New treatment sees through parasites' disguises

Trypanosomes, the parasites that cause sleeping sickness, dodge capture and destruction by the immune system by routinely altering their surface proteins to prevent recognition; however, a newly developed drug delivery strategy may defeat their stealth strategy.

The key to the trypanosome's disguise acumen is the variable surface glycoprotein (VSG), which undergoes constant alteration to help bloodstream parasites stay at least one step ahead of host immune detection. As a result, drug-based therapeutics are more practical than vaccination, but existing drugs bring with them the risk of severe toxicity and the potential for the emergence of drug-resistant strains.

Recent research has identified a naturally occurring human protein, apolipoprotein L-I (apoL-I), which is capable of inducing lysis in certain trypanosome strains. Now, in new work published in the May issue of *Nature Medicine*, Toya Nath Baral of the Vrije Universiteit Brussel (Belgium) and his colleagues describe a scheme for targeted delivery of this protein that seems to bypass the parasite's natural defense mechanisms.

The trypanosome species responsible for sleeping sickness is normally resistant to apoL-I, but a minor modification to this protein is enough to render these species vulnerable to destruction. For delivery, Baral and colleagues used a nanobody—a small, single-protein fragment derived from camel antibodies—that is capable of generically recognizing a variety of different VSGs. Linking modified apoL-I to this nanobody seemed to do the trick; *in vitro*, trypanosomes exposed to the conjugate perished completely, and *in vivo*, trypanosome-infected mice showed total clearance of parasites within a week of treatment. Mice receiving optimal doses of this therapeutic agent remained parasite-free and in apparently good health for the duration of the *in vivo* studies, as long as 60 d after treatment.

The authors indicate that the sequence similarity between nanobodies and human antibodies should lower the risk of unwanted host immune response for this therapy, and that this strategy may also prove useful for treating other infectious diseases.

Michael Eisenstein

NEUROGENESIS NOT NEEDED FOR EFFECTIVE ENRICHMENT

Access to environmental enrichment alters behavior and learning in rodents, but not because they grow new brain cells, according to a new study. These results contradict the commonly held idea that enrichment-induced neurogenesis causes behavioral alterations and improved performance in learning tasks.

Previous research has demonstrated that laboratory rodents exposed to environmental enrichment, such as toys and running wheels, show improved learning and memory and decreased anxiety-like behaviors. Research has also shown that environmental enrichment enhances neurogenesis in the dentate gyrus, a part of the hippocampus in which the birth of new neurons and glia continues in adulthood. This observation has led researchers to suspect that it is the increased neurogenesis that causes the changes in behavior and learning.

Now, a recent *Nature Neuroscience* paper (published online 30 April; doi: 10.1038/nn1696) by a research team led by René Hen of Columbia University (New York, NY) calls this hypothesis into question. Hen's team used targeted x-irradiation directed at the hippocampus of mice to block cell division in the dentate gyrus. After allowing the mice to recover for 2 months from radiation-induced inflammation, they assigned the animals to two groups. The control group lived in standard rodent cages without enrichment, whereas the experimental group lived in large, multicompartment cages with access to toys and running wheels. After 6 weeks Hen's team tested the mice for spatial learning using the Morris water maze, and for anxiety-like behaviors using the novelty-suppressed feeding protocol.

In the Morris water maze irradiated mice housed in the enriched environment took shorter paths to the hidden platform, demonstrating improved spatial learning abilities. In the novelty-suppressed feeding protocol these mice showed decreased latency to feed, suggesting that enrichment decreases anxiety-like behaviors. The researchers also tested unirradiated mice in both tasks and failed to detect significant differences in the results obtained with these animals and their irradiated counterparts. Immunohistochemical analysis of the brains of irradiated and control mice confirmed that exposure to enrichment spurs adult neurogenesis in the hippocampus.

If neurogenesis is not the cause of environmental enrichment-induced changes in behavior, other mechanisms yet to be identified must be responsible. Writing in *Nature Neuroscience*, the authors propose that "upregulation of growth factors such as brain-derived neurotrophic factor, as well as morphological changes such as increased dendritic branching and synaptogenesis" may be responsible.

Tanja Schub