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Targeting Trends

Reporting the latest news in Molecular Surgery

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Denise Higgins, Editor

ADVANCED TARGETING SYSTEMS

A New Immunotoxin for Targeting Dopaminergic Neurons

Targeting results with anti-DAT-SAP shown in Figure 1 are reprinted by permission of Kluwer Academic/Plenum Publishers. The original was published in Cell Mol Neurobiol *23:839-850, 2003.*

Dopaminergic neurons are widely studied because of their role in one of the devastating diseases of old age, Parkinson's. Lesioning studies using 6-hydroxydopamine or MPTP have been useful in research on Parkinson's Disease. However, these reagents have limitations such as MPTP affecting catecholaminergic neurons and 6-OHDA stability and specificity issues.

Targeting dopaminergic neurons with an antibody provides maximal specificity and overcomes the limitations of previous methods. Here we announce the availability of an immunotoxin against cells that express the dopamine transporter (DAT). DAT, because of its importance in dopamine use, is an indentifier of dopaminergic neurons. The DAT antibody used as the targeting agent in the immunotoxin recognizes a unique extracellular domain sequence and does not recognize other transporters.[1] This new immunotoxin is called anti-DAT-SAP and is described in Wiley *et al.*[2]

Figure 1 shows the removal of dopaminergic neurons in a dose-dependent manner after direct injection into the striatum. Cells can also be eliminated by intracerebroventricular injection; the immunotoxin will seek out the dopamine transporter, and the saporin moiety will be transported to the cell body to inhibit protein synthesis.

References

1. Hersch SM, Yi H, Heilman CJ, Edwards RH, Levey AI (1997) Subcellular localization and molecular topology of the dopamine transporter in the striatum and substantia nigra. *J Comp Neurol* 388(2):211-227.
2. Wiley RG, Harrison MB, Levey A Lappi DA (2003) Destruction of midbrain dopaminergic neurons by using an immunotoxin to the dopamine transporter. *Cell Mol Neurobiol* 23:839-850.

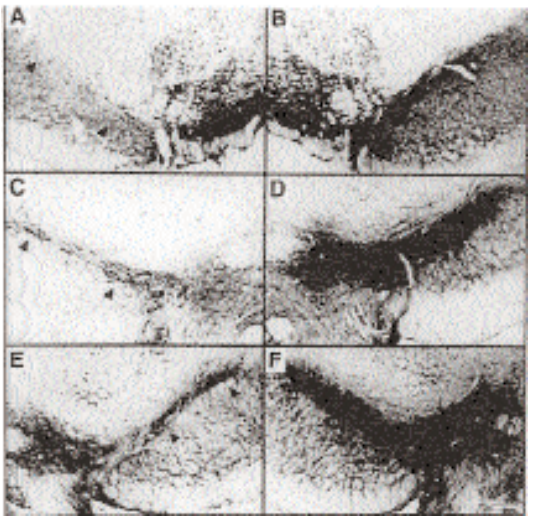

Figure 1. Representative sections stained for tyrosine hydroxylase from rats with intrastriatal injections of anti-DAT-SAP two weeks prior to sacrifice. Panels A, C, and E are ipsilateral to the striatal injections. Panels B, D, and F are contralateral, from the same sections. The anti-DAT-SAP doses were 2.8 µg in A, 0.56 µg in C, and 0.28 µg in E. Note loss of dopaminergic neurons from the ipsilateral substantia nigra, pars compacta (arrowheads) with the greatest extent of cell loss in A and the least in E. The magnification bar in F indicates 100 µm and applies to all panels.