Targeting Talk: *Neuropeptide Toxins*

by Dr. Ronald G. Wiley

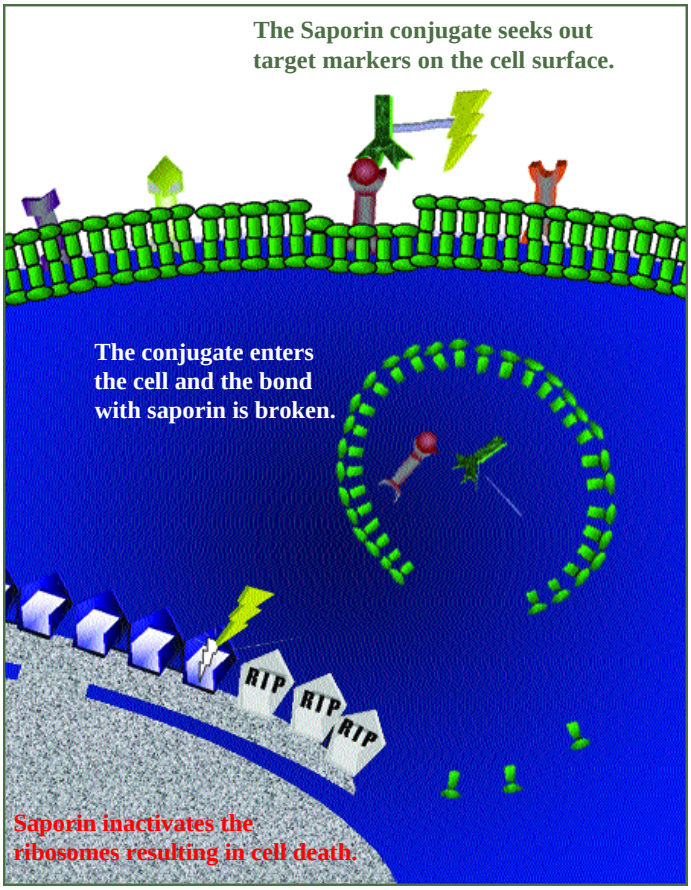
Q: What are neuropeptide-toxins and how do they work?

A: Neuropeptide-toxin conjugates are made up of the ribosome-inactivating protein, saporin, coupled to a naturally-occurring or synthetically-modified neuropeptide such as Substance P or dermorphin. The conjugate has binding specificity similar to the native, unconjugated neuropeptide.

When the neuropeptide binds to its cognate receptor, the conjugate is internalized. Once inside the target cell within an endosome, the neuropeptide and saporin separate and some of the saporin translocates into the cytoplasm where it catalytically inactivates ribosomes resulting in cell death.

Q: Are neuropeptide-toxins effective suicide transport agents?

A: The general answer to this question is not currently known. However, in the instance of intrathecally-injected dermorphin-SAP (Cat. #IT-12), the evidence does NOT favor suicide transport of the neuropeptide-toxin conjugate. When supramaximal doses of dermorphin-SAP (750 ng) are injected into the lumbar subarachnoid space of adult rats, less than 1% of lumbar dorsal root ganglion cells show evidence of saporin activity. This is in spite of the fact that many of these neurons express the targeted mu opioid receptor on their central terminals in the superficial dorsal horn of the spinal cord. This assertion is based on analysis of over 16,000 neurons from dorsal root ganglia in six rats.



Dermorphin-SAP (Cat. # IT-12)
a conjugate of the mu opioid receptor (MOR) agonist dermorphin and the ribosome-inactivating protein, saporin

Eliminates mu-opioid receptor-expressing cells

Substance P-SAP (Cat. # IT-07)
a conjugate of Substance P and the ribosome-inactivating protein, saporin

Eliminates Substance P (SP) receptor-bearing neurons

Also available using a more stable analog of Substance P:
SSP-SAP (Cat. #IT-11)

Blank-SAP (Cat. # IT-21)
a conjugate between a non-targeted peptide and the ribosome-inactivating protein, saporin

This molecule is the perfect control for use with peptide conjugates such as: SP-SAP, SSP-SAP, Orexin-SAP, Dermorphin-SAP and CRF-SAP.