

# 'Wimpy' antibody protects against kidney disease in mice

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An antibody abundant in mice and previously thought to offer poor assistance in fighting against infection may actually play a key role in keeping immune responses in check and preventing more serious self-inflicted forms of kidney disease, researchers say.

Led by researchers at the University of Cincinnati (UC) and Cincinnati Children's Hospital Medical Center and published online Nov. 2, 2014, in the journal *Nature*, the study finds that the mouse antibody IgG1, which is made in large quantities and resembles a [human antibody](#) known as IgG4, may actually be protective.

"Antibodies protect against pathogens, in large part, by clumping them together and by activating other defenses, including a set of serum proteins, known as complement, and cells that have antibody-binding molecules on their surface called Fc receptors," says Fred Finkelman, MD, Walter A. and George McDonald Foundation Chair of Medicine and professor of medicine and pediatrics at UC.

Finkelman is also an immunobiology researcher at Cincinnati Children's Hospital Medical Center. Richard Strait, MD, an assistant professor of pediatrics at UC and an attending physician at Cincinnati Children's, is the first author of the research published in *Nature*.

"Surprisingly, most of the antibody made by mice is IgG1, which is relatively defective in its ability to clump pathogens, activate complement, and activate cells by binding to their Fc receptors," says

Finkelman, also a physician at the Cincinnati Department of Veterans Affairs (VA) Medical Center. "Humans have a similar type of antibody, called IgG4, which is also relatively defective in these abilities.

"Why should you have such a wimpy antibody? It's the antibody made in the largest amount. Our thought was that in biology, you don't get anything for free," says Finkelman. "If an antibody can kill bacteria and viruses very well, it might also cause inflammation that can harm the animal that makes it. So maybe you need some of these wimpy [antibodies](#) to protect against that type of self-inflicted damage."

Researchers tested their hypothesis by studying what happens when genetically bred mice that cannot make IgG1 are injected with a foreign protein that would spur a normal mouse's immune system to produce IgG1. The genetically bred mouse instead produced another antibody known as IgG3, which affected capillaries in the kidneys and ultimately led to renal failure.

"The mouse's kidneys turned yellow because they essentially shut off blood flow and within a few days there was total destruction of the filtering part of the kidney called the glomerulus," explains Finkelman.

However, injecting IgG1 into mice that could not make the antibody prevented them from developing kidney disease, says Finkelman.

"These findings support our hypothesis about the reason for making antibodies such as mouse IgG1 and human IgG4," says Finkelman.

"They also demonstrate a new type of [kidney disease](#) that can be caused by certain types of antibody, such as mouse IgG3, even without complement or Fc receptors. In addition, our findings suggest that antibodies such as human IgG4 might be useful for treating people who have diseases caused by other types of antibody."

These diseases include [myasthenia gravis](#) and blistering skin diseases, says Finkelman.

Myasthenia gravis is a chronic autoimmune neuromuscular disease characterized by varying degrees of weakness of the skeletal (voluntary) muscles of the body. Individuals with the ailment lose the ability to contract their muscles because their body produces an antibody that destroys acetylcholine receptors in muscle.

"The nerves in their muscles continue to fire and they release the chemical acetylcholine, but there is not much for the acetylcholine to bind to," says Finkelman. "These people become very weak and can actually die because they can no longer swallow well or breathe well."

Individuals with blistering skin diseases make antibodies against the molecules that hold skin cells together, says Finkelman. As a result, the skin cells separate from each other, forming blisters.

"People can lose a lot of fluid and can get infected very easily," says Finkelman. "These are very serious diseases and the treatment is not very good."

**More information:** IgG1 protects against renal disease in a mouse model of cryoglobulinaemia, *Nature*, 2014. [DOI: 10.1038/nature13868](https://doi.org/10.1038/nature13868)

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