Molecular cell recognition - putting the brain in order

Drosophila melanogaster fruit flies are often found in droves in the kitchen. This annoys some people, but not others. The neurogeneticists in the group of Professor Karl-Friedrich Fischbach at the University of Freiburg actually quite like the small flies because they enable the development of the brain to be looked into closely. The scientists are investigating how the complex optical areas of the brain are organised.

"The fruit fly navigates around a room without ever colliding with anything," said Karl-Friedrich Fischbach from the Institute of Biology III at the University of Freiburg. "The flies behave rather intelligently."

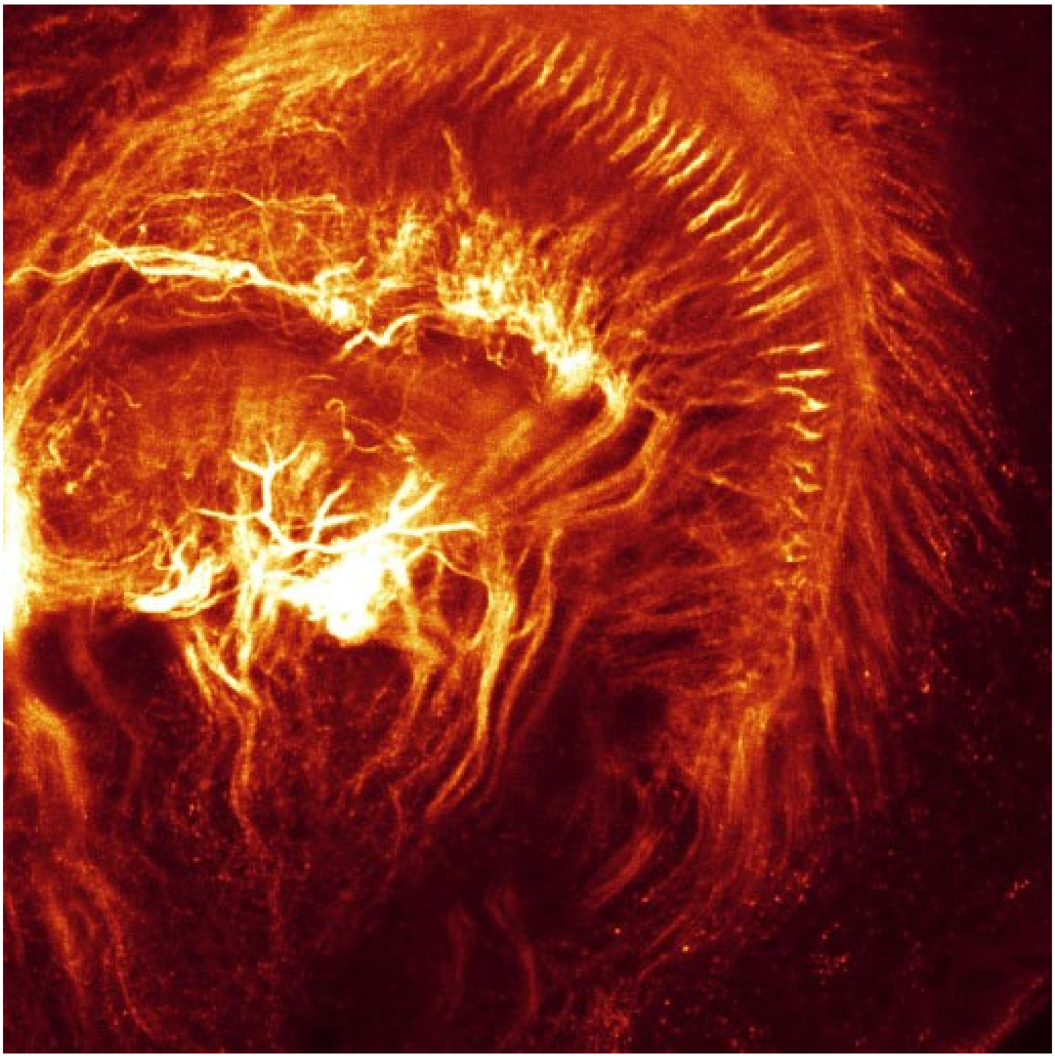
Cross section of a Drosophila melanogaster brain (Figure: www.flybrain.org)

The brain of fruit flies is a lot smaller than the human brain and also looks quite different. But human and fly brains also have some things in common, for example in the brain areas that mediate vision. Human and fly optical areas have a visuotopic organisation.

Neurons originating from the eye and transmitting information from neighbouring areas of the field of vision, also innervate neighbouring areas in the optical area. In addition, in both humans and flies, individual cell layers have different functions. In flies, the nerve cells that code the vertical movements (upwards and downwards) of objects, form their synapses in layers different from those required for coding horizontal movements (forward or backward).

In Drosophila, these highly ordered neural networks are fully developed when the flies emerge. The axons of nerves, which are located in the individual ommatidia of the complex fly eye, migrate and move towards their target, thereby crossing several cell layers. "But how do they recognise this target?" asks Fischbach and also, "How do they know when they have reached their target region and which cells they have to attach to?"

A group of molecules used to recognise the final destination



The inner chiasm in the brain of a fruit fly larva (Figure: www.flybrain.org)

When looking for genes, the mutated versions of which lead to mistakes in the organisation of the brain, Fischbach and his colleagues identified the gene irregular chiasm C (irreC) more than 10 years ago. A mutated irreC gene leads to malformations in those regions of the optical area that are referred to as outer and inner chiasms. The axons from the eyes find their cell targets in the lower brain regions via detours.

The neurogeneticists then found out that the irreC-encoded protein is a member of the immunoglobulin family. It thus resembles the antibodies of the immune system that appear to have the same precursor molecules. IrreC has a sister molecule, the protein Kirre. Both proteins are located in the membrane of axon endings, extend into the extracellular space and can bind defined proteins on the surface of other cells. “That is how the growing axons recognise their target cells,” said Fischbach. The scientists also found the protein partners on the membranes, which are bound by IrreC and Kirre. These proteins are also part of the immunoglobulin family and fit with IrreC and Kirre like a key and a lock. Since these proteins form a functional unit, Fischbach and his colleagues decided to call the entire group “irre cell recognition module” (IRM).

A universal principle

The scientists have also identified IrreC and the other proteins in other tissues, for example in embryonic muscle founders and fusion-competent myoblasts involved in the development of Drosophila muscles. The IRM proteins make sure that the two cell types find each other and merge into multinuclear muscle cells. The proteins also play an important role in the compound fly eye. Without the IRM proteins, the ommatidia do not arrange in the order they should, instead orienting their axis in all kinds of directions. Only when the outer cells of the ommatidia and the surrounding interommatidial cells recognise each other by way of IRM proteins and bind permanently, will this lead to a fixed order.

In evolutionary terms, the IRM is not only found in the fruit fly. Independently from Fischbach’s group of researchers, the Freiburg physicians, Gerd Walz and Thomas Benzing, discovered this class of molecules in the cells of human kidneys. Caenorhabditis elegans and mice brain also express IRM proteins. “It seems likely that these proteins have similar functions to those in the fruit fly,” said Fischbach who hopes to investigate further details of the functions of these proteins using Drosophila. Fischbach and his colleagues are interested in the role of the IRM in the formation of synapses in the optical area of the brain. New genetic methods enable the scientists to switch on and off particular IRM genes in the nerve cells. Modern staining techniques can then be used to observe what then happens in individual or groups of neurons.

mn - 9th April 2008

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Article

14-Apr-2008
BioRegion Freiburg