C-Fos Got Your Back!

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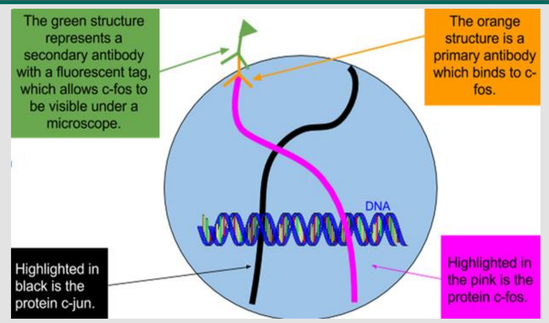
I. A Little C-Fos in a Big World

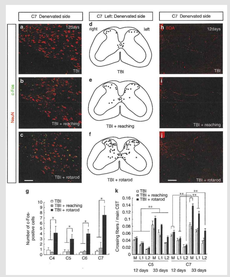
Every day, we take for granted activities like walking, talking, and climbing steps. Basic movements in the human body require the use of the spinal cord. However, when the spine is injured, all bodily movement is limited beyond the point of injury, making these simple tasks impossible. When other parts of the body are injured, new cells are generated to replace the damaged cells. On the other hand, the spinal cord is strikingly different because nerve cells don't regenerate, making the process of rehabilitating injured spines complex and nearly impossible. This is even more drastic when we take into account that the spine is a part of the central nervous system, controlled directly from the motor cortex in the brain, and if it does not function properly, there can be major repercussions in terms of movement elsewhere in the body. That is where a transcription factor known as C-fos becomes important. Transcription factors are proteins that are involved in the process of transcribing DNA into RNA. C-fos is a specific transcription factor that is present at higher levels when neurons are active. The presence of C-fos allows scientists to see the active neurons and assess the potential for rehabilitation.

II. Immunohistochemistry



Primary antibodies, specifically designed to attach to c-fos, are put in the cell. Since these are still too difficult to see, secondary antibodies designed to attach to the primary antibodies are coupled with the primary antibodies. These secondary antibodies give a fluorescent color anywhere c-fos is present, allowing us to locate the protein using a microscope and determine c-fos activity levels under certain test conditions.Primary antibodies, specifically designed to attach to c-fos, are put in the cell. Since these are still too difficult to see, secondary antibodies designed to attach to the primary antibodies are coupled with the primary antibodies. These secondary antibodies give a fluorescent color anywhere c-fos is present, allowing us to locate the protein using a microscope and determine c-fos activity levels under certain test conditions.

III. Neuron Activity 101



C-fos is a transcription factor that needs a partner such as c-jun in order to work; however, we look specifically at c-fos in cells beyond the injury site. This is done because c-fos is expressed more specifically when active neurons are growing to make more connections, allowing this transcription factor to act as an indicator of activity important for rehabilitation.

C-Fos Interactions

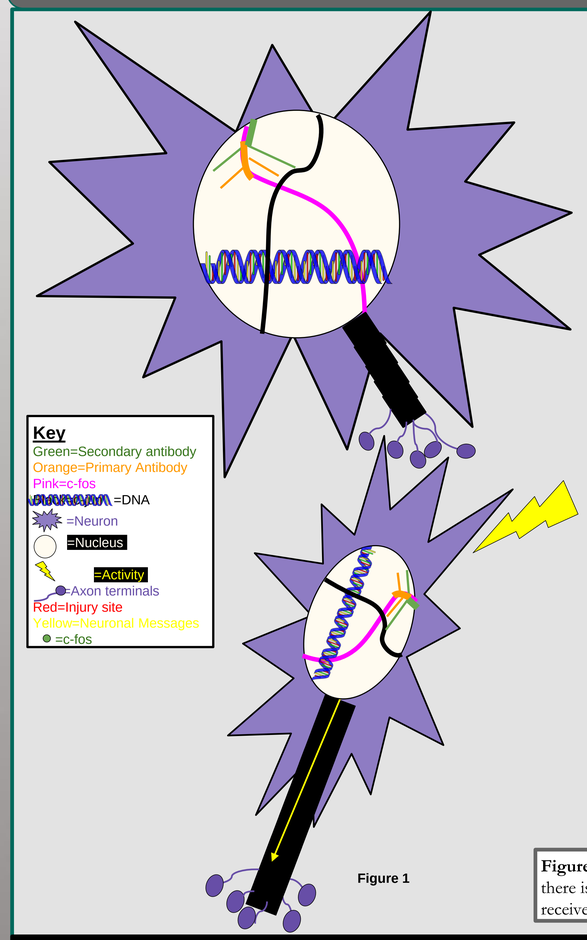


Figure 1

Figure 1 shows an active neuron interacting with another neuron. When there is no damage to the neuron then messages can be sent and received.

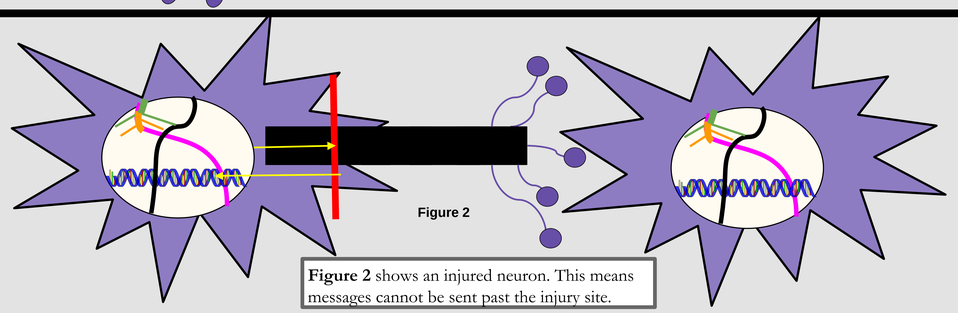


Figure 2

Figure 2 shows an injured neuron. This means messages cannot be sent past the injury site.

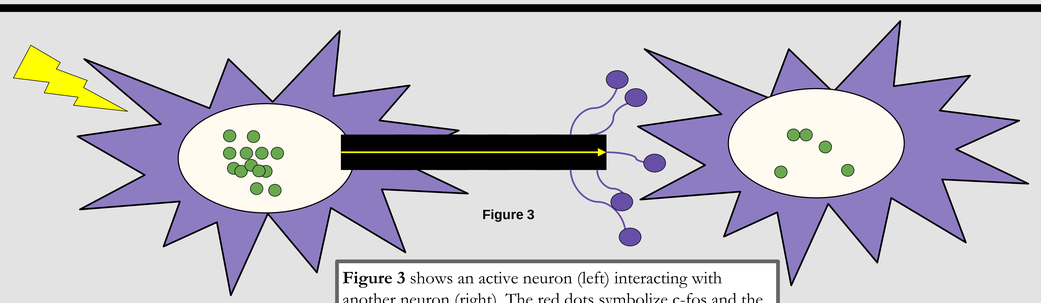
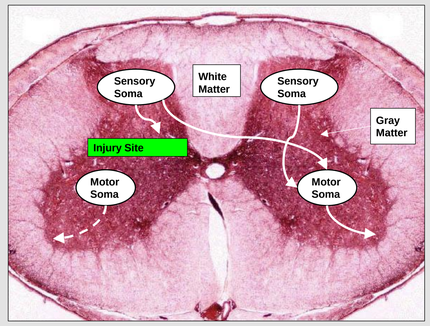


Figure 3

Figure 3 shows an active neuron (left) interacting with another neuron (right). The red dots symbolize c-fos and the heightened expression of c-fos is shown in the active neuron.

Figure 4 (Nakagawa, 2013)**:** This is an image of the model of c-fos. Shown in a darker gray is c-jun and shown in a coral is c-fos. The active site is shown by the teal colored portion on the helix. The bonds are shown in an orange and the green circles represent important amino acids. PDB Number: 1FOS

IV. A Step Towards Neuronal Rewiring



This is a transverse cross section of the lumbar portion of the human spinal cord. C-fos works in neurons in the central nervous system, which includes the spinal cord and the brain. It is a transcription factor that works in conjunction with another transcription factor (such as c-jun) to regulate the production of several proteins. Increased c-fos levels are indicative of neuronal activity because it is only expressed when the cell is active. In active cells, c-fos is differentially expressed and is expressed at a higher level when the cell is active. Normally when the spinal cord is injured information cannot be sent past the injury site (from the sensory soma to the motor soma). Therefore, with the use of extensive therapy signals are sent across the cord in an attempt to relay messages past the injury site. C-fos then becomes useful as it can be used to assess whether therapy has been successful or not.

V. More Than a Transcription Factor

C-fos has been classified as a basic transcription factor that details the activity of cells; our study specifically focused in on neuronal cells. The expression of c-fos is an indirect marker because it is expressed when neurons fire action potentials. The current research on how c-fos behaves lays the foundation for our knowledge regarding the recovery of neural cells. Application to the real world can be seen through how c-fos interacts with other factors, how regenerating axons make synaptic connections, and how using c-fos grants us the ability to identify postsynaptic cells. Building on the foundation of our knowledge could allow us the development pharmaceutical drugs to treat spinal diseases and comprehend the mystery of the human body a little bit better.

VI. References

Primary Citation: Glover, J. N. M. & Harrison. (1995). Crystal structure of the heterodimeric bZIP transcription factor c-Fos–c-Jun bound to DNA. *Nature* 373: 257-261.

Secondary Citation: Nakagawa, H., Ueno, M., Itokazu, T., Yamashita, T. (2013) Bilateral movement training promotes axonal remodeling of the corticospinal tract and recovery of motor function following traumatic brain injury in mice. *Cell Death and Disease 4*, 5. doi:10.1038/cddis.2013.62

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