The most natural drug

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In the fight against infection, the human immune system isn't ready for a war. Vaccines push the immune system to create defenses against illness, but they take time to work. A new process developed by scientists at the Oklahoma Medical Research Foundation (OMRF) and Emory University stands to revolutionize the process.

In an advance online publication in *Nature*, the researchers describe a method that can identify and clone human antibodies specifically tailored to fight infections. The new technology holds the potential to quickly and effectively create new treatments for influenza and a variety of other communicable diseases.

When an infection invades, the immune system goes to work manufacturing antibodies to fight it. Most of the antibodies created will have no effect, but a very few will bond to the invader and replicate to neutralize the enemy.

The new process develops a "smart bomb" for the immune system, using fully human monoclonal antibodies specifically designed to fight the infection without doing any harm to the body. The work was led by OMRF's Patrick Wilson, Ph.D., and J. Donald Capra, M.D., and Emory's Rafi Ahmed, Ph.D., and Jens Wrammert, Ph.D.

In the past, it took years of work and great expense to create what are known as monoclonal antibodies—lab-produced antibodies derived from a single line of cells. "It was kind of the 'needle in a haystack' approach," said OMRF's Wilson, senior author on the paper. "The problem is they

couldn't pick the cells that made the antibodies against the pathogens that you wanted to fight."

A second method, making hybrid antibodies from mouse B cells (white blood cells that produce infection-fighting antibodies), is faster but more dangerous. If the proteins in the hybrid antibodies weren't compatible, the body could reject the antibodies or react with them in unforeseen ways.

The new process doesn't use traditional antibody derivation methods or human-mouse hybrids. Instead, the OMRF and Emory researchers isolated antibody-secreting cells (plasma cells) from people who had received the influenza vaccine, then cloned the antibody genes from these cells.

"We can recognize which cells are made and then make antibodies from them directly," Wilson said. "It's a rapid and efficient way to make fully human antibodies."

While the research is aimed at combating influenza, it can be used to create treatments for any condition—such as anthrax or smallpox—for which there is already a vaccine. Antibodies might also be produced from the immune responses of people with active or chronic infections. This technology has the potential to serve as therapy for someone who is already infected or provide passive immunity to protect against future infection.

"Vaccines can activate the immune system, but they need time to take effect, and many offer less than 100 percent protection and carry risks of side effects," OMRF President Stephen Prescott, M.D., said. "With further research and testing, this new method might allow a nurse going into the center of an outbreak to receive a shot to keep her safe from infection. Soldiers in the field could keep a shot of anti-anthrax in their

packs in case of a biological attack."

With more research, this new technology could also be key to fighting diseases such as multiple sclerosis and cancer, Prescott said.

Wilson and his clinical collaborator, OMRF's Judith James, M.D., Ph.D., are currently working to make more antibodies from other infections—including hepatitis C, pneumococcal pneumonia, and anthrax. They're also seeking a partner to help produce large quantities of the influenza antibodies.

"We now have an outstanding opportunity to create antibodies against a host of diseases," James said. "This discovery has great clinical potential."

Source: Oklahoma Medical Research Foundation