For discussion purposes with qualified bioinformatics professionals, the document affixed to this article is provided to address CT1 activities.

https://medicalxpress.com/news/2019-04-multitasking-nerve-cell-individual-cells.html

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Multitasking with perfection: Nerve cell works like 1400 individual cells

by Max Planck Society

CT1 is different. In general, a nerve cell receives input from a number of presynaptic cells, processes the signals, and passes its output to downstream cells. In the cell CT1, however, each of the approximately 1400 cell areas works like a separate neuron. This allows CT1 to access information from all facets of the fly's complex eye and to contribute locally to the calculation of motion direction. Using a computer model of the cell, Alexander Borst and Matthias Meier from the Max Planck Institute of Neurobiology show that CT1 is reaching biophysical limits.

"That's an amazing cell!" This was the first impression of Alexander Borst, as Matthias Meier showed him the results. Together, the two neurobiologists have demonstrated what is also suspected for amacrine cells in the mammalian retina: It is possible that numerous isolated microcircuits exist in a single nerve cell.

Borst and Meier investigate the visual system of fruit flies, whose complex eyes each consist of about 700 facets. CT1 contacts each of the cell columns that connect to these facets in the brain. In addition, the synapses of CT1 reach into two different brain regions, responsible for the processing of light or dark edges. Thus, CT1 connects to about 1400 areas in the fly brain. This, however, should corrupt the whole system. Each cell column processes changes in light perceived by "their" facet. If the signals of the columns were mixed, the entire image information for downstream cells would be lost.

As flies see very well, a loss of image information does not seem to be an issue. The two neurobiologists could show that each contact area of CT1 is an electrically isolated, independent functional unit. Each of these units receives input from its associated column and returns its output to the same column. Calcium measurements and computer modelling show that essentially there is no cross-talk between neighboring units or with the cell body.

For the cell units to be electrically isolated from each other, their connections should be thin and long, which increases the electrical resistance. CT1 achieves this with connections of merely 100 nanometers in diameter. In addition, the "connection cables" often form loops. In this way, the connections between neighboring units are about ten

times longer than needed to bridge the distance. "It wouldn't be possible for the connections to get much thinner or longer in the fly brain," says Borst.

Why CT1 is so different from most other cells is still a mystery. "It saves cell bodies, but that is certainly not the only reason", muses Matthias Meier. "If that was the case, such huge amacrine cells wouldn't be so rare." So far, only very few cells are known with such a structure. Amongst them, CT1 is an extreme example, of which only two cells exist in a fly brain, one per hemisphere.

The scientists are also not yet sure about the exact functions of CT1. The output of the CT1 subunits goes to T4 or T5 cells, depending on their location. These calculate the direction of images moving in front of the fly's eye. Interestingly, CT1 cells specifically target the motion-sensitive T4 and T5 cells only on one-half of their dendrites. How CT1 thereby affects motion vision is one of the next questions the Max Planck neurobiologists want to investigate.

MCFIP - Epigenetic modeling will identify three forms of Cardiotrophin exist; i.e. CFT1 - 3. While minimal research exists to identify the amino acid constituents, quantum biology modeling identifies phenylalanine - tyrosine and tryptophan as being the near certain configuration.

How significant is this information? CFT1 -3 can be verified as being bioidentical to the three forma of troponin; i.e. C - I and T.

Based on these finding, additional research is needed to ascertain if CT1 cells constitute the cytokine IL-3 that creates the troponins and 4 other epigenetic molecules; i.e. TNNT1 - 3, TNNC1 - 3, TNNI1 -3 and the enzyme calcineurin.

If CT1 is the cytokine, its use as tPA has previously been identified as a means of stimulating cardiac activity.

https://medicalxpress.com/news/2017-08-heart.html

How to trick your heart into thinking you exercise

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The far right image shows how a cardiotrophin treatment repaired heart muscle after a heart attack in a rat model. The blue areas are scar tissue and the red sections are healthy heart muscle. Credit: *Cell Research*

Researchers have discovered that a protein called cardiotrophin 1 (CT1) can trick the heart into growing in a healthy way and pumping more blood, just as it does in response to exercise and pregnancy. They show that this good kind of heart growth is very different from the harmful enlargement of the heart that occurs during heart failure. They also show that CT1 can repair heart damage and improve blood flow in animal models of heart failure. The results are published in *Cell Research*. The research team is from The Ottawa Hospital, the University of Ottawa, the University of Ottawa Heart Institute and Carleton University.

Heart failure is a leading cause of death and disability in high-income countries and a growing problem around the world. It occurs when the heart can't pump enough blood through the body, often because a heart attack has damaged the heart muscle tissue.

"When part of the heart dies, the remaining muscles try to adapt by getting bigger, but this happens in a dysfunctional way and it doesn't actually help the heart pump more blood," said Dr. Lynn Megeney, senior author of the study and a senior scientist at The Ottawa Hospital and professor at the University of Ottawa. "We found that CT1 causes heart muscles to grow in a more healthy way and it also stimulates blood vessel growth in the heart. This actually increases the heart's ability to pump blood, just like what you would see with exercise and pregnancy."

Dr. Megeney and his colleagues conducted a variety of studies in mice, rats and cells growing in the lab. In addition to CT-1, some of the studies involved a drug called phenylephrine (PE), which is known to cause the bad kind of heart growth. They found:

- Heart muscle cells treated with CT-1 become longer, healthier fibres, while those treated with PE just grow wider.
- CT-1 causes blood vessels to grow alongside the new heart muscle tissue and increases the heart's ability to pump blood, while PE does neither.
- When CT-1 treatment stops, the heart goes back to its original condition, just like it does when exercise or pregnancy end. However, the dysfunctional heart growth caused by PE is irreversible.
- CT-1 dramatically improves heart function in two animal models of heart failure - one caused by a heart attack (affecting the left side of the heart) and one caused by high blood pressure in the lungs (pulmonary hypertension, affecting the right side of the heart).
- Both CT-1 and PE stimulate heart muscle growth through a molecular pathway that has traditionally been associated with promoting cell suicide (apoptosis), but CT-1 has a better ability to control this pathway.

"This experimental therapy is very exciting, particularly because it shows promise in treating both left and right heart failure," said Dr. Duncan Stewart, a cardiologist, senior scientist and co-senior author on the paper who is also Executive Vice-President of Research at The Ottawa Hospital and a professor at the University of Ottawa. "Currently, the only treatment for right heart failure is a transplant. And although we have drugs that can reduce the symptoms of left heart failure, we can't fix the problem, and left heart failure often leads to right heart failure over time."

"An intriguing aspect of this research was how human CT1 was able to promote a healthy growth response in multiple animal models," said co-author Dr. Patrick Burgon, scientist at the University of Ottawa Heart Institute and assistant professor at the University of Ottawa. "This suggests the action of CT1 is universally conserved and puts us much closer to therapy."

The researchers also note that while exercise could theoretically have the same benefits as CT-1, people with heart failure are usually limited in their ability to exercise. Dr. Megeney and Dr. Stewart have patents pending for the use of CT-1 to treat heart conditions and they hope to develop partnerships to test this protein in patients. If this testing is successful it will take a number of years for the treatment to become widely available.

Explore further: **Study examines altered gene expression in heart failure**
More information: Mohammad Abdul-Ghani et al. Cardiotrophin 1 stimulates beneficial myogenic and vascular remodeling of the heart, *Cell Research* (2017). **DOI: 10.1038/cr.2017.87**

Journal reference: Cell Research