Targeted toxins in pain

(continued from page 1)

Making selective neural lesions has long been an important experimental strategy in neuroscience. The power of this approach depends in large part on the specificity of the lesions. The term "molecular neurosurgery" refers to the use of targeted toxins to produce specific neural lesions based on targeting surface molecules on the neurons of interest.

This work began with suicide transport agents, such as ricin, that were delivered to target neurons by retrograde axonal transport. Suicide transport agents produce anatomically specific lesions but lack cell type selectivity. In order to selectively destroy specific types of neurons, we developed anti-neuronal immunotoxins such as anti-DBH-SAP, anti-SERT-SAP (Cat. #IT-23), and 192-IgG-SAP (Cat. #IT-01). These agents consist of monoclonal antibodies that recognize molecules expressed on the surface of specific types of neurons; the antibody is armed to kill by coupling to the ribosome-inactivating protein, saporin. (The more recent approach to cell type selective lesioning is neuropeptide-toxin conjugates such as SP-SAP and dermorphin-SAP.) Saporin, by itself, normally enters cells very inefficiently, but when coupled to a carrier that induces receptor-mediated endocytosis, saporin uptake can be highly efficient and limited to cells displaying the target molecule. The table below summarizes the targeted toxins available for the study of pain.

Molecular Neurosurgery Agents of Interest in Pain Research

Agent	Target	Lesioning Use
192-IgG-SAP *Cat. #IT-01*	**P75^{NTR}, low affinity NGFr** (cholinergic basal forebrain, cerebellar Purkinje neurons, postganglionic autonomic neurons and some primary sensory neurons)	Immunolesioning
Anti-DBH-SAP *Cat. #IT-03*	**Dopamine beta hydroxylase** (adrenergic and noradrenergic neurons)	Immunolesioning by application to either dendrites/soma or by retrograde axonal transport
Anti-SERT-SAP *Cat. #IT-23*	**Serotonin transporter** (serotonergic neurons)	Immunolesioning
Dermorphin-SAP *Cat. #IT-12*	**Mu opioid receptor** (striatal neurons, lamina II dorsal horn nociceptive interneurons, ventromedial medulla)	Direct application, spinal intrathecal injection
OX7-SAP *Cat. #IT-02*	**Thy-1** (all rat neurons and some T lymphocytes)	Suicide transport in both peripheral and central nervous systems
SP-SAP and SSP-SAP *Cat. #IT-07 and IT-11*	**Neurokinin-1 receptor (NK-1R)** (striatal cholinergic interneurons, dorsal horn nociceptive projection neurons)	Direct application to dendrites/soma, spinal intrathecal injection

Note: Only antibody-toxin conjugates undergo retrograde transport; see Page 5 for discussion

References

1. Khasabov SG, Ghilardi JR, Mantyh PW. *J Neurosci* 22:9086-9098, 2002.
2. Mantyh *et al. Science* 278:275-279, 1997.
3. Nichols *et al. Science* 286:1558-1561, 1999.
4. Vierck CJ, Kline RH, Wiley RG. *Neuroscience* 119:223-232, 2003.
5. Wiley RG, Lappi DA. *Neurosci Lett* 230:97-100, 1997.
6. Wiley RG, Lappi DA. *Adv Drug Deliv Rev* 55:1043-1054, 2003.
7. Burgess *et al. J Neurosci* 22:5129-5136, 2002.
8. Gardell *et al. J Neurosci* 23:8370-8379, 2003.
9. Porreca *et al. J Neurosci* 21:5281-5288, 2001.

Please visit www.ATSbio.com to see a complete list of references using these targeted toxins.