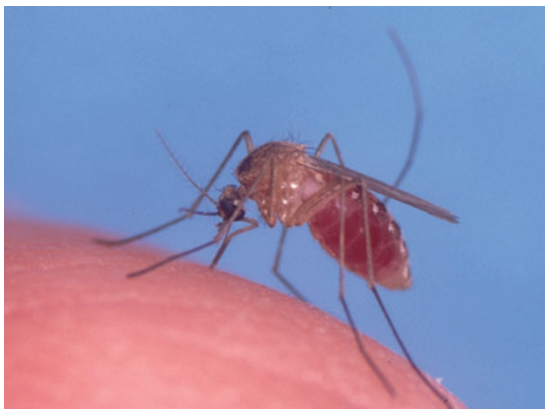
Antibody neutralizes West Nile virus

A newly developed therapeutic antibody, capable of neutralizing West Nile virus (WNV) even several days after the onset of infection, may prove an important breakthrough for preventing WNV-related deaths and for tackling other related viruses.

Although birds are the primary carrier of WNV, scientists and doctors have been aware for some time that the mosquitoes that transmit the virus can also pass it along to mammals—including humans. The majority of the population experiences no ill effects from WNV exposure, but those who do are at risk for encephalitis and meningitis, both severe and potentially fatal afflictions of the brain. Patients older than 50 years of age are at particular risk.

At present, there is no human vaccine available for WNV, although research has shown that the body can mount a successful immune response with antibodies that neutralize viral infection. In an effort to explore the potential of monoclonal antibodies as anti-WNV therapeutics, Michael Diamond of the Washington University School of Medicine (St. Louis, MO) and his colleagues immunized mice with recombinant viral envelope protein, which is generally known to be a primary target for immune recognition. They generated nearly 50 different monoclonal lines, a dozen of which proved capable of neutralizing WNV more effectively than human polyclonal antisera (*Nat. Med.*, May).

One of the most effective antibodies, E16, was capable of blocking infection of several different mouse and human cell lines by several different WNV strains; at the same time, the antibody was specific enough not to neutralize closely related, non-WNV viruses. The antibody proved equally effective in mice; for mice that had been injected 2 days after infection with E16, the survival rate rose from 10% to >90%. E16 even offered protection when injected several days later, when infection had progressed to the central nervous system. Increased doses of E16 given 5 days after infection still conferred 90% survival rates, and 9 days later all virus had been cleared from the brains of 68% of the treated mice.



Diamond's team has also developed a 'humanized' version of E16, which is equally effective in mice but may prove more effective for human patients. "Our results are the first successful demonstration of a humanized monoclonal antibody as postexposure therapy against a viral disease," the authors write, "and suggest that antibody-based therapeutics may have more broad utility than previously appreciated."

Michael Eisenstein

GROWTH FACTOR DISCOVERY PROMISES ADVANCE IN DIABETES RESEARCH

A recently discovered growth factor seems to have a surprisingly prominent role in the regulation of glucose metabolism and may offer a valuable therapeutic target for the treatment of diabetes mellitus.

Researchers have traditionally linked the fibroblast growth factor (FGF) family of proteins, which currently contains 22 known members with activities relating to the regulation of cell growth and division. However, some recent evidence has suggested that certain of these FGFs may also participate in metabolic regulation. In a recent article from the *Journal of Clinical Investigation* (published online 2 May; doi:10.1172/JCI23606), Alexei Kharitonenkov and his colleagues at the Lilly Research Laboratories (Indianapolis, IN) report the surprising finding that FGF-21, one of the more recently discovered and enigmatic of the FGFs, may be involved in the regulation of glucose homeostasis.

Adipocytes treated with FGF-21 assimilate more glucose from the culture medium than treated cells, in response to a signaling pathway that seems to be fully insulin independent. Following several days of treatment with FGF-21, the researchers observed a significant drop in blood glucose in a number of genetically obese and diabetic rodent strains; accompanying this effect was a decrease in blood triglyceride levels, and an increase in insulin sensitivity and glucose clearance.

Kharitonenkov's team followed these experiments by generating a transgenic mouse line that overexpresses FGF-21 specifically in the liver; unlike other FGFs, FGF-21 does not seem to trigger cell proliferation, and transgenics were not predisposed to tumor formation. By the age of 9 months, the transgenics weighed less, had lower fasted blood glucose levels and more brown fat, and showed greater insulin sensitivity and more efficient glucose clearance than their wild-type counterparts. Surprisingly, there was no hypoglycemia observed in fasted FGF-21–treated or transgenic mice, reinforcing a model in which FGF-21 acts independently of insulin. The transgenics also proved resistant to diet-induced obesity.

Beyond these intriguing findings, the authors are uncertain of FGF-21's precise mode of action. Among other possibilities, they speculate that its effects could be mediated by increasing the expression of a glucose transporter protein or by downregulating secretion of glucagon, insulin's counterpart hormone. Nevertheless, the metabolic effects of FGF-21 could potentially make it a prime target for the design of future therapeutics and may suggest an exciting new direction for diabetes research.

Michael Eisenstein