



**WEAPONS OF
MICROSCOPIC
DESTRUCTION**
HOW YOUR IMMUNE SYSTEM KEEPS YOU SAFE FROM ATTACK



Assemble your defences in time
The V(D)J recombination jigsaw game

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ANTIBODIES...HOW ARE THEY CREATED?

V(D)J recombination – the jigsaw that generates your antibody repertoire...

In response to threats of attack your body has developed an immune system, an army of specialist cells equipped with high-tech weapons (e.g. antibodies) and sophisticated communication systems. Antibodies are also known as **immunoglobulins (Ig)** and are 'Y' shaped proteins made by B cells.

Each antibody has a different '**variable**' region, the top of the 'Y' shape, where **antigen-recognition** and binding takes place. A single pathogen can have many different antigens, for each there may be many antibodies. Our immune system has the potential to produce 10 billion different antibodies, even before it meets an invader! This diversity ensures our immune system can detect and eliminate the 1000s of pathogens we encounter each day.

There are many processes which take place to create the different variable regions on our antibodies. The first process involved in generating the huge collection of antibodies is called '**V(D)J recombination**', scientists at the Babraham Institute have been investigating this. The variable region (the top of the 'Y') is encoded by numerous gene segments which are known as variable (V), diversity (D) and joining (J) gene segments.

The V, D and J genes are joined together via a 'cut and paste' mechanism by two enzymes known together as the **Recombinase Activating Gene**, or RAG complex. There are 195 V genes, 10 D genes and 4 J genes; initially the D and J genes join, followed by a V gene. Because there are so many different Vs, Ds and J genes many different combinations can be used to generate the variable antigen binding region of the antibody – producing millions of different antibodies which can recognise millions of different invaders.

Nuclear Dynamics and Immunology

Collaboration to understand our immune system

At the Babraham Institute we also study nuclear dynamics, a field of science which investigates processes that alter gene expression without changing the DNA sequence. These include 3D organisation of chromosomes, and several epigenetic mechanisms, such as DNA looping which ensure that the gene segments are brought together correctly. Scientists at the Babraham Institute are trying to understand how the 3D architecture of antibody genes influence V(D)J recombination. In particular we have found that these genes make a lot of non-coding RNA. Non-coding RNA doesn't make protein and 98% of the RNA in our body is non-coding. We are trying to understand how non-coding RNA influences V(D)J recombinations. Our research has already shown that as we age approximately half of our V genes are no longer used properly to generate new antibodies – leading to a reduced resistance to infection. We aim to understand which of these epigenetic mechanisms are faulty during ageing, so that we can design new treatments to boost antibody production, improving the ability of elderly people to fight infection.

For more details visit <http://bit.ly/1lzsvvz>

Can you assemble your defences in time?



Have a go at our V(D)J recombination jigsaw game. How many different antibodies can you make in 2 minutes?

These antibodies patrol your body until they find a foreign invader that they recognise. Then they attack the invader and remove it from your body.



Remember

- You must use 1 'V' gene, 1 'D' gene and 1 'J' gene
- You can use the same genes more than once, but not in the same combination

How did you get on?

5-10

If you got between 5 and 10 V(D)J recombinations, then you've made/created the antibody repertoire of a baby or old person.

20-80

If you got between 20 and 80 V(D)J recombinations, then you've made/created the antibody repertoire of a middle aged person.

80-100

If you got between 80 and 100 V(D)J recombinations, then you've made/created the antibody repertoire of a young adult.