Babraham Institute Schools' Day 2015 Four Example Project Descriptions

One of the biggest decisions of your life and you're not even asked about it?
Dr Anne Corcoran

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You think you've got big decisions to make!?! How do you think your cells feel? They have to decide what type of cell they want to be and never ask you any questions! What makes a red blood cell a red blood cell and a skin cell a skin cell? By switching on different genes, a cell is able to become specialised so that it is able to perform a specific task within your body. A red blood cell will express the globin gene, but a skin cell will not. For genes to be expressed, DNA must be in the form of a double helix. But how do you get 2m of DNA in to your cell's nucleus? Also, if it is all in there in the double helix form, how do you regulate which genes are switched on and off?

Well, both of these problems are solved by tightly packaging your entire DNA so that it will fit within one of your cells. The first level of packaging is the wrapping of DNA around a group of proteins that gives it the appearance of beads on a string. This beads on a string is then further packaged by twisting so that it forms a thicker more dense structure. Think of it like twisting twine to form a rope. As well as saving space, another major function of DNA packaging is to regulate what genes can be read. By 'undoing' the packaging in specific areas around genes that are required by a cell it is possible to control the type of cell it is and the specialised function it performs.

As part of your project while working with us you will examine cells under a microscope. You will then isolate the DNA from these cells and perform an enzymatic digestion that will cut the DNA between the groups of protein that form part of the beads on a string structure. To determine if the enzymatic digestion has worked, you will separate the different sized fragments of DNA produced by using gel electrophoresis.

In Anne Corcoran's Group, we are interested in which genes are switched on and off in white blood cells that produce antibodies, which fight infection. In doing so, we hope to understand why in some people this process does not function correctly resulting in an increased risk of disease and infection.

Cutting and pasting DNA

Dr Gavin Kelsey

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This practical provides an opportunity to extract DNA and get to grips with the principles of cloning. Recombinant DNA technology has revolutionised biology and lies at the heart of the biotechnology industry. The term 'recombinant' originates from the fact that separate DNA molecules, perhaps DNA molecules from different species, can be joined together - recombined - in the test tube.

Providing these recombinant molecules carry the appropriate genetic elements, they can be introduced into and propagated in a host organism, very often the enterobacterium Escherichia coli. This process is often loosely known as molecular cloning. By expansion in cultures of the host, large amounts of the new DNA molecule can be produced for any number of procedures. Recombinant DNA technology relies critically on a variety of enzymes by which DNA molecules can be modified. These include:

- enzymes that can cut DNA at specific sites - restriction endonucleases;
- enzymes that can rejoin compatible DNA ends - DNA ligases;
- enzymes that can copy messenger RNA into a DNA strand - reverse transcriptases;
- enzymes that can copy DNA strands from a DNA template - DNA polymerases.

In this practical, the function of two of these classes of enzyme will be demonstrated: a restriction endonuclease and a DNA ligase. Briefly, a DNA molecule will be digested with a restriction endonuclease and then ligated together again. The products of these reactions will be visualised by electrophoresis through an agarose matrix. This is a simple demonstration of techniques that are fundamental to molecular biology and used in labs on a daily basis.

Identifying genetically modified organisms

Dr Jon Houseley

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In the last fifty years, we have gained the ability to manipulate the genomes of organisms from simple bacteria to up to humans. **G**enetically **m**odified **o**rganisms or GMOs have revolutionised the study of biology, allowing great leaps forward in our understanding of how life works.

The use of GMOs in research is in theory very simple – if you are interested in the function of a particular gene, create a GMO with a mutation in that gene and see what goes wrong. However, there are significant challenges in this process. For example, my lab routinely makes genetically modified yeast strains carrying mutations, but having made such strains we must ensure that the mutations are in the correct genes.

This is not simple as the genetically modified strain will only differ from an unmodified strain at a single site in the whole genome. Genomes are composed of bases, each of which represents a simple piece of information, much like a letter in a book. The yeast genome contains 12 million bases (for comparison, the complete works of Shakespeare contains about 6 million letters), so to test for the correct mutation we need a technique that can rapidly search the whole genome for the gene of interest.

We use a technique called PCR to test for genetic modifications – if you used PCR to look for a needle in a haystack it would make so many copies of the needle that you would no longer see the haystack! Having amplified the gene of interest to such an extent, it then becomes easy to tell if it has been mutated or not. In this project, the students will use PCR to differentiate yeast strains that have a particular gene mutated from those that do not.

Cells of the Immune System

Klaus Okkenhaug
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Immune cells are present to defend against infection throughout the life of an organism. We will look at the different types of immune cells present in the body, especially lymphocytes, the cells responsible for immunity to a wide range of diseases. Two types of lymphocyte, T- and B-cells, are part of the adaptive immune response. This is the part of the immune system responsible for "immune memory". These immune cells are affected by vaccination, and are present in the blood as well as in many organs of the body, such as the spleen and lymph nodes.

In this project we will look at a sample of immune cells using a microscope and determine which type of cell they are by their morphology. We will then stain the cells, using a range of fluorescently-conjugated antibodies. The stained cells will be passed through a flow cytometer, a machine that directs several lasers at the cells in order to determine their size, shape and the amount of fluorescent antibody bound by every cell.

From this data it is possible to determine some of the surface proteins expressed by the cells to carry out their function, and hence if the cells belong to the antibody-producing B-cell, killer T-cell (CD8-expressing) or helper T-cell (CD4-expressing) populations. In HIV patients, CD4-expressing T-cells are infected by the HIV; B-cells and killer T-cells form the major defence against the virus.