Geneticists study how individual nerve cells assemble into specific nerves

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(Medical Xpress)—Geneticists from Trinity College Dublin interested in 'reverse engineering' the nervous system have made an important discovery with wider implications for repairing missing or broken links. They found that the same molecular switches that induce originally non-descript cells to specialise into the billions of unique nerve cell types are also responsible for making these nerve cells respond differently to the environment.

The geneticists are beginning to understand how these molecular switches, called 'transcription factors', turn on specific cellular labels to form complex bundles of nerves. These bundles function to ensure we respond and react appropriately to the incredible amount of information our brains encounter. Understanding how to precisely program nerve cells could help to target missing or broken links following serious injury or the onset of degenerative diseases such as Alzheimer's or Parkinson's.

Commenting on the importance and wider implications of this discovery, Assistant Professor in Genetics at Trinity, Juan Pablo Labrador said: "We know very little of how individual nerve cells are programmed to assemble into specific nerves in living organisms to make specific circuits, so our work is like reverse engineering the nervous system."

"To restore damaged or missing connections in the nervous system – for example, after spinal cord injuries or degenerative diseases such as Alzheimer's or Parkinson's – we need to know how nerve cells are programmed to make those connections in the first place. For that we

require a complex 'builder's manual' that tells us how to program the neurons to make the connections. What we are doing in my lab is trying to write this manual."

The nervous system can be thought of as an incredibly complex network of wires, which are all arranged into different, related bundles to coordinate complex tasks. The wires are the cellular extensions from the individual nerve cells that assemble into bundles to form specific nerves. The geneticists have begun to understand how varied combinations of transcription factors work to generate different nerve cells and direct their wiring to form specific nerves.

By studying the behaviour of individual nerve cells that make connections with muscles, the geneticists discovered specific 'footprints' of labels that induced these nerve cells to assemble into specific bundles that link to their target muscles. Individual transcription factors are only able to turn on specific labels to some extent. It is only the action of all of them together that programmes the nerve cells to turn on all the labels required.

The research was just published in the high-profile journal *Neuron*. The team led by Assistant Professor Juan Pablo Labrador, found that the actions of the transcription factor influencing nerve cell differentiation in flies ('Eve') controls nerve cell surface labels.

The team also showed that if these labels, targeted by Eve, are expressed erroneously, the nerve cells will not form the correct nerves. Additionally, the team discovered that different combinations of transcription factors including Eve work as codes for different groups of labels that guide individual nerve development.

More information: "A Transcription Factor Network Coordinates Attraction, Repulsion, and Adhesion Combinatorially to Control Motor

Axon Pathway Selection." Aref Arzan Zarin, Jamshid Asadzadeh, Karsten Hokamp, Daniel McCartney, Long Yang, Greg J. Bashaw, Juan-Pablo Labrador. *Neuron* - 20 February 2014 DOI: 10.1016/j.neuron.2014.01.038