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B Fragment of Cholera Toxin Conjugated to Saporin

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INTRODUCTION

Saporin conjugates have proven extremely versatile and valuable in the selective destruction of a variety of cell types. In the nervous system, the use of saporin-conjugated toxins has generally been directed toward neurons. We were interested in whether saporin conjugates could be used to target other nervous tissue cell types, particularly the myelin-forming cells. Taking advantage of the fact that myelin is rich in G_{M1} ganglioside and that the B fragment of cholera toxin has a high affinity for G_{M1}, we used a conjugate of the B fragment of cholera toxin and saporin (CTB-sap) to target myelin-producing cells (oligodendrocytes) in the central nervous system (CNS) (Fig. 1). We found that CTB-sap is effective in removing oligodendrocytes in addition to other glial cells and largely leaves neurons intact. We successfully used CTB-sap to study demyelination and remyelination in the spinal cord *(1)*, and our preliminary results suggest that CTB-sap will be useful for inducing demyelinating lesions in other parts of the CNS.

CTB-SAP: INTERNALIZATION, TOXICITY, AND EFFECTS

The Conjugate: Structure and Toxicity

Cholera toxin is an oligomeric protein composed of an A subunit and five identical B subunits. The A subunit of the toxin massively increases cyclic adenosine 5'-monophosphate (AMP) levels; the B pentamer is the receptor-binding portion of the molecule and by itself has no toxic activity. As men-

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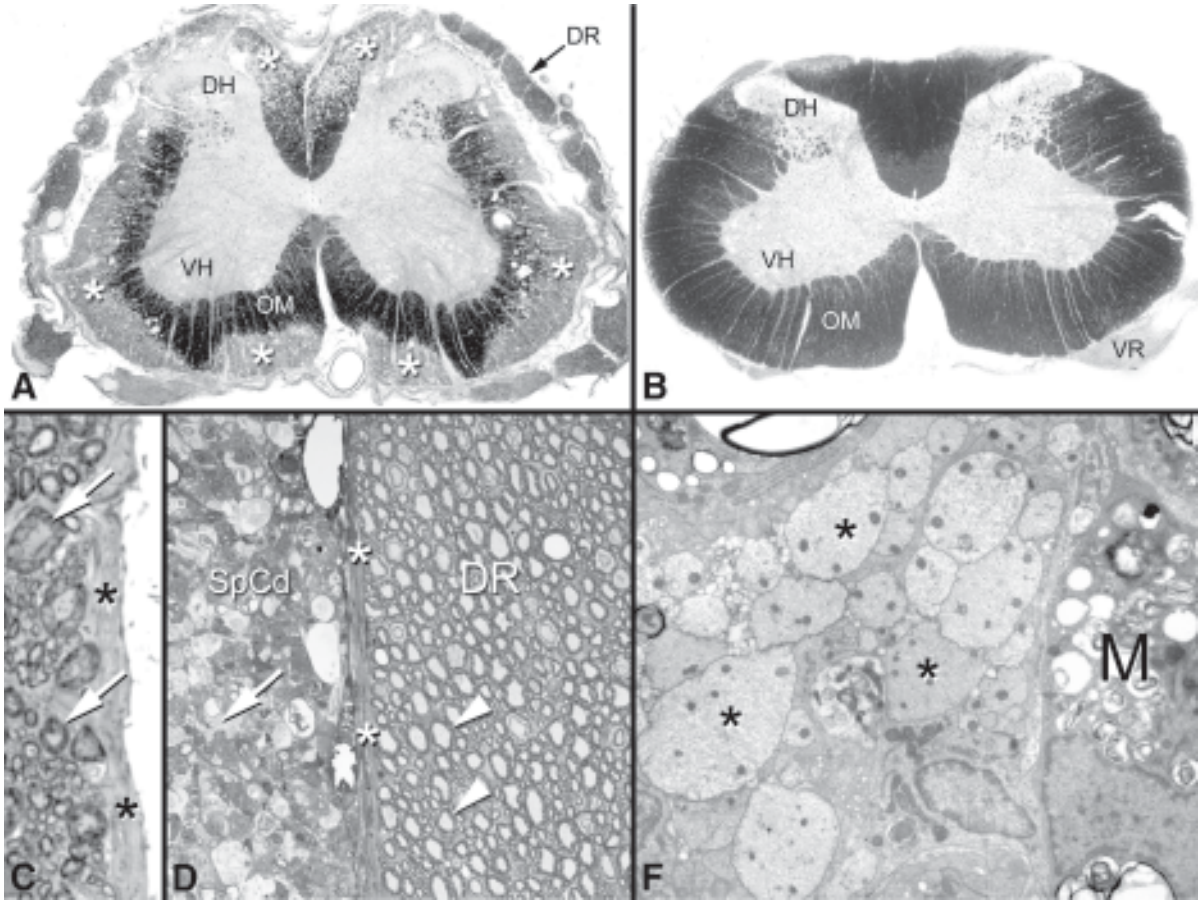

Fig. 1