

# Mystery microscope images



## Equipment:

- 6X framed microscopy images
- 6X cards saying what each microscope image shows
- 6X cards with the different microscopy techniques written on them
- 6X cards with the different magnifications of the images written on them

## Audience Experience:

Participants are invited to match up six images (generated by Crick scientists using a variety of microscopy techniques) with what the image shows, the microscopy technique used and the magnification.

The activity can be made easier or harder by withholding info (e.g. what the image shows or the techniques used).

## Hooks:

We've got six amazing images here made by Crick scientists. Can you figure out what they are, and what type of microscope was used to capture them?

The Crick uses state-of-the-art microscopy techniques to generate images that are really useful in research. Can you figure out what these six images are?

## Key messages:

The invention of the microscope has opened up a whole new world to science - a world too small for our eyes to see. By using microscopes scientists have discovered the existence of microorganisms, studied the structure of cells, and seen the smallest parts of plants, animals and fungi.

Today, scientists at the Crick are using a number of state-of-the-art microscopy techniques to investigate everything from cancer to developmental biology and infectious disease.

## The images:



## Image 1:

### Guess what?

Compound eye of the fruit fly

### Guess how?

Scanning electron microscopy

**Magnification:** 4,600x

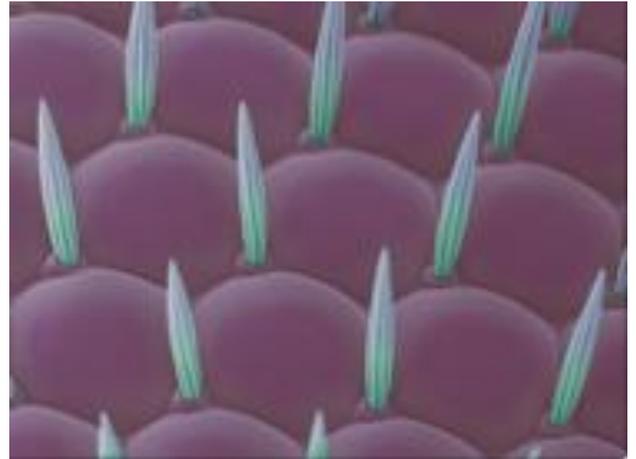


Photo credit: Anne Weston

### Extra info:

#### What the image shows:

What you can see is a part of the compound eye from a wild type fruit fly (or *Drosophila melanogaster*). The wild type has not been genetically altered or drug treated in any way so is a good example of what a normal healthy fly's eye should look like.

The compound eye of *Drosophila* is composed of many optical units called ommatidia. Each hexagonal structure (purple) is a single ommatidium. The hair-like structures (turquoise) are called setae and it is thought that these may help to reduce glare. The image is about 50 micrometres in length.

#### What it tells:

*Drosophila* are very important in research. They are used extensively in genetic research due to about 75% of known human genes having a recognizable match in the genome of a fruit fly.

Having standard wild type images is important when looking at how drugs or genetic modifications affect organisms. The appearance, shape and structure (morphology) of the eye of *Drosophila* can be affected by any genetic modifications. By looking at a wild type specimen this is a base-line to which one can compare the outcomes of various experiments.

#### How it was made:

The image was captured using a Scanning Electron Microscope and has been false coloured using Adobe Photoshop post-acquisition.

The Crick has an electron microscopy Science Technology Platform, which provides an EM service to the institute's labs and is where Anne Weston works. It does not carry out research on *Drosophila* but images the flies on behalf of some of the labs that do.



## Image 2:

**Guess what?**  
A dying cell

**Guess how?**  
Confocal microscopy

**Magnification:** 4,200x

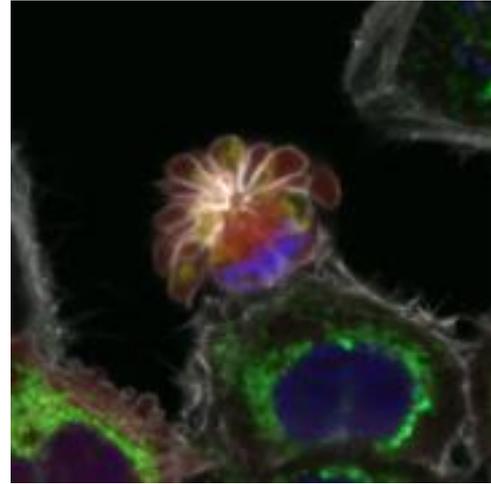


Photo credit: Anna Dowbaj

### Extra info:

#### What the image shows:

The image shows a dying HeLa cell, amongst other healthy cells. HeLa cells originate from the cervical cancer tumour of a patient named Henrietta Lacks in the 1950s. They were the first type of human cells to be successfully grown, and kept alive, in the laboratory. They are now the most widely used human cell line in biomedical research.

Here, the cell's DNA is shown in blue, the white is actin cytoskeleton and the green is mitochondria. Components of the signalling pathway of interest are labelled with mCherry fluorescent protein, which shows up red. The image is about 55 micrometres in length.

#### What it tells:

The Francis Crick Institute is interested in understanding cell signalling pathways in tumours. Often cancerous cells will exploit pathways involved in cell growth, metabolism, immune suppression and cell survival. This image is part of a set of images that Anna took while studying protein signalling between tumours and the tissue microenvironment.

#### How it was made:

The cells were fixed and stained with immunofluorescence dyes, before being imaged under a confocal microscope.



### Image 3:

**Guess what?**  
The head of a mouse embryo

**Guess how?**

High resolution episcopic microscopy

**Magnification: 50x**

**What the image shows:**

The image shows a horizontal slice through the head of a mouse embryo. When this image was taken at 14.5 days gestation, the embryo was just over a centimetre long (from head to rump).

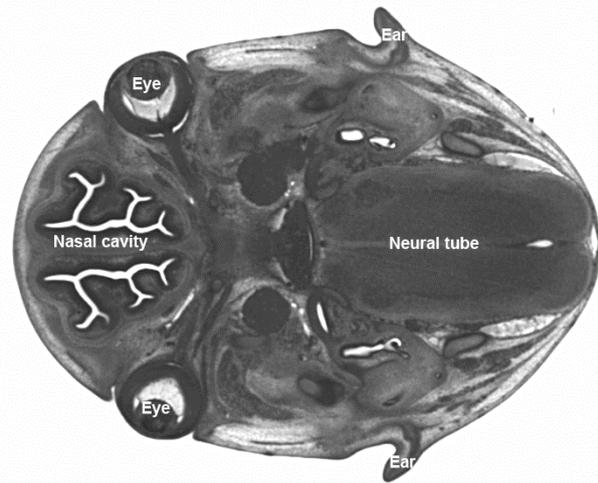


Photo credit: Mohun Lab, DMDD Collaboration

In the image you can see a cross section of the eyes, ears, nasal cavity and the neural tube. The neural tube is the structure inside an embryo that eventually develops into the central nervous system (the brain and spinal cord). The head is about 50 millimetres in length.

**What it tells:**

Although we look very different, humans and mice have around 95% of their genome in common and can develop similar diseases. This means that the results of genetic research with mice often gives us valuable information about human genetic diseases.

The DMDD programme at the Francis Crick Institute studies mice where an individual gene has been deleted from their genome and, as a result, the embryos do not survive to be born. The programme looks at the effects of the gene deletion on their growth, appearance and internal organs. By studying high-resolution images of the embryos and their placentas, any abnormal features of the embryo can be identified. These abnormalities give insights into the role that the missing gene would normally play in the development of the mouse.

By studying many different gene deletions in mice, the programme hopes to gain clues about how different genes could contribute to diseases affecting human development.

This mouse is called a 'wild-type'. It didn't have any genes removed from its genome, and it is used as a control against which to compare the development of mice that have had a gene removed.

**How it was made:**

The image was generated via a technique called High Resolution Episcopic Microscopy, which allows us to see the structure of organs and tissue in incredible detail, despite the tiny size of the embryo. The technique was invented by Tim Mohun (who leads the DMDD programme) in 2006.



## Image 4:

**Guess what?**  
Optic nerve entering the retina

**Guess how?**  
Confocal microscopy

**Magnification: 720x**

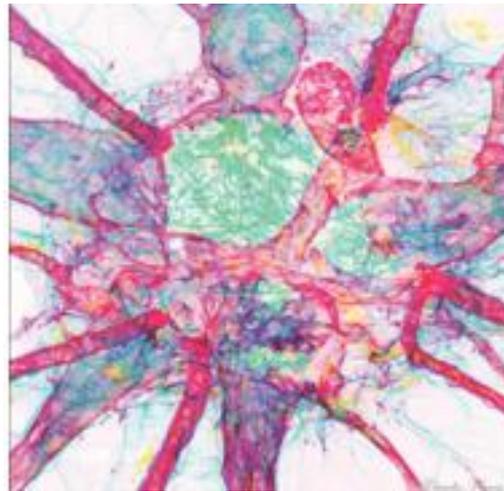


Photo credit: Claudio Areias Franco

### Extra info:

### What the image shows:

This image was taken at the point where the optic nerve meets the retina of a six day old mouse. It shows blood vessels surrounding the optic nerve, which actually enter the retina through it.

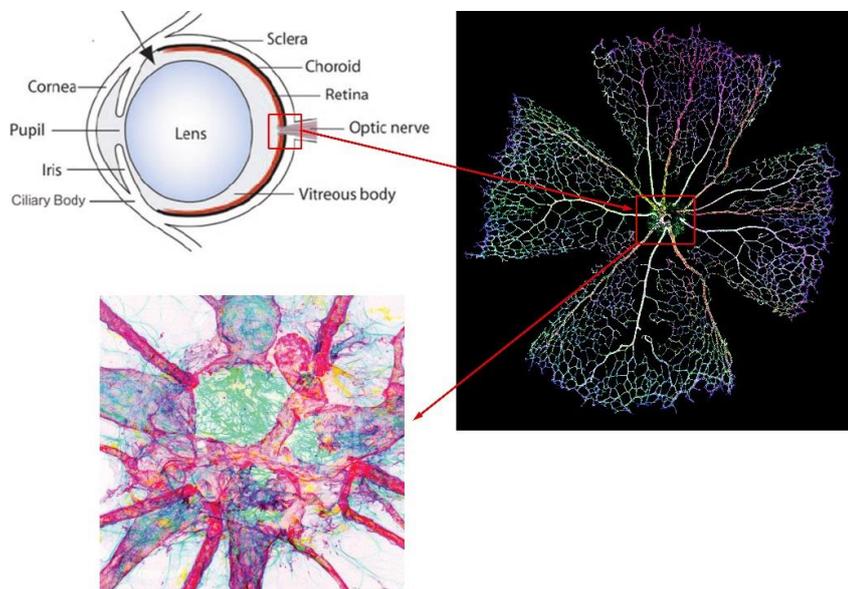
The blood vessels are shown in red, the optic nerve stem in green, and endothelial cells in yellow. The image is about 320 micrometres across.

### What it tells:

The Crick is interested in understanding how neurons in the visual system develop and form a circuit, but in Claudio's own words: 'In terms of usefulness, [the image] was not useful at all. I just took this picture because I found it was pretty!'

### How it was made:

The sample was stained with fluorescent markers, before being imaged under a confocal microscope. Claudio inverted the colours and played with the contrast to generate the final image.





## Image 5:

**Guess what?**  
Influenza virus fusing with liposomes

**Guess how?**

Cryo electron microscopy

**Magnification:** 3,750,000x

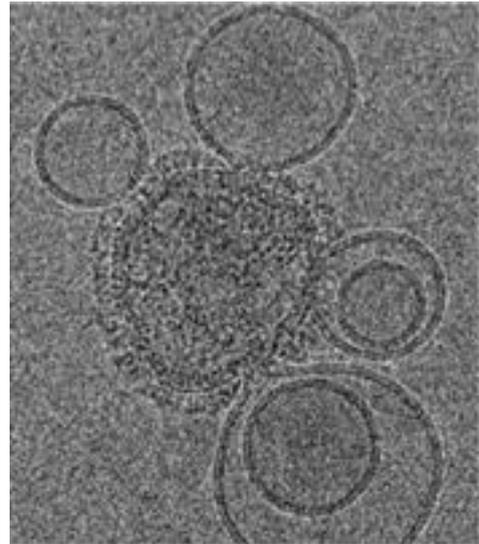


Image credit: Lesley Calder and Peter Rosenthal

**Extra info:**

**What the image shows:**

The image shows influenza virus (in the middle), covered with protein spikes, fusing with spherical objects called liposomes. The liposomes are spheres made of bilayer membranes, such as the membranes that surround mammalian cells, but liposomes are much smaller than cells.

The virus is about 1200 Å (or 120 nanometers) in diameter, and the spikes on the surface (the hemagglutinin protein) are about 135 Å. The magnification is higher than the typical magnification achieved by cryo-EM because the image was enlarged when printed.

**What it tells:**

Influenza virus is surrounded by a membrane, and when it infects a cell it must attach to the target cell membrane and then fuse with it. The fusion event usually happens in membrane compartments within the cell after the virus has been engulfed by the host cell membrane). Here the liposomes are used as simple models for how the virus interacts with cell membranes. Such images tell us how the proteins in the virus membrane mediate the fusion event that is an essential step in entry.

**How it was made:**

The technique used is cryo electron microscopy. The specimen is rapidly plunge-frozen, so fast that ice crystals cannot form, and then imaged using electrons in this frozen state. Electron microscopes allow one to see much smaller features than from light microscopes. However, low electron exposures are used to prevent damage to the structures of interest during imaging.



## Image 6:

**Guess what?**  
Fruit fly embryo

**Guess how?**  
Confocal microscopy

**Magnification:** 460x

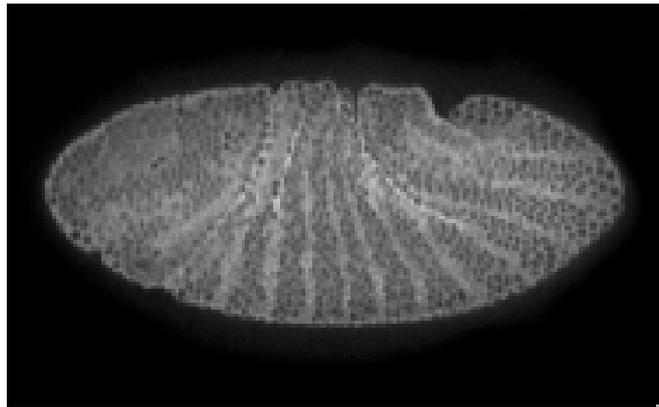


Image credit: Sam Crossman

### Extra info:

#### What the image shows

This image shows a 5-hour old fruit fly embryo that has been stained to reveal the outline of each of its cells. This approach also highlights a pattern of repeating stripes. The cells in these stripes express a gene that helps form the segments that make up the body of the adult insect. A single fruit fly embryo is around half a millimeter in length.

#### What it tells

Embryonic development is a vastly complex process and we still know relatively little about the mechanisms that transform a single fertilised egg into a fully-grown animal with billions of cells. One of the fundamental problems of biology is understanding how seemingly identical cells in the embryo go on to form the various tissues that make a fully developed organism

Questions like this are hard to answer by studying humans, so we aim to understand how smaller and more simple animals like the fruit fly manage these tasks. Remarkably, many of the genes involved in the formation of segments in insects perform important roles in humans; meaning studies on these simple systems can reveal new insights into human health and development.

#### How it was made

Embryos are collected on plates of grape juice jelly before they are harvested and stained to reveal the location of the gene of interest. These are then transferred to a glass slide and imaged with a confocal microscope at 100x magnification.