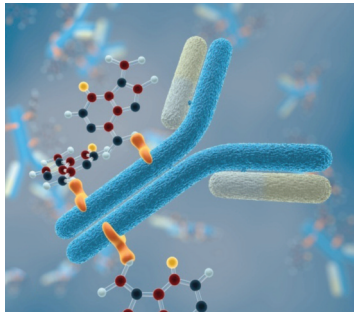
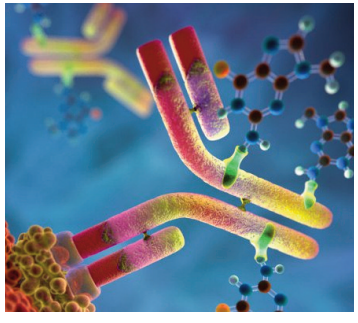
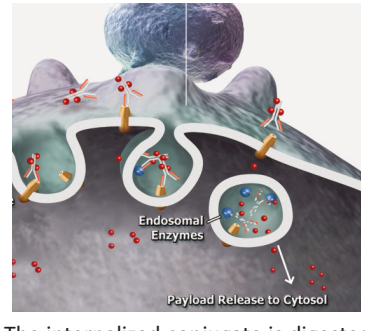


A targeting agent is conjugated to a payload. Here the conjugate is an antibody linked to a small molecule.



The targeted conjugate binds only the cells that are specific to the antibody causing the receptor to internalize.



The internalized conjugate is digested by enzymes releasing the payload into the cytosol. The payload is then free to alter the cell.

The Advanced Targeting Systems' technology . . .

Molecular Surgery

is a modification of one of the most widely used techniques in the neurosciences: lesioning of a region by surgical means and observation of the effect.

KnockOut Models

Using Molecular Surgery, scientists can establish an animal model by eliminating a specific cell type.

Check out this recent publication.

The Establishment of a CSF-Contacting Nucleus "Knockout" Model Animal

Song S-Y, & Zhang L-C. (2018). *Frontiers Neuroanat*, 12:22-32.

Dose: 3 µl (500 ng) CTB-SAP was microinjected into the lateral ventricle.

Objective: To establish a cerebrospinal fluid (CSF)-contacting nucleus-deficient model animal using cholera toxin B subunit-saporin (CTB-SAP).

Summary: The complete ablation occurred by Day 7 after CTB-SAP microinjection. A model animal that had no CSF-contacting nucleus was established after survival beyond that time point. No obvious effects were observed in the vital status of the model animals, and their survival was ensured. The common physiological parameters of model animals were stable. The present study provides a method to establish a CSF-contacting nucleus "knockout" model animal, which is similar to a gene knockout model animal for studying this particular nucleus *in vivo*.

ADVANCED TARGETING SYSTEMS

Stratech

Targeted Toxins

Cell-specific targeting and removal:
Cheaper and Quicker than knockouts
with high impact results

stratech.co.uk/atsbio

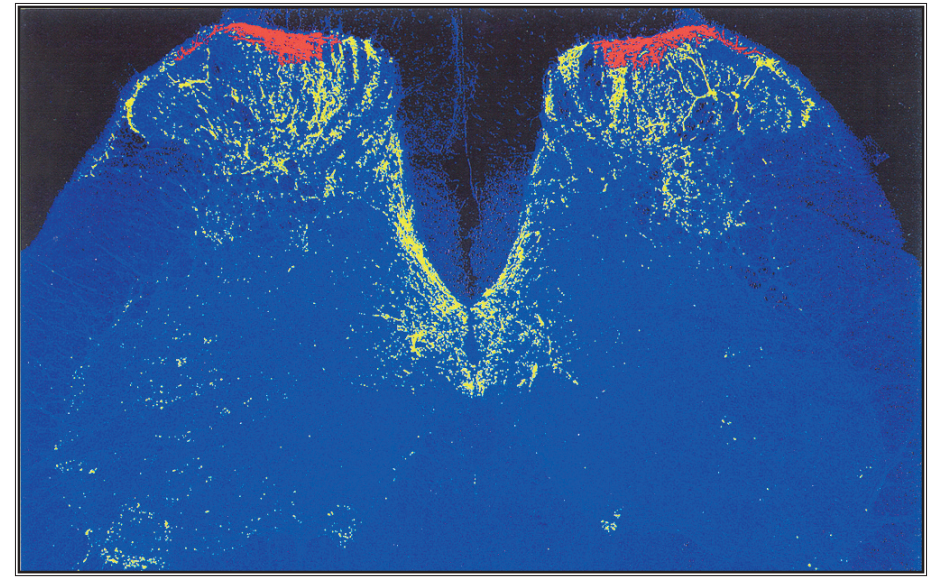
Knockout models are helpful tools in scientific research. They have been useful in studying and modeling in all sorts of research in biology; so much so that the pioneers – Smithies, Capecchi and Evans – won a well-deserved Nobel Prize for Physiology and Medicine in 2007. But there are some reasons not to go down that path:

- About 15% of gene knockouts are developmentally lethal (from www.genome.gov).
- According to information posted on a major university's core facility website, it will take a minimum of 40 weeks to produce a knockout mouse. The cost for this best-case scenario is at least $11,000. And that doesn't include the time and money spent for the molecular biology construction.
- Statistics published by university core facilities range from 10% to 50% success rate in producing gene-based knockout models.
- You are pretty much limited to mice. Of course, if you want to spend more, you can try rats.

That's a lot of time and money for a grad student or post-doc to find out, "Gee, that didn't give me a high impact result."

Here's an alternative that has a high rate of success, can give high impact results, takes about 10 days to see behavioral results, and costs $200 to $700 to treat about 20 mice. You also have the option to use rats, ferrets, or many other species.

Targeted toxins offer the ability to develop "knockouts" through cell surface-based targeting that has several advantages over the gene-based approach. The "knockout" has a slight but important difference: instead of knocking out a gene, you eliminate a particular cell type. And this happens at your convenience: you inject the animal, put it back in its cage and then usually four days later, behavioral differences begin to show. These usually become permanent after a week or so. So you don't have to wait 40 weeks to even start your experiments. People usually begin immunohistochemistry after a couple of weeks.



*Internalization of Substance P receptor (SPR) after injection of SP-SAP into the cerebrospinal fluid. This figure shows, in **red**, concentrated areas of SPR on the cell membrane after internalization of the saporin conjugate. Lesser concentrated areas of SPR that are not targeted are shown in **yellow**.*

This figure illustrates how targeted toxins can be used to 'knockout' specific, cell surface-based targets without affecting untreated areas.

The Cost

Let's say you're using a rat. Well, there's the cost of the rat and its boarding. Often people use 100 ng of the targeted toxin. Since the price is usually $350 per 25 micrograms, for a single injection that would be $1.40 per animal. Then there's the 2-week wait, the cost of the behavioral experiment, and the IHC; all at a cost less than $11,000. Much less. And then publish in Science, Nature, Journal of Neuroscience, Diabetes, Cancer Research, Endocrinology, Journal of Immunology, or many others.

The Animal Model

Using targeted toxins, you can begin with a fully mature, healthy animal. And the result is a fully mature, healthy animal that is ready to run through mazes.

Now you know you've got a choice!