Targeting Talk: *Retrograde Transport*

by Dr. Douglas Lappi

Q: I spoke with someone from your technical service over the phone and got the impression that your product dermorphin-SAP (Cat. #IT-12) is not a retrograde and will only affect the terminals or the cells that express mu opioid receptors in the injection site in the brain. I have three questions: 1) Do you have any written document on this issue? 2) Will dermorphin-SAP also kill terminals in the injection site or just cell bodies? And 3) If it also kills terminals, will it affect their remote cell bodies?

A: 1) That the peptide-toxins don't undergo retrograde transport is an example of negative data, so people haven't really been publishing too much on that. But two articles deal specifically with it: Lappi and Wiley[1] and Bugarith *et al*.[2] The latter, in particular, presents solid data on the inability of the peptide ligand toxin NPY-SAP (Cat. #IT-28) to undergo retrograde transport.

I don't think we have a single example of a peptide-ligand toxin that undergoes retrograde transport. In order for a peptide-toxin to kill cells, the cell body must have the receptor and the toxin must be injected within reach of the cell body. We've made a mistake in not putting that in the data sheets, and will begin to change that.

2) Let me cite for you: Tokuno *et al*., Efferent projections from the striatal patch compartment: anterograde degeneration after selective ablation of neurons expressing mu-opioid receptor in rats.[3] As the title implies, they address the issue of elimination of processes following cell body destruction.

3) I'm not sure I understand this question, but that won't stop me from trying to answer it: The situation is the contrary, because the destruction of processes comes from the action taking place in the cell body. Our experience is that once the cell body is gone, it's just a matter of time for the process to go away. This makes these toxins a little different than others. In fact, we recommend that you wait two weeks at least to see immunohistological evidence of a toxic effect after injection of a saporin toxin *in vivo*. That's how long it takes the removal process to get rid of all the antigens that you might want to use for evidence of cell loss.

Q: Can I inject NPY-SAP to destroy projections through retrograde transport?

A: Regarding NPY-SAP, a peptide-toxin, see previous response. The antibody-toxins such as 192-IgG-SAP (Cat. #IT-01) or anti-DBH-SAP (Cat. #IT-03) will undergo retrograde transport from terminals to cell bodies. Thus, you can put 192-IgG-SAP into the cortex and it will destroy neurons in the basal forebrain, because the saporin (probably the whole conjugate) is transported from the projection to the cell body. Likewise, anti-DBH-SAP in the spinal cord destroyed hindbrain catecholaminergic neurons by retrograde transport.[4] All the antibody-toxins appear to undergo retrograde transport. (See table on page 6.)

Finally, the lectin-toxins, CTB-SAP (Cat. #IT-14) and IB4-SAP (Cat. #IT-10) undergo retrograde transport, just like the native lectins do. CTB-SAP is well-described in Llewellyn-Smith *et al*.[5] and several others. Please see our website and the references on the CTB-SAP page. For IB4-SAP, Vulchanova *et al*.[6] describe use, along with several other articles on our reference page.

In addition, detailed discussions are available in the book *Molecular Neurosurgery with Targeted Toxins*,[7] available from Humana Press.

References

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2. Bugarith K, Dinh TT, Li AJ, Speth RC, Ritter S. (2005) *Endocrinology* 146(3), 1179-1191.
3. Tokuno H, Chiken S, Kametani K, Moriizumi T, Mounir S, Parent A. (2002) Efferent projections from the striatal patch compartment: anterograde degeneration after selective ablation of neurons expressing mu-opioid receptor in rats. *Neurosci Lett* 332:5-8.
4. Ritter S, Bugarith K, Dinh TT. (2001) Immunotoxic destruction of distinct catecholamine subgroups produces selective impairment of glucoregulatory responses and neuronal activation. *J Comp Neurol* 432(2), 197-216.
5. Llewellyn-Smith IJ, Martin CL, Arnolda LF, Minson JB. (1999) Retrogradely transported CTB-saporin kills sympathetic preganglionic neurons. *NeuroReport* 10, 307-312.
6. Vulchanova L, Olson TH, Stone LS, Riedl MS, Elde R, Honda CN. (2001) Cytotoxic targeting of isolectin IB4-binding sensory neurons. *Neurosci* 108(1):143-155.
7. Molecular Neurosurgery With Targeted Toxins. Wiley RG, Lappi DA, eds. (2005) *Humana Press*, Totowa NJ.