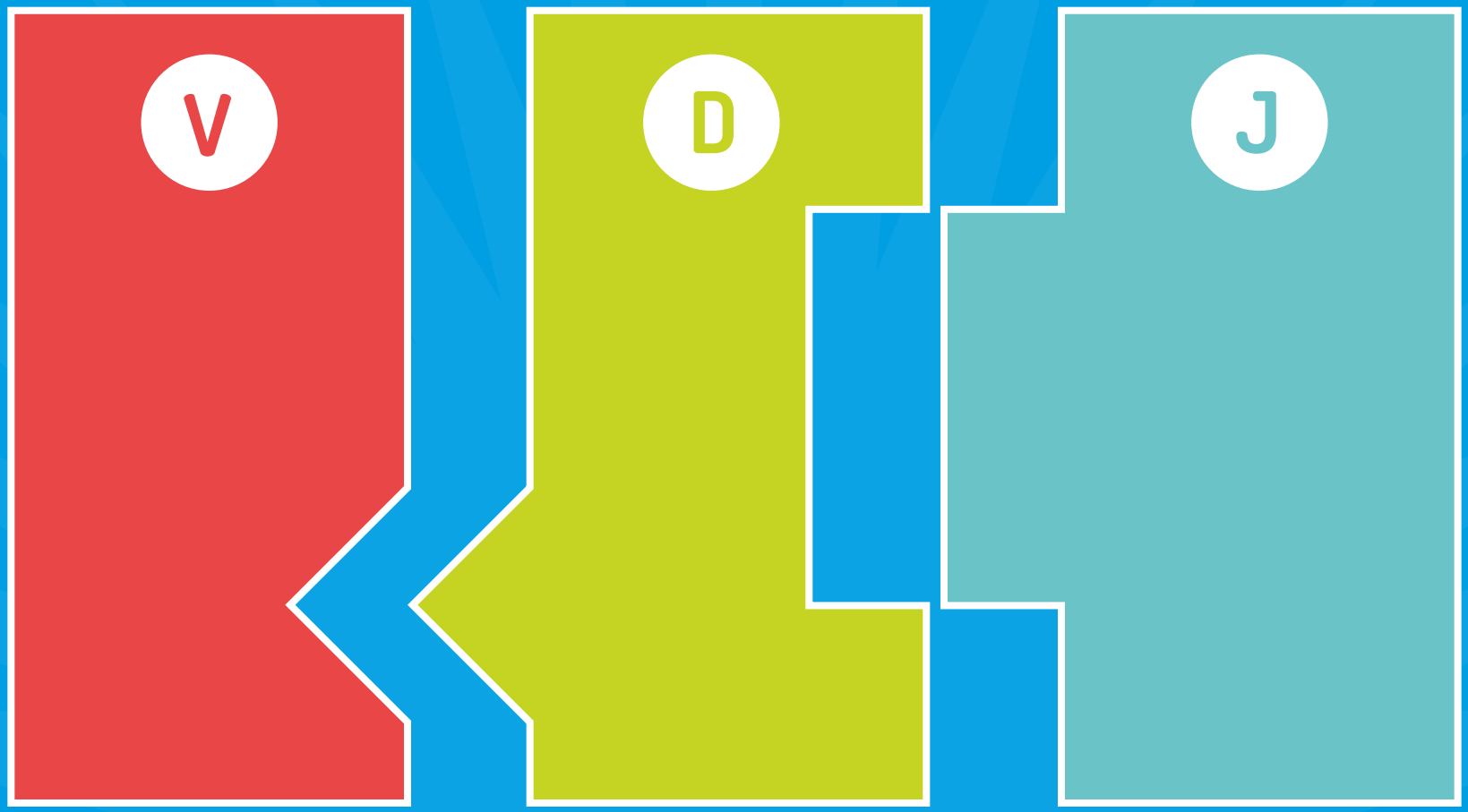
How do our B cells make enough **different antibodies** to catch all the different germs that could attack us?



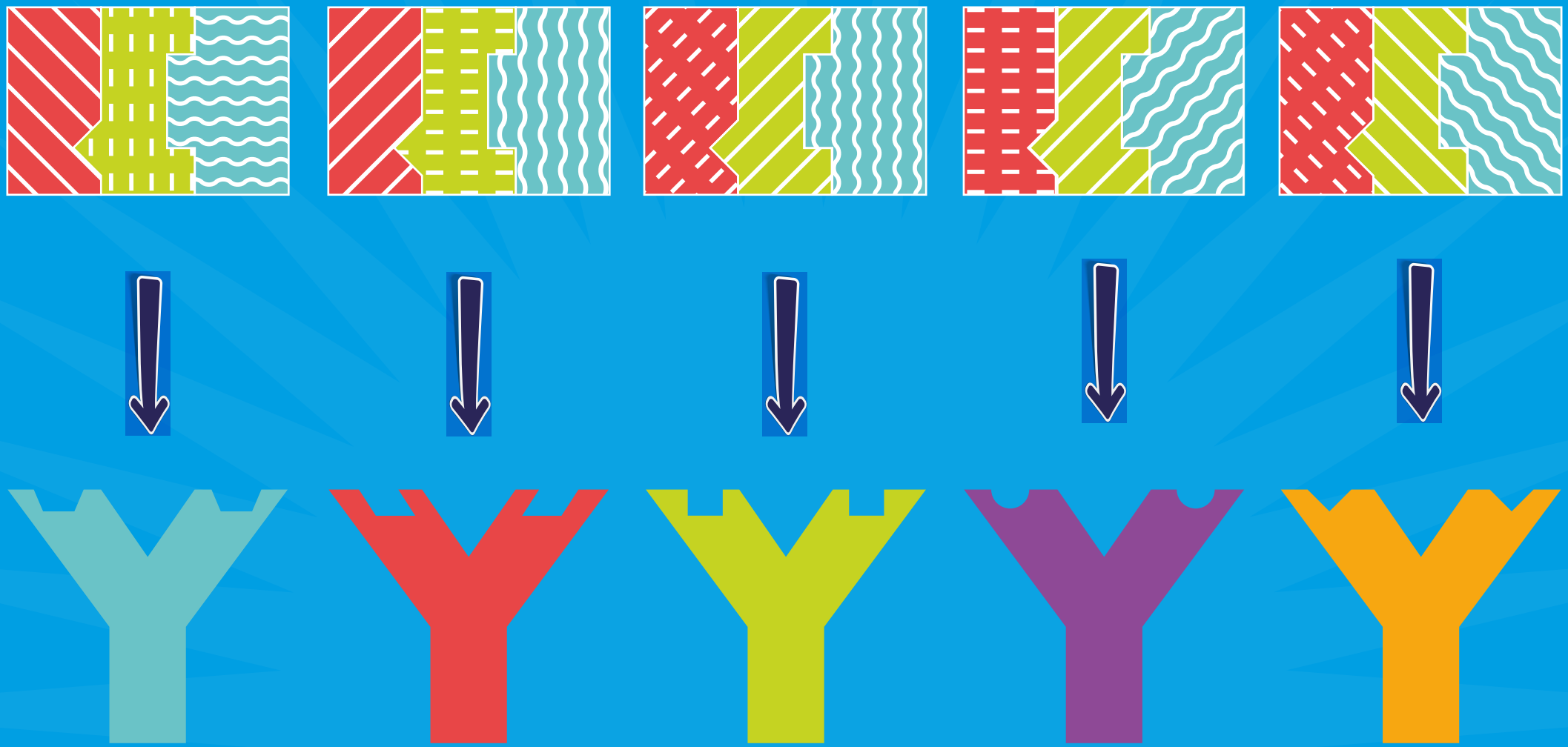
If we had a gene for every antibody we can make, our genome would be **over 1,000 times longer** than it already is...

...that's too much DNA to carry around!

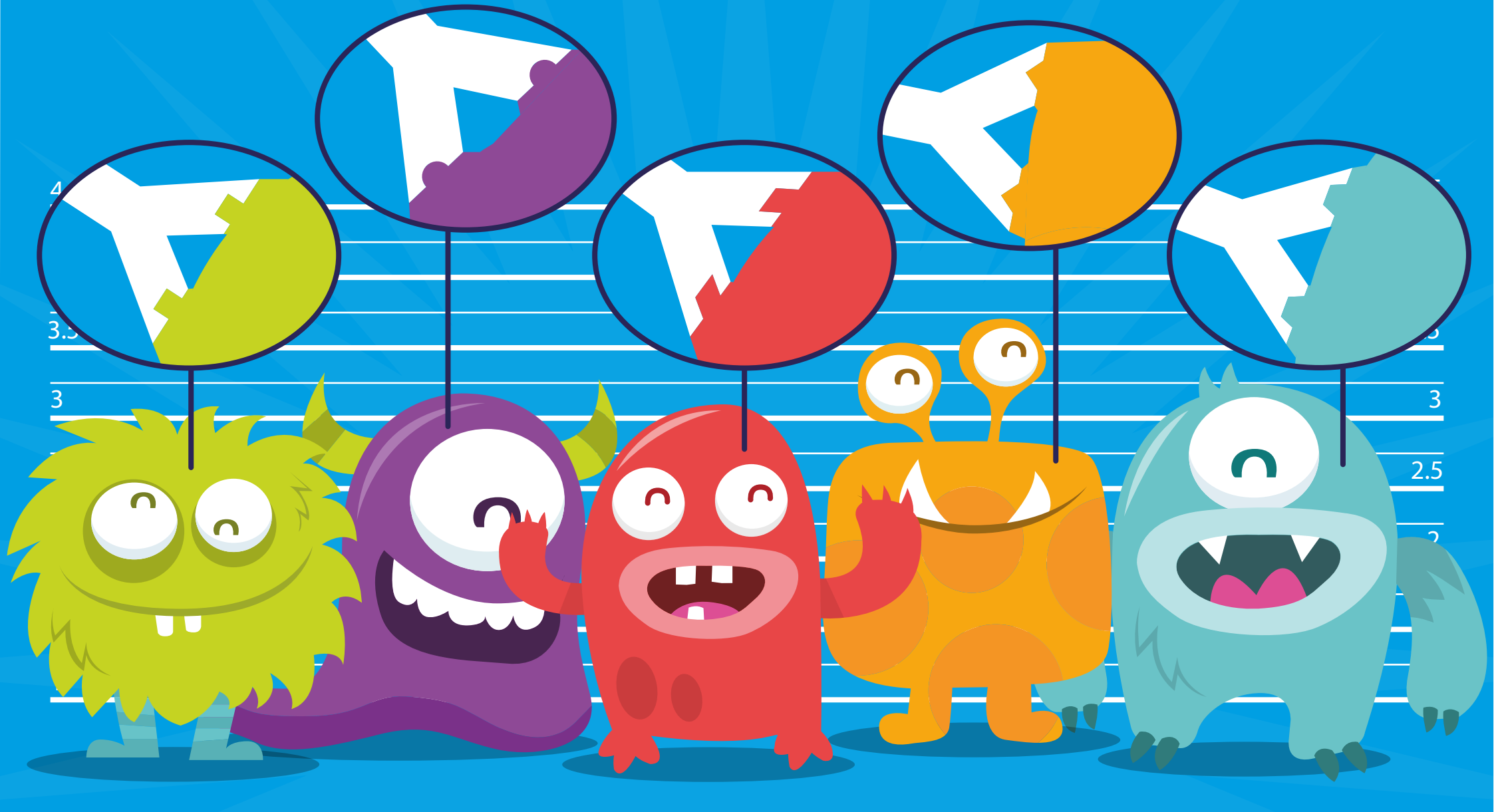
Instead, every B-Cell makes its own **unique antibody** out of a small set of components – **V**, **D** and **J** gene segments:



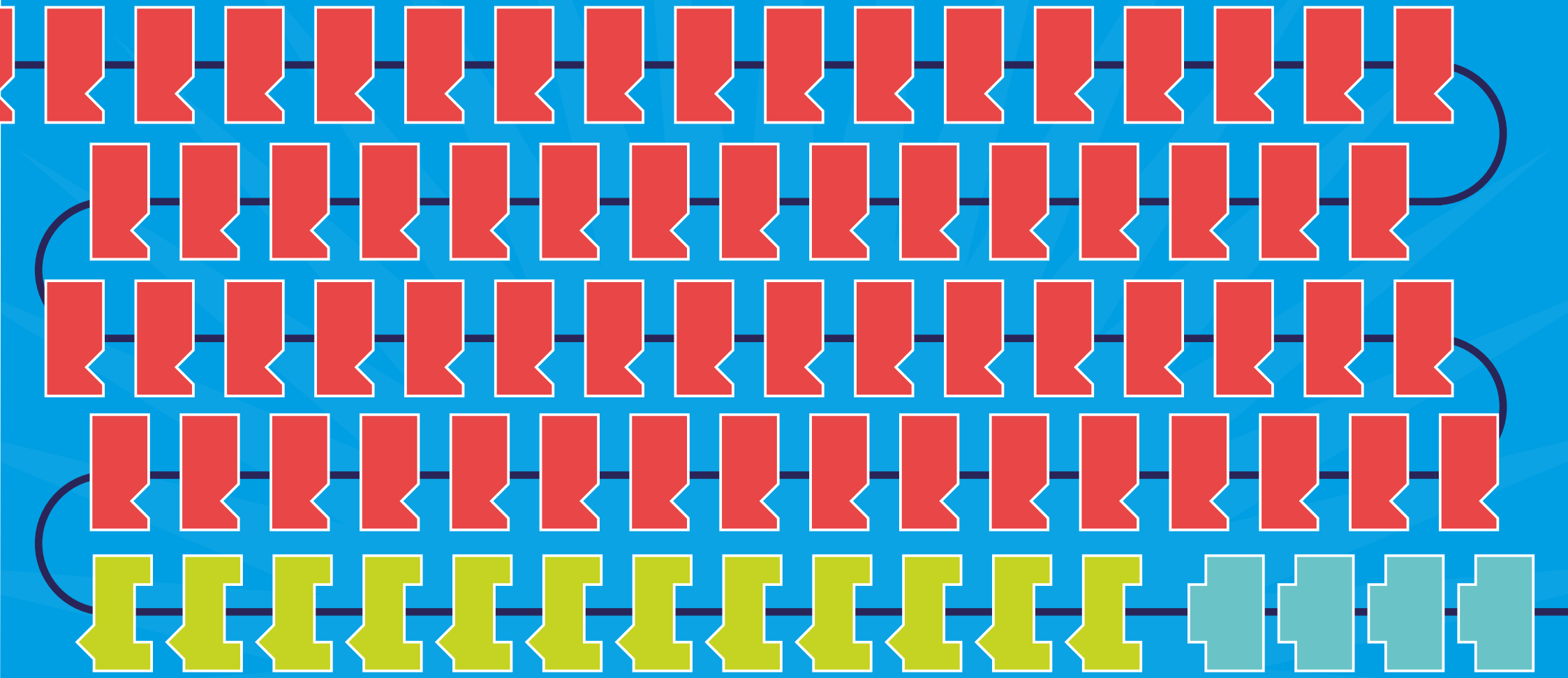
Different combinations of gene segments connect to each other to make the antibodies.



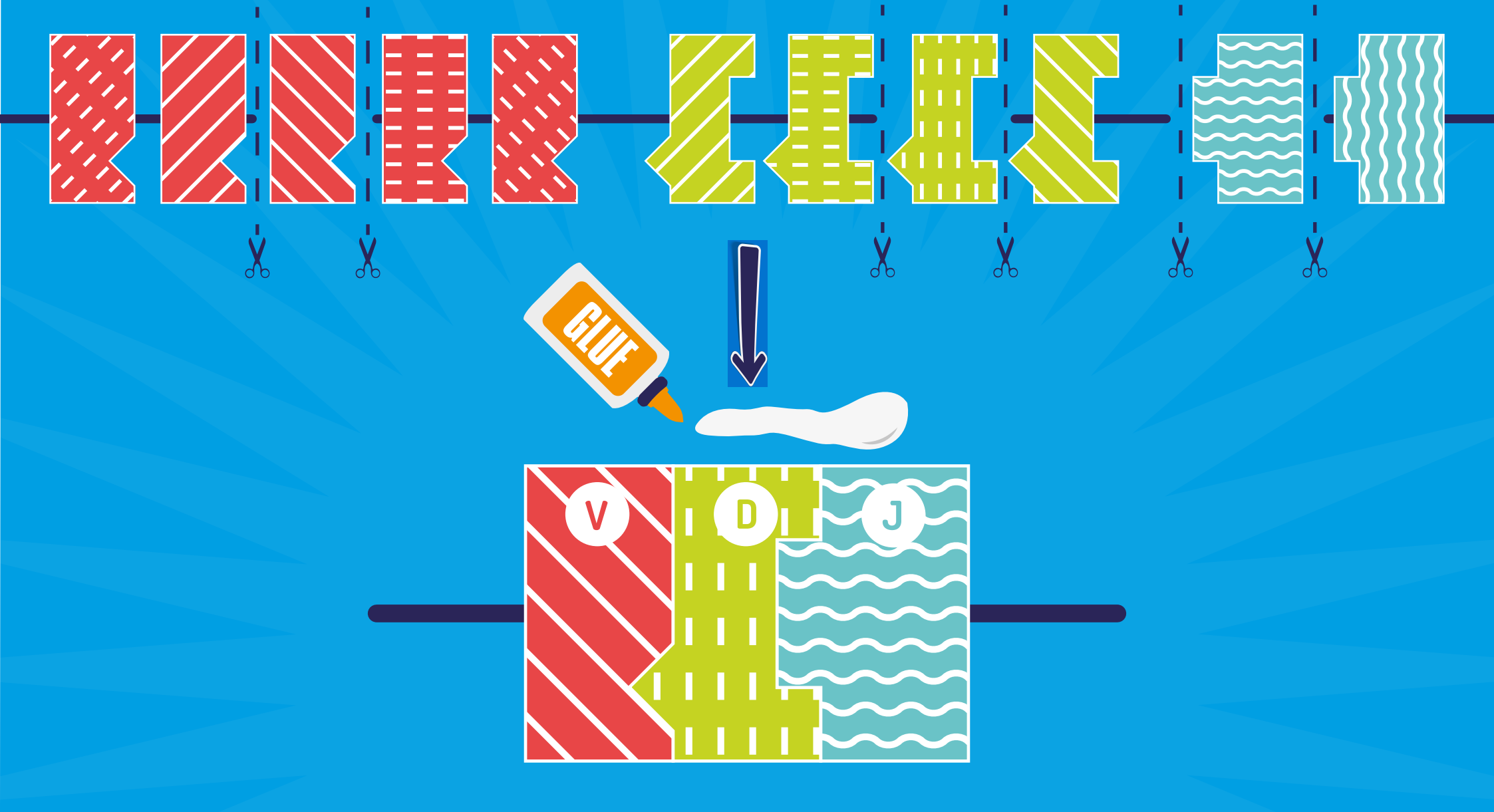
The antibodies are then able to **recognise and stick** to markers on pathogens (germs), known as antigens.



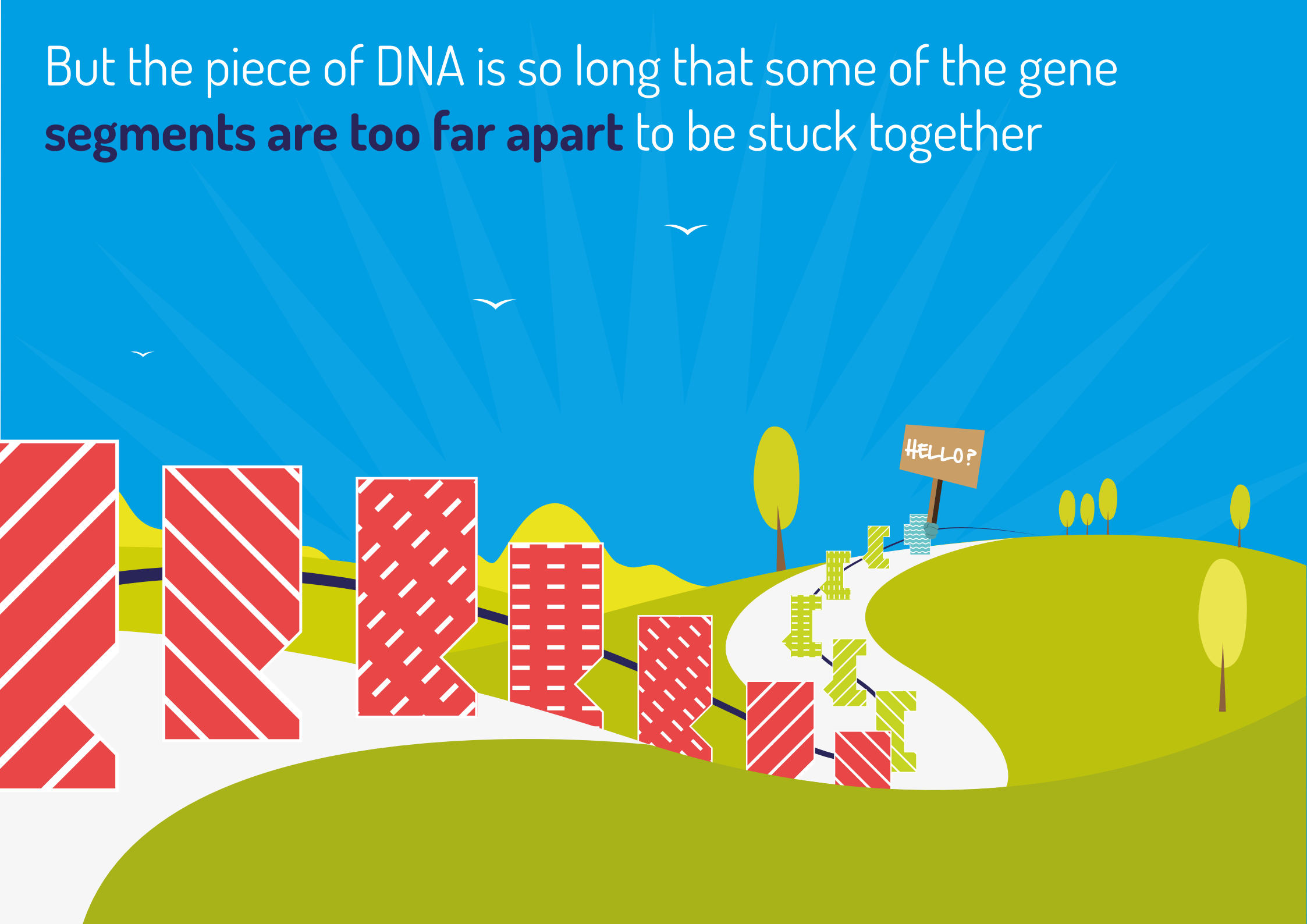
The V's, D's and J's are all on **one long piece of DNA**.



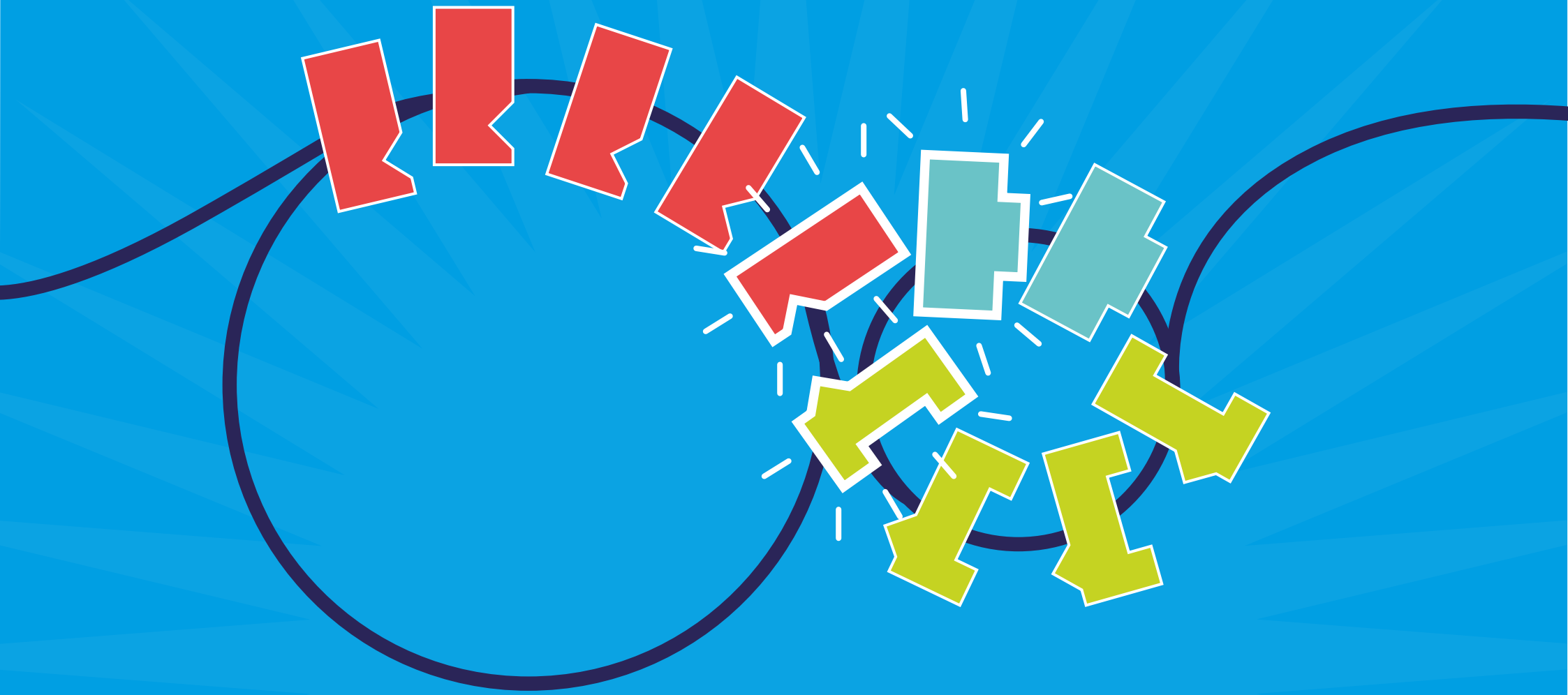
The DNA has to be **cut up and stuck back together** again to make an antibody.



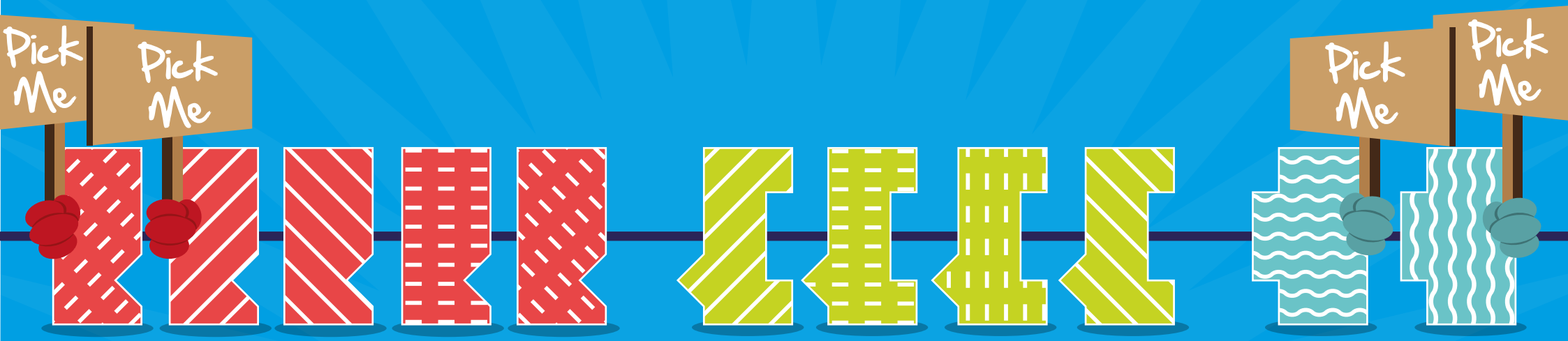
But the piece of DNA is so long that some of the gene **segments are too far apart** to be stuck together



B-Cells get around this problem by making loops in the DNA, pulling **far apart** gene segments **closer together**.

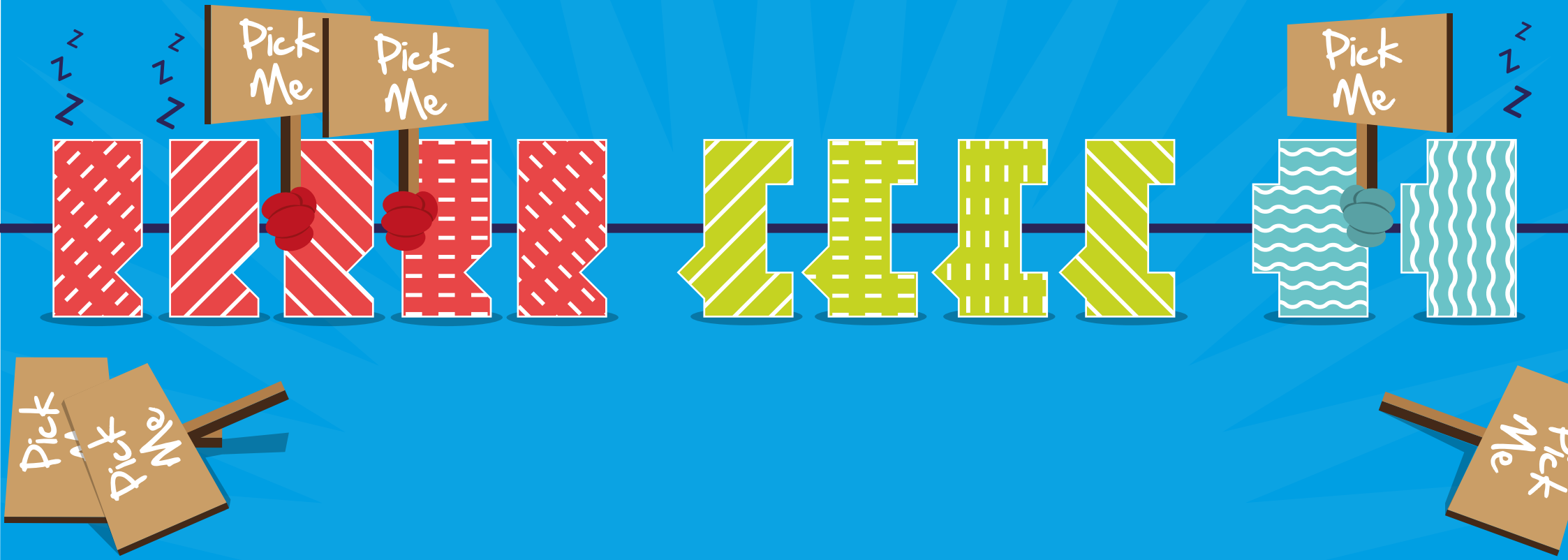


They also give special help to far away segments by giving them **epigenetic marks** to help them get chosen.



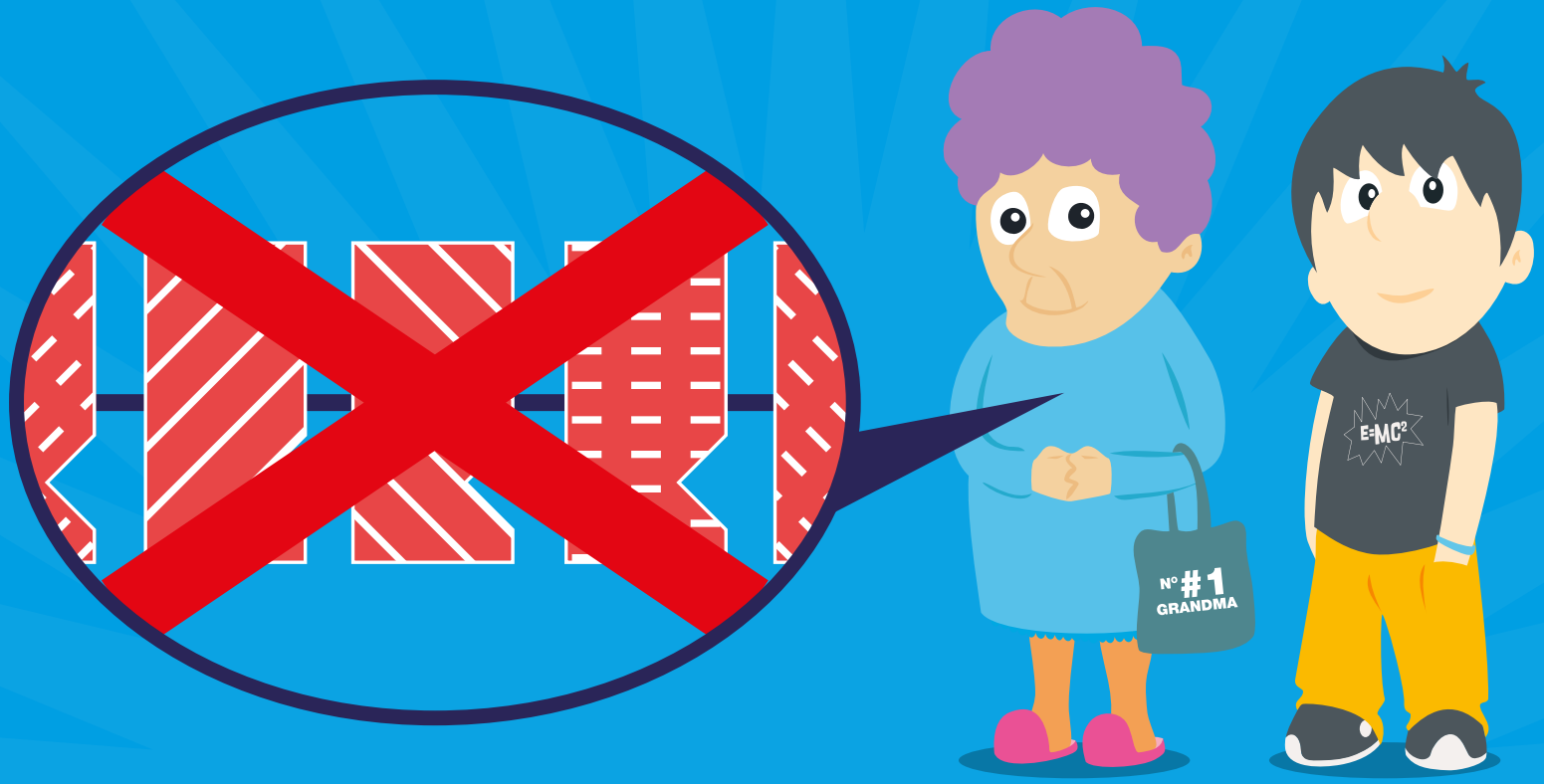
We have created a new technique called **VDJseq**. It lets us sequence the VDJ's in B-Cells so we know which V's, D's and J's were chosen in each cell.

This sequencing helps us find out **which genes are chosen and why**. It could also help find out what's wrong in people who have a weak immune response to infection.



Do some of their gene segments get ignored so they can't make as many antibodies?

Older people have a weakened immune response. VDJseq shows that **in older mice the far away V genes don't get chosen** as much as in younger mice.



We hope to understand whether problems with DNA looping or epigenetic marks cause this defect.

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Research in the Corcoran Lab focuses on understanding the role of chromatin and nuclear organisation in controlling gene expression during the development of the immune system:

www.babraham.ac.uk/our-research/lymphocyte/anne-corcoran