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# Targeting Trends

*Reporting the latest news in Molecular Surgery*

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***Denise Higgins, Editor***

ADVANCED TARGETING SYSTEMS

## Immunolesioning Hippocampal Inhibitory Interneurons

*Dr. Robert Sloviter, University of Arizona, contributes this issue's article from the laboratories of ATS customers. Dr. Sloviter summarizes his research with SSP-saporin, which he and his graduate student Jennifer Martin used to examine the role of inhibitory neurons in maintaining normal network excitability.*

The mammalian hippocampus is perhaps the most intensely studied brain region for a variety of reasons. Hippocampal structure and function are highly conserved among mammalian species, and its highly laminar organization greatly facilitates experimental design and interpretation. However, its greatest attractions are its involvement in the normal functions of learning and memory, and in a variety of neurological disorders including stroke, Alzheimer's Disease, and epilepsy. One of the major issues of hippocampal research involves the structure and function of hippocampal inhibitory interneurons, and how they determine the behavior of excitatory hippocampal principal cells. We and others have sought to determine whether certain network behaviors might be the result of inhibitory neuron dysfunction or loss, but it has always been difficult to remove or disable inhibitory neurons selectively, without producing significant collateral damage.

After some failed attempts to lesion specific neuronal populations, we were excited to read the paper by Pat Mantyh and his colleagues,[1] in which they reported the efficacy of Substance P-saporin (SP-SAP) for removing SP receptor-positive cells in the spinal cord. Because some hippocampal inhibitory interneurons had been reported to express SP receptors (SPRs),[2] we purchased SP-SAP,

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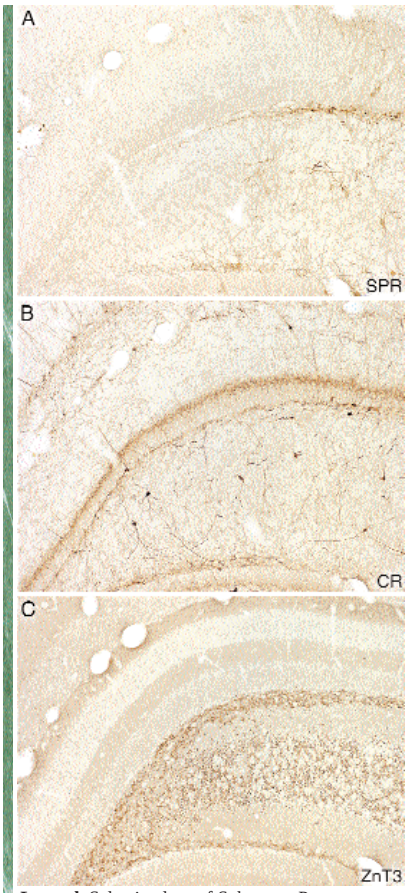


**Legend.** Selective loss of Substance P receptor (SPR)-immunoreactive cells after intrahippocampal injection of SSP-SAP. (A) All SPR-positive cells and dendrites have been ablated on the left side of the photograph. (B) Calretinin (CR)-immunoreactive cells and fibers in an adjacent section survive in the SPR depletion zone. (C) In another adjacent section, zinc transporter-3 (ZnT3)-positive terminals are similarly unaffected in the SPR depletion zone.

## ATS Receives $900,000 in NIH Funding

In September, Advanced Targeting Systems received two Small Business Innovation Research (SBIR) awards from the National Institutes of Health. The first is a Phase II grant from the National Institute of Neurological Disorders and Stroke. This project continues a collaboration with Drs. Joanne Berger-Sweeney (Wellesley College) and Mark Baxter (Harvard University) to further develop the mouse p75 immunotoxin. More than three-quarters of a million dollars will be invested in characterizing this lesioning agent for use in modeling and studying neurodegenerative diseases such as Alzheimer's disease (AD). Part of the project will include use of the immunotoxin in a transgenic mouse model of AD.

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