CrossMark

https://doi.org/10.1017/S1551929500050513 Published online by Cambridge University Press

Watching Neurons Hand Off Molecules

Continued from page 4

synaptic neuron. The points of DsRed were demonstrated to be at pre-synaptic sites by co-localizing the DsRed signal with an immunocytochemical stain for a protein known to be associated with synaptic vesicles. referred to as synapsin I. Of particular interest, it was shown in the plasmid-injected neurons that GFP-BDNF and DsRed had virtually the identical distribution, whereas the nerve cell body of the post-synaptic neuron was only labeled with GFP-BDNF. These results suggest that BDNF was transferred from the pre-synaptic axon to the post-synaptic neuron because only the pre-synaptic neuron received the injection of plasmid, and the DsRed was not similarly transferred.

Next, Kohara *et al.* addressed the question whether the transfer of the GFP-BDNF was mediated through the BDNF receptor, referred to as TrkB. When the receptor was blocked with TrkB-immunoglobulin G, the GFP-BDNF was not transferred to the post-synaptic neurons. This suggested that TrkB mediates the transfer of BDNF. Finally, the relationship between neuronal activity and BDNF transsynaptic transfer was examined. When plasmid-injected neurons were paralyzed with tetrodotoxin, the nerve cell bodies of the neuron adjacent to the DsRed-positive terminals did not show any GFP signal. The results indicated that the transsynaptic transfer of BDNF was dependent on neuronal activity. This was further confirmed when picrotoxin, a molecule that excites neurons, was in the presence of plasmid-injected cells, the GFP signal almost doubled in the post-synaptic neurons, indicating that increased neuronal activity resulted in an increased transfer of BDNF.

Kohara *et al.* have used an elegant, although technically challenging technique to demonstrate the direct transsynaptic transfer of a neurotrophic factor. This almost certainly occurred in an anterograde direction. It is possible that axon terminals of the post-synaptic neuron may have contacted the nerve cell body of the plasmid-injected neuron and that BDNF might have been transported retrogradely to the nerve cell body of the post-synaptic neuron but this possibility appears to be unlikely because fluorescent signal was not detected in axons that came from post-synaptic neurons. These results indicate transneuronal transfer of BDNF is dependent on neuronal activity and is not part of a general movement of protein between neurons because the DsRed was not transported to post-synaptic neurons. The co-expression of two fluorescent proteins in the study made it possible for Kohara *et al.* to directly observe the activity-dependent, transneuronal transfer of BDNF. Quite an accomplishment! ■

1. The author gratefully acknowledges Professor Tadaharu Tsumoto for reviewing this article.

2. Kohara, K., A. Kitamura, M. Morishima, T. Tsumoto, Activity-dependent transfer of brain-derived neurotrophic factor to postsynaptic neurons, **Science** 291:2419-2423, 2001.

Does The World Need A Traceable Ruler?

Joseph D. Geller, Geller MicroAnalytical Laboratory
jg@gellermicro.com

According to the International Standards Organization (ISO), for companies that are in compliance with ISO-9000 or QS-9000, traceable measurements shall be made when products or processes require dimensional measurements be made to a known uncertainty. These measurements are often made with a traceable ruler or micrometer. For magnification (the ratio of object size to image size) to be traceable, both the image and object size must be measured with calibration standards that have traceable dimensions. In the current ISO jargon the "uncertainty" of the instruments used to make the measurements must be known. The word "accuracy" is now only considered to be a subjective term and shall remain dimensionless. The uncertainty "budget" must consider all the factors, which may degrade the measurement result. This procedure is detailed in section 4.7 of the ISO-17025 (which replaced ISO Guide 25) "General Requirements for the Competence of Testing and Calibration Laboratories". This document is available from the International Standard Organization at www.iso.org.

In microscopy, the magnified image is usually measured with a ruler having millimeter graduations. To determine the magnification, the object that is magnified (calibration standard) shall also have dimensions with a known uncertainty. The resultant magnification is useful only under the specific conditions used. For details and procedures using the SEM see ASTM E766-98. For optical microscopy see ASTM E1951-98. These ASTM documents are available from www.astm.org.

So, do we really need a traceable ruler? How inaccurate can a ruler be? If we had the answer to that question we would not need one! During a trade show within the last several years I happened to visit a stand occupied by a national laboratory (many countries have national laboratories). They were giving away plastic rulers - both long and short ones. When I placed the mm markings on the long and short rulers together there was a discrepancy of about 0.5 mm over a length of 80 mm. Which, if either, was accurate? All we know is that the measurements did not agree. If we had a traceable ruler the uncertainty of the "give aways" could be determined.

We have addressed this subject and developed a "traceable ruler". The MR-1 has a scale of 150 mm in length with minimum markings of 0.01 mm. It is pretty "accurate". The uncertainty over the whole length of the scale is +/- 2.5 µm, and +/- 1 µm over the first 10 mm. Further information can be obtained at http://www.gellermicro.com/micro-ruler.pdf. Geller MicroAnalytical Laboratory is ISO-9001 certified and accredited to ISO-17025. ■