

Targeting Talk: *In Vivo* Delivery of Targeted Toxins

Q: What are the options for delivery of targeted toxins?

A: The options for toxin delivery are varied and limited only by investigator ingenuity. Generally, injection has been the route of choice. Some toxins can be given intravenously, such as 192-Saporin (Cat. # IT-01) or anti-DBH-SAP (Cat. # IT-03), in which case all cells expressing p75 or dopamine beta-hydroxylase and exposed to the systemic circulation are potential targets. Intravenous injections will not deliver toxins to the CNS.

Subarachnoid injections have been used successfully for immunotoxins and peptide toxins such as SP-SAP (Cat. # IT-07).

Direct intraparenchymal injections have been used to restrict toxin application to just a few target cells. However, intraparenchymal injections require careful attention to injection technique and are impractical for large target structures.

Q: When injecting directly into tissue, are there any special techniques that should be used?

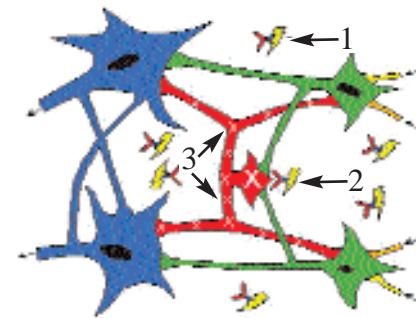
A: Direct injections into brain or spinal cord have been used successfully by some investigators. Specifics of toxin dose, concentration, injection volume and speed of injection have varied considerably. If a high concentration of toxin is deposited locally, lesion specificity is often lost. Presumably, if toxin concentration is too high, cellular uptake by non-specific bulk fluid-phase endocytosis (pinocytosis) can internalize enough saporin to be lethal.

There is currently interest in “convective” delivery techniques developed in the laboratory of Dr. Edward Oldfield at the NIH. The basic principle is to deliver a relatively large concentration slowly over an extended period, often using a rather dilute solution. The parameters for any given species and injection site need to be determined by pilot experiments.

Q: What sort of special care should be given to the animal after administration of the targeted toxin?

A: The toxins generally bind and internalize within minutes, although some immunotoxins circulate for longer periods if injected intravenously. However, no significant amount of active toxin is excreted. So, animals can be returned to group housing immediately after toxin injection. The only special requirements may derive from the specific target being studied. For example, rats given intraventricular 192-Saporin (Cat. # IT-01) develop decreased fluid and food intake for several days after injection. Since the adipsia is significant, providing the animals with fresh, juicy vegetables, such as cucumber or potatoes, can help.

Rats injected intraventricularly with anti-DBH-SAP (Cat. # IT-03) will lose considerable body weight and are slow to regain. They, too, may benefit from food supplements, including nuts and other high calorie appetizing treats. Otherwise, common sense care of any neurologic deficits is indicated depending on the target and toxin being used.



1. Saporin is conjugated to specific targeting agent.
2. Conjugate is bound to receptor/antigen and internalized.
3. Target cells are eliminated; other cells are left untouched.