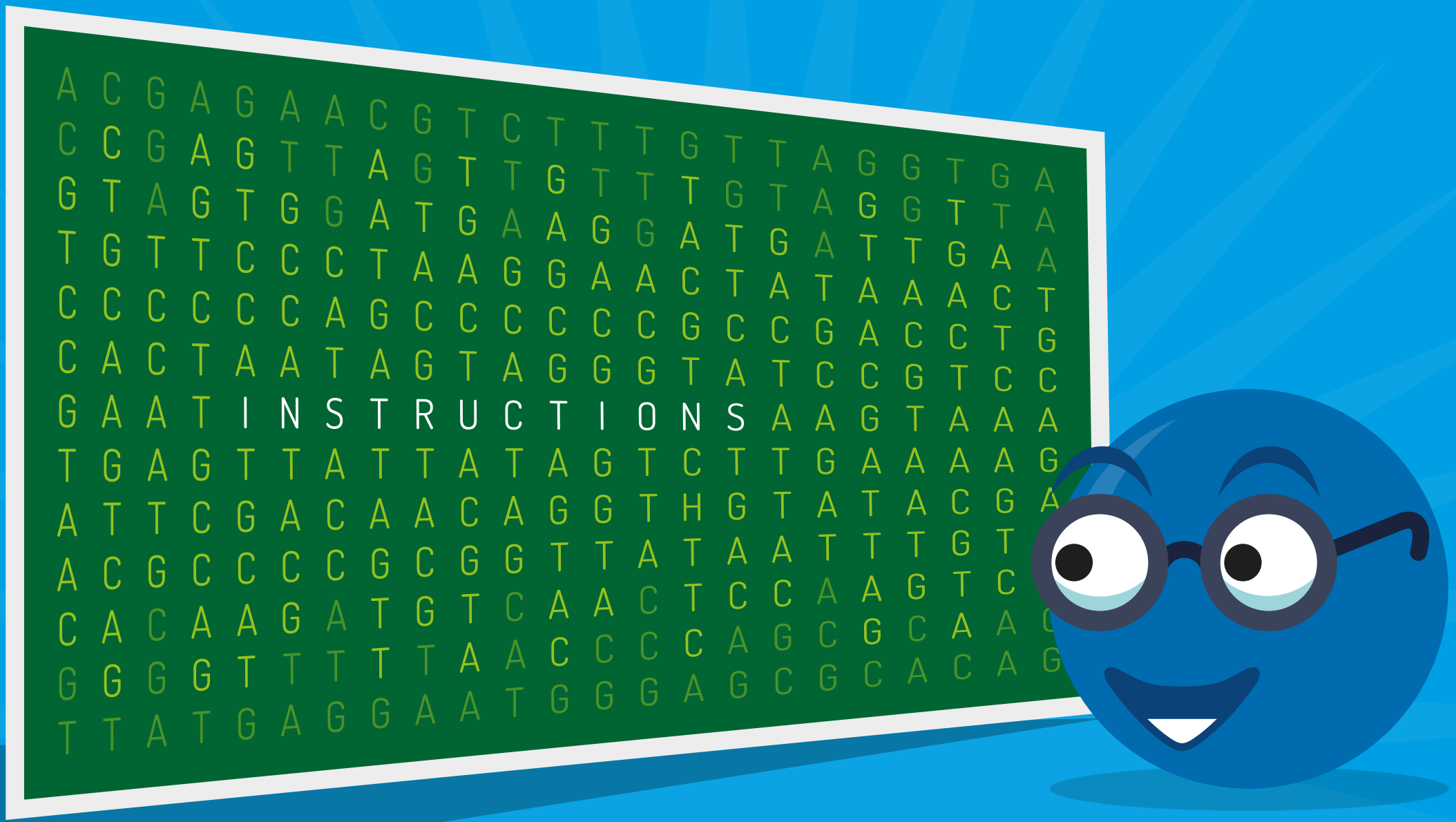
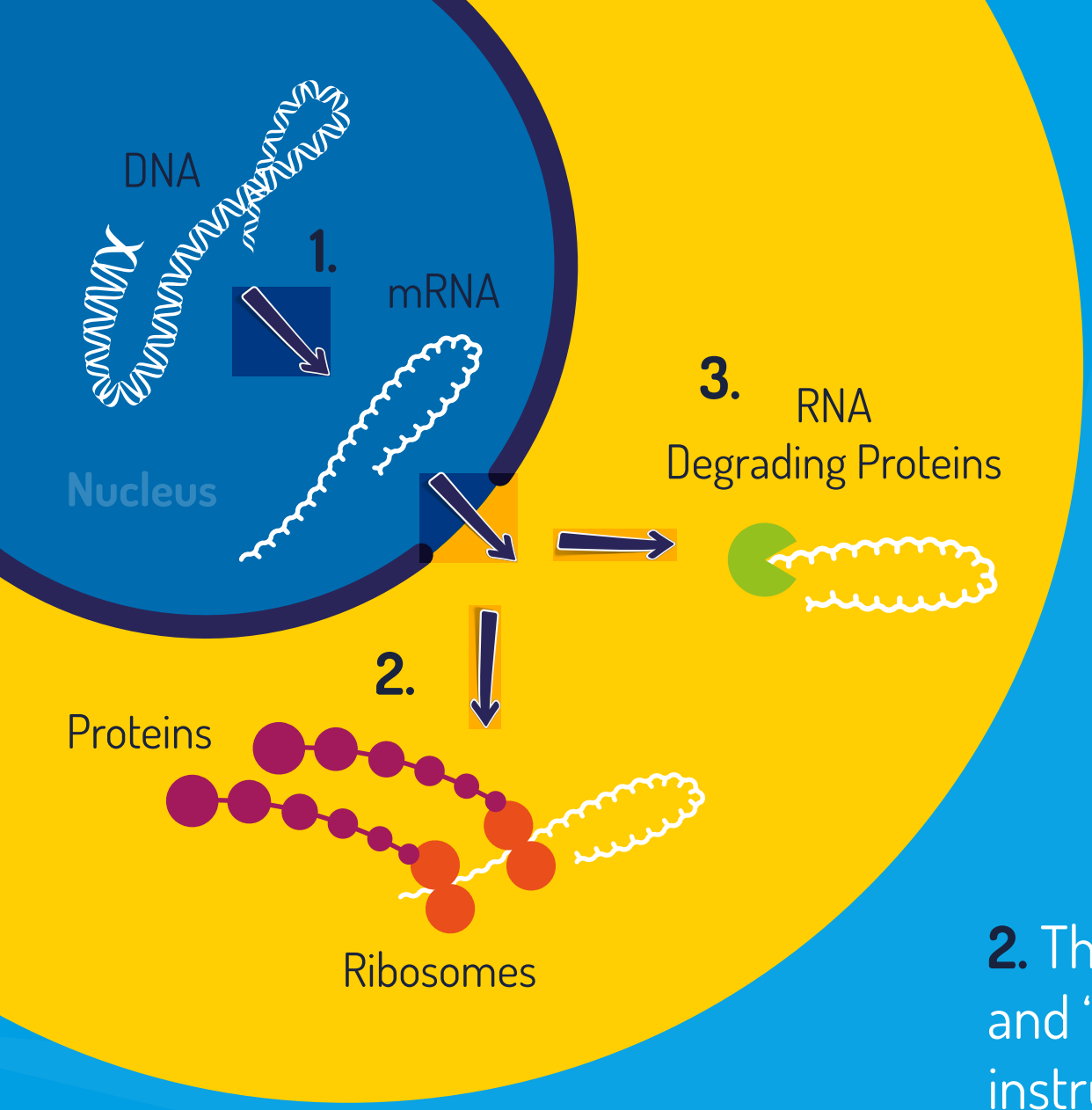
The development and function of immune cells

Our research focusses on the development and function of immune cells.

For cells to develop and carry out their jobs properly, instructions must be read and translated from our DNA.





Protein-coding genes contain the instructions to make proteins, which are involved in lots of processes including DNA synthesis, the immune cells response, cell structure and more!

The instructions are read like this:

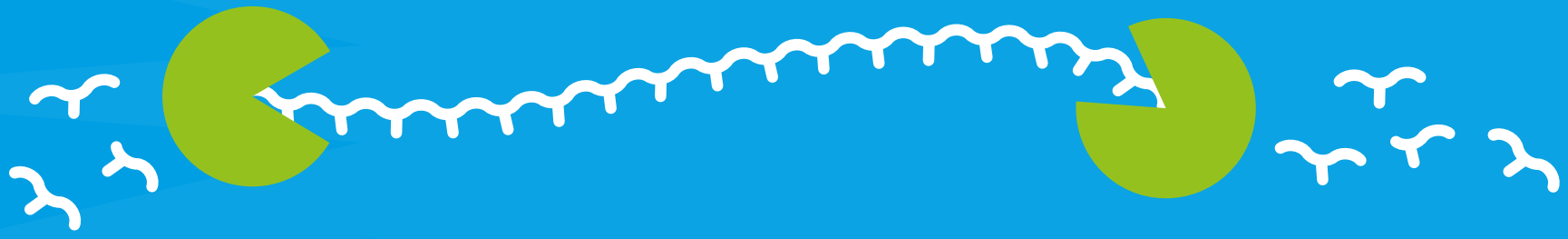
1. Information in DNA is transferred to messenger RNA (mRNA)

2. The mRNA leaves the nucleus and 'ribosomes' translate the instructions in to proteins

3. Sometimes, the mRNA is not needed and so RNA degrading proteins are recruited

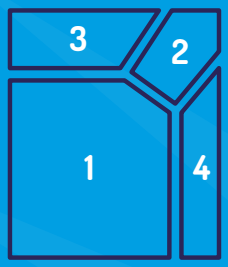
We study two RNA binding proteins called **ZFP36L1** and **ZFP36L2** which bind to the mRNA...

...and recruit the **'RNA degrading proteins'** to break up the mRNA.



To understand how important the RNA binding proteins were to immune cell development, we generated mice that don't make these proteins in their T cells or B cells.

We use markers on the surface of the cells to determine which cells we are looking at. Each dot on the plot represents an individual cell.

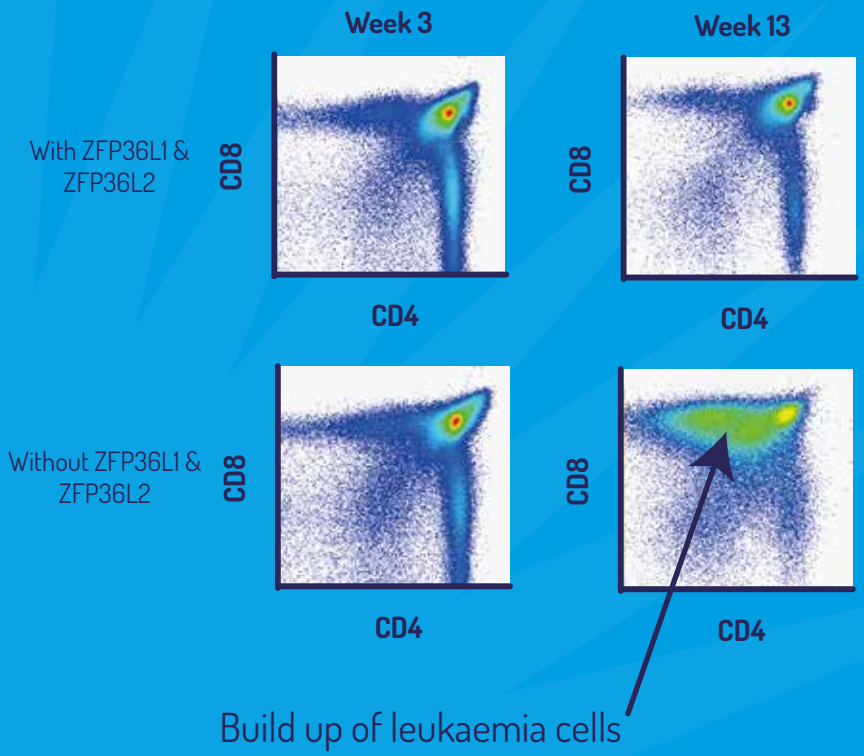


1. **Double negative cells:**
the earliest stage of T-Cell development in the thymus, make the first half of their T-Cell receptor.

2. **Double positive cells:**
later in development finish making their T-Cell receptors.

3. **CD8 single positive:**
contain immature T-Cells between the double negative and double positive stage of development as well as killer T-Cells.

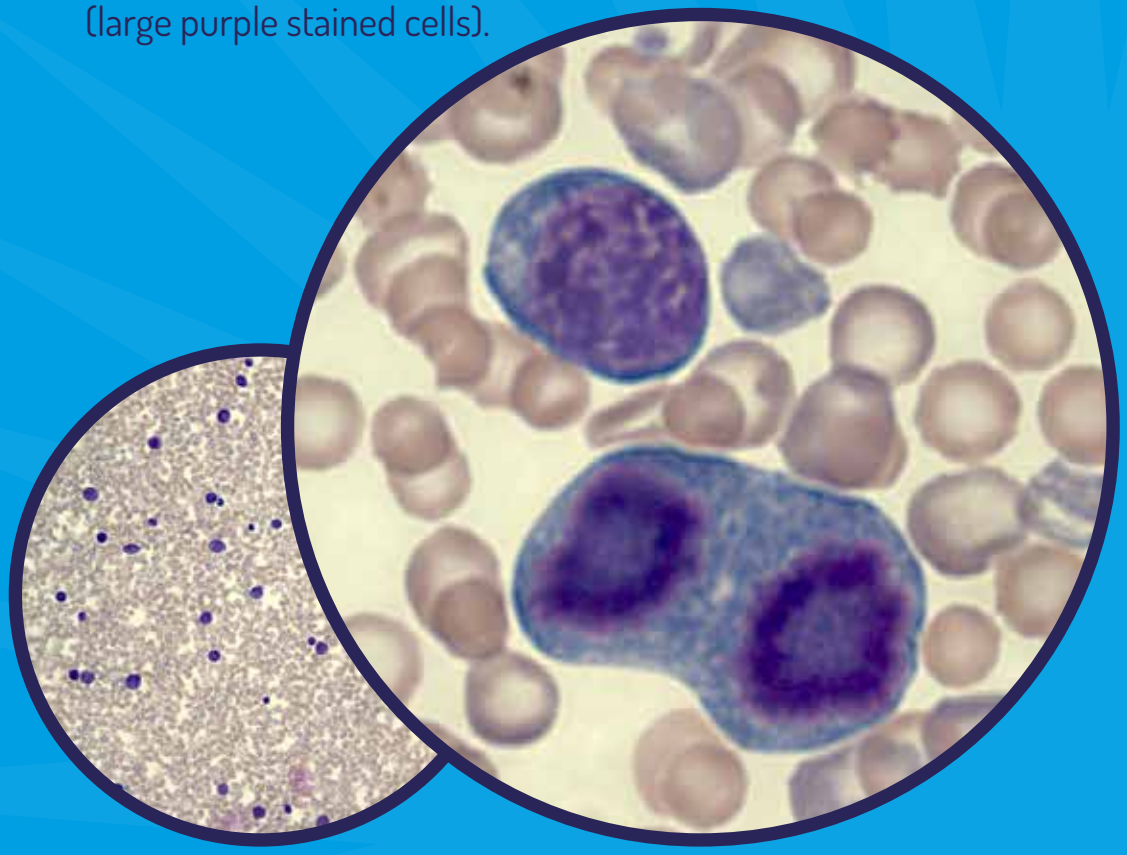
4. **CD4 single positive:**
contain the helper T-Cells.



We found that these mice developed leukaemia (cancer of white blood cells) at about 14 weeks of age.

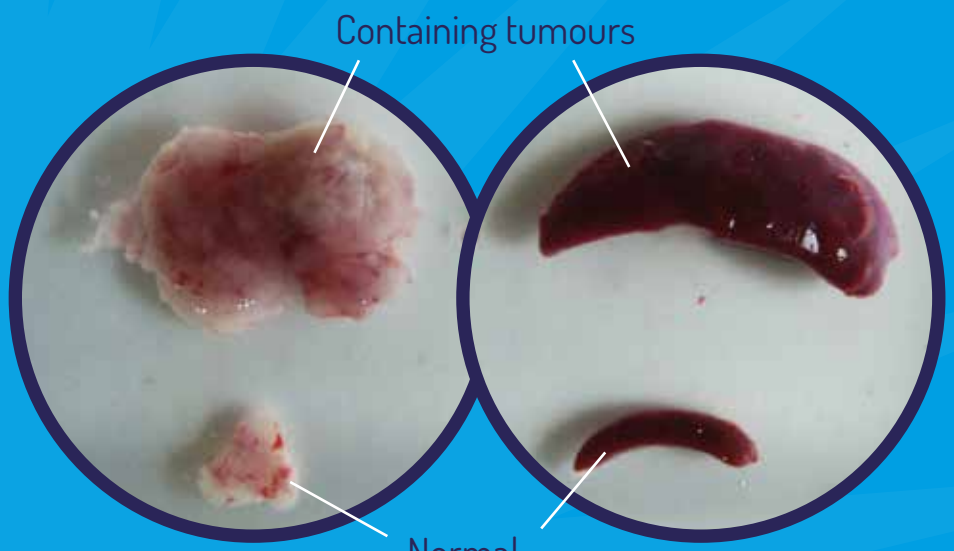
The leukaemic cells formed tumours in the thymus and spread to other immune cell organs such as the spleen and lymph nodes.

Blood smears showing leukaemic cells (large purple stained cells).



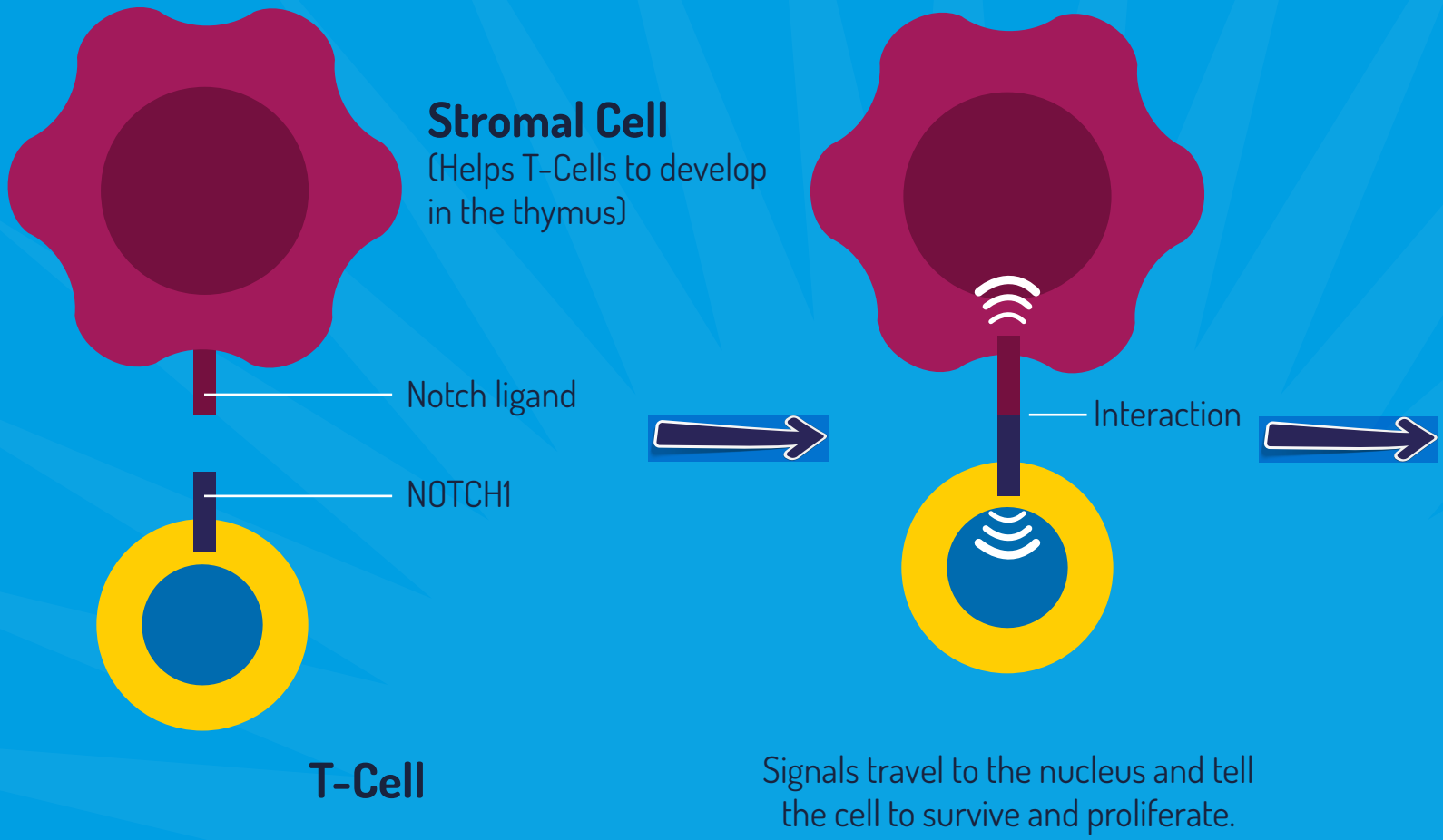
Low Magnification **High Magnification**

Images of thymus and spleen showing tumours



Thymus **Spleen**

Upon further study we found that the T cells which lacked these two RNA binding proteins had an increase in a protein called NOTCH1.



This protein is important in T-Cell development.
But, when it is over-active it can cause leukaemia.

We found that the NOTCH1 mRNA has a site where ZFP36L1 and ZFP36L2 can bind and recruit RNA degrading enzymes.

So, if ZFP36L1 and ZFP36L2 are not active during T cell development this can cause leukaemia.

This is just one mechanism by which these RNA binding proteins control immune cell development and functions. We are working to understand how these RNA binding proteins and their target mRNAs are regulated in immune cells.

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Research in the Turner Lab focuses on understanding the fundamental mechanisms that control immune cell development and function throughout the life-course.
www.babraham.ac.uk/our-research/lymphocyte/martin-turner

For more information on this research:
www.ncbi.nlm.nih.gov/pubmed/20622884