Infection-fighting antibodies made in plants as effective as costlier conventional version

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The first head-to-head comparison of therapeutic monoclonal antibodies produced from plants versus the same antibodies produced from mammalian cells has shown that plant-produced antibodies can fight infection equally well.

Scientists from Washington University School of Medicine in St. Louis and Arizona State University conducted the comparison as a test of the potential for treating disease in developing nations with the significantly less expensive plant-based production technique.

The results are reported online in the Proceedings of the National Academy of Sciences.

Antibodies, which are part of the immune system, bind to foreign invaders to disable them and label them for destruction. Because of their finely tuned targeting capabilities, scientists have developed ways to mass-produce a particular antibody. They have used such monoclonal antibodies in a variety of contexts.

For example, a monoclonal antibody against West Nile virus, originally developed at Washington University School of Medicine in St. Louis, is in clinical trials by a company that licensed the antibody from Washington University.

Monoclonal antibodies are also in development for a variety of other diseases, but the expense of manufacturing such antibodies makes it

economically infeasible to use them to treat disease in the developing world. So researchers at Washington University and Arizona State University decided to see if they could adapt the West Nile virus monoclonal antibody for production in a much less expensive factory: genetically modified plants.

Plants normally do not make antibodies, but in 1989 scientists developed a technique to genetically alter a tobacco plant so it would produce monoclonal antibodies. Proponents of the new technique noted that it had the potential to make antibodies much more affordable. In addition, plants do not carry viruses that can infect humans.

Researchers had to adjust the West Nile virus antibody to adapt it for production in Nicotiana benthamiana, a relative of tobacco.

"We altered the genetic coding of the antibody slightly, not changing its parts but using alternate forms of the coding for those parts to maximize the plant's ability to produce it," says co-senior author Qiang Chen, Ph.D., of Arizona State. "We also stabilized the antibody, preventing copies of it from being degraded inside the plant cells. Together, those two techniques increased our average antibody yield by 60 percent above any previous efforts."

Scientists then tested regular and plant-produced monoclonal antibodies in mice both as preventatives against West Nile infection and as treatments for animals already infected with the virus. They found the antibodies from plants were equally effective at preventing infection and fighting existing infections.

Researchers at Macrogenics Inc., the company that licensed the antibody from Washington University, analyzed the plant-produced antibody's ability to bind to West Nile virus particles. They found that one important receptor was binding appropriately, but the strength of a

second receptor's bond was lowered.

"This results from the fact that plants combine their proteins with slightly different sugars than mammals," says co-senior author Michael Diamond, M.D., Ph.D., professor of medicine, of molecular microbiology and of pathology and immunology at Washington University. "We're already working on genetically modifying the plants to humanize the sugars the plants combine with the antibody's proteins."

Diamond stresses that the study was not designed to make a case for using plant-produced antibodies to treat West Nile virus infections, which continue to occur throughout the United States.

"That's a decision for manufacturers and governmental regulators to make," he says. "Our hope is that once this technology is proven and widely available, it will be taken up by innovative, technology-savvy nations like India and Brazil where the need for more affordable solutions for endemic diseases is much greater."

More information: Huafang L, Engle M, Fuchs A, Keller T, Johnson S, Gorlatov S, Diamond MS, Chen Q., "Monoclonal antibody produced in plants efficiently treats West Nile virus infection in mice", *Proceedings of the National Academy of Sciences*, online edition.

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