Abstractions

LAST AUTHOR

A specialized cellular network that protects the brain has proved a hurdle to therapeutic drug delivery. Now researchers have found a way to breach the blood–brain barrier, which safeguards the brain from potentially dangerous molecules in the bloodstream. Manjunath Swamy, an immunologist at the CBR Institute for Biomedical Research in Boston, Massachusetts, and his colleagues had previously shown that small interfering RNA molecules (dubbed siRNAs) could treat viral brain infection when delivered directly to the brain. Now they may have found an easier way to deliver siRNAs — using a key peptide from the rabies virus that is able to traverse the blood–brain barrier (see page 39).

Was your goal simply to cross the blood–brain barrier?

Not exactly. We've been working on treatments for severe viral brain diseases. We've shown that synthetic siRNAs drastically suppress viral encephalitis. We started this line of research to find a better way to deliver these siRNAs to the brain.

What led you to try the rabies virus?

Twenty-five years ago, researchers trying to find the rabies-virus receptor showed that a protein on the virus binds to a neuronal receptor to infect brain cells. There were indications that you didn't need the virus, or even the entire viral protein, but simply a short protein fragment to bind to brain cells.

What else was needed to engineer this peptide fragment to deliver the siRNA?

We added a positively charged amino acid to the peptide so it could bind to the siRNA. After intravenous delivery, we found siRNA localized in brain cells. When we treated mice infected with the encephalitis virus with siRNA the survival rate was 80%.

Are there any risks associted with crossing the blood–brain barrier?

So far we've found the peptide to be nontoxic, but we need to understand how it is metabolized before it can be used in humans. We also don't know what happens to the specific neuronal receptor, which is involved in neurotransmission.

What ripple effects might your findings have in the greater research community?

This delivery approach has huge potential. The blood–brain barrier poses a problem for delivering promising gene therapy and RNA-interference agents. Researchers have already shown that siRNAs might be effective in neurological disorders such as Alzheimer's disease. The good thing about this peptide carrier is that you can attach any siRNA, and possibly antibodies or enzymes, to it. ■

MAKING THE PAPER

Hannah Rowland

Experimental foragers put 100-year-old mimicry debate to the test.

Whether species whose markings mimic those of less palatable species are mutualistic or parasitic has divided theoreticians and field ecologists for more than 100 years. Now a group of experimentalists has gone some way to settling the debate (see page 64).

Two types of mimicry exist in nature. Müllerian mimics are unpalatable species that evolve to resemble another unpalatable, model species. Such mimics share the cost of educating predators and so, the thinking goes, have a mutualistic relationship with their model. But batesian mimics — which are completely palatable and edible — receive all the benefit of their model's protection without making any contribution. These mimics are therefore viewed as having a parasitic relationship with their model species.

Debate has centred on situations in which a müllerian mimic is unequally defended — that is, its chemical defence renders it only slightly unpalatable compared with its highly unpalatable model. Theoreticians, including Michael Speed of the University of Liverpool, UK, proposed that such a situation would be quasi-batesian and would degrade the model species' protection, because a predator would take longer to learn that the markings meant 'not tasty'. But field workers believed that any level of defence in a müllerian mimic would be mutualistic.

Speed and his doctoral student, Hannah Rowland, took advantage of a 'novel world' set-up devised by their collaborators, Johanna Mappes and Leena Lindström at the University of Jyväskylä in Finland. Wild-caught great tits (*Parus major*) were pre-trained to open a paper-wrapped almond piece as a new type of prey. Then, in the novel-world aviary, Rowland and her Finland-based co-author Eira Ihalainen presented naive birds with several scenarios that represented batesian and differently defended müllerian mimics of a very unpalatable model prey — a piece of almond soaked in the bitter-tasting antimalarial drug chloroquine.

The students could test various factors individually, such as a mimic's level of defence (none, moderate or high), the quality of the mimicry (perfect or imperfect) and the number of mimics in relation to the model prey. In addition to the model and mimic prey items, the birds could choose a completely palatable prey item camouflaged against the background of the aviary.

In the unequally defended müllerian situation, Rowland and her colleagues observed an overall mutualistic relationship. In other words, Rowland says, "everyone's mortality — both the mimic and the model — gained from association with the model's markings". Under these conditions there was no quasi-batesian parasitic relationship.

The authors found that introducing a batesian mimic to the system didn't increase the model's mortality. In fact, the model's mortality stayed flat with increasing numbers of edible mimics. This indicates that the dilution effect of adding more total prey to the system overwhelmed any parasitic relationship from the batesian mimic.

"In a forest, you could have a situation where a highly defended butterfly has a batesian mimic migrate into the area, and although it might affect the community's risk of predation, it wouldn't have a massive impact on the species survival," says Rowland. She thinks this work "resolves a certain amount of the debate". She adds that the novel-world aviary provides an opportunity to put other theoretical models of ecological interactions to the test. ■

FROM THE BLOGOSPHERE

What is open science? A post on Nautilus (http://tinyurl.com/2kauqz) discusses an essay on the topic by Frank Gibson of Newcastle University, UK. His role in an e-neuroscience project, Gibson writes, exposed him to a life-science domain in which "data sharing and publicly exposing methodologies has not been readily adopted", largely owing to privacy issues and data set sizes.

The Nature journals' policies on data availability can be found on our author and reviewers' website. There, you can comment on emerging policies on data availability in a range of disciplines.

The Postgenomic website, Gibson notes, produces an "up-to-the minute list of the open science discourse". "Although early days," he continues, "maybe even the 'open science group' on Scintilla will be the place in future for fostering the open science community."

NPG's Scintilla site collects data from hundreds of news outlets, scientific blogs, journals and databases and allows users to find and share information. It is free to join, so take a look and, if you wish, contribute.

(All articles and websites can be accessed from the Nautilus URL above.) ■

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