Max-Planck-Institut für Neurobiologie

Navigational aid for growing nerve cells

A protein governs the growth of nerve cells and guides them to their target

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The human brain consists of a hundred billion nerve cells, each of which makes thousands of connections with other cells. In all of this, how do nerve fibers know where to grow and when to establish a contact? Scientists at the Max Planck Institute of Neurobiology in Martinsried now found a protein that guides growing nerve cells in the eye of the fruit fly. In addition, the protein also acts as spacer between neighboring nerve cells. Similar mechanisms could also play a role in the development of the vertebrate nervous system.

Finding your way in a large and unknown city without the aid of a navigational device or a fellow passenger is tough: each intersection requires a new decision on the right way to go, while at the same time dozens of traffic rules need to be observed and collisions to be omitted. In a very similar situation are young nerve cells, when they try to find their way in their "megacity", the brain. In a vast tangle of other cells, growing nerve cells have to decide at numerous points in which direction to continue in order to find the cell they need to contact. To make this task even more difficult, thousands of other nerve cells have the same aim and project their cell extensions (axons) towards their partner cells. Unwanted collisions between these cells could thus quickly lead to a "traffic jam" with severe consequences: functional impairment is often the result when a nerve cell is unable to contact its partner cell.

What guides a nerve cell to its target?

In order to answer this question, scientists of the Max Planck Institute of Neurobiology took a closer look at the eye development of the fruit fly *Drosophila*. The eye of the fruit fly is especially suited for such research: It is much simpler than that of a vertebrate and thus easier to study. At the same time, it is complex enough to elucidate the general mechanisms responsible for neuronal path-finding. Another benefit of choosing the fruit fly is that a wide variety of genetic tools are available. This enables scientists for example to alter genes specific to the development of the eye while all other nerves remain untouched. And this is exactly what the neurobiologists have done: they specifically disabled a gene in the fly eye and found its product, the protein Gogo (Golden Goal), which not only functions as a navigational aid for growing nerve cells, but also maintains the spacing between neighboring cells.

Truly a complex eye

The compound eye of the fruit fly consists of 800 independent photoreception units, each of which contains eight photoreceptor cells. These specialized nerve cells convert light into electrical signals which are transported to the brain. The axon of each receptor cell grows during the eye's development towards the next site of neuronal processing, the lamina (Figure 1). Parallel growth of the eight axons results in the formation of the visual rod in the center of each photoreceptor unit. Reaching the lamina, two of the eight axons continue to grow to the next brain layer, the medulla. On their way to the medulla, the visual pathways cross each other, resulting in a rotation of 180° of the original picture. The Max Planck scientists now showed how nerve cells find their correct partner cells in this complex growth pattern: The protein Gogo is located in the membrane right at the tip of the growing axon. In the absence of Gogo due to genetic manipulation, cells are unable to maintain their parallel growth – they collide and clump together and the visual rod cannot form. In addition, the two axons that continue to grow towards the medulla are unable to find their partner cell – they stray before or overshoot their correct target layer (Figure 2). It is thus clear: the fly eye cannot develop correctly without Gogo.

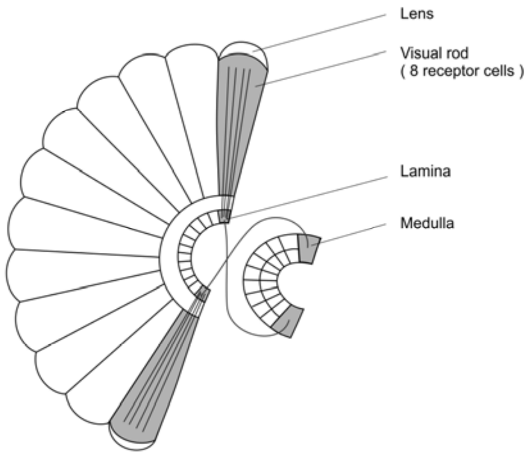

Figure 1: Nerve connections in the fly eye

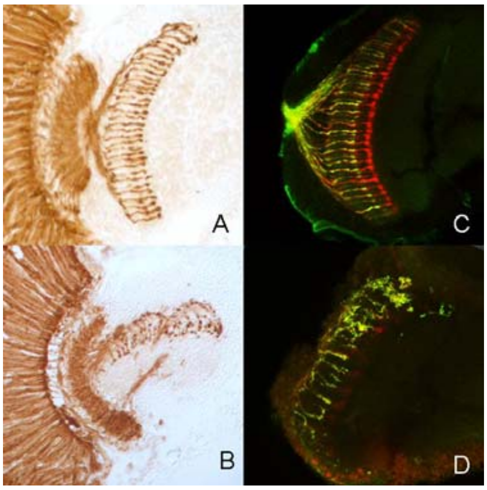

Figure 2: A protein with great impact. The comparisons show quite vividly that the orderly axonal growth (A & C) cannot be maintained without the navigational guiding of the protein Gogo (B & D)

Navigational aid also for other nerve systems?

"Based on the genetic and cell biological evidences, we assume that Gogo is a receptor protein, whose binding to its signal molecules leads to an attraction or repulsion of the axons", explains Takashi Suzuki who supervised the study. Other signal molecules probably enable Gogo to aid the nerve cell to its correct partner cell in the medulla. It is likely that other receptor proteins and their signal molecules also play a role in guiding the axons; however, there are probably less than ten, assumes Suzuki. "If we understand the combination and function of these molecules we hope to understand the development of the whole system." Many of the genes found in the fruit fly play also a role in the development of nervous systems in other organisms. The insights into the development of the eye of the fruit fly are therefore also important to understand our own nervous system.

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Tatiana Tomasi, Satoko Hakeda-Suzuki, Stephan Ohler, Alexander Schleiffer, Takashi Suzuki
The transmembrane protein Golden Goal regulates R8 photoreceptor axon-axon and axon-target interactions
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