Allergy genes flew the coop, according to evolutionary analysis

An estimated 400 million people worldwide suffer from hay fever, and 300 million have the associated condition of asthma, according to the first-ever global allergy impact report published in June by the World Allergy Organization. Allergies have become increasingly common during the last few decades, and experts expect the trend to continue.

Now a team of scientists says that a closer look at the avian immune system might help new and better allergy treatments take flight.

A key culprit in allergies is the antibody immunoglobulin E (IgE), a protein produced by the human immune system. Scientists believe that IgE evolved because it protected our ancestors against parasitic infections. But IgE can also goad the immune system to launch all-out war against innocuous substances like pollen and peanuts.

Instead of producing IgE, birds, reptiles and amphibians make an antibody called IgY. From a structural standpoint, IgY looks similar to IgE, and both are believed to have descended from a common ancestor. But, until recently, scientists did not know if these two antibodies behaved similarly.

In people with allergies, IgE binds white blood cells for long periods of time and instructs these cells to unleash chemicals such as histamines. This cascade of events triggered by IgE can cause anything from itchy eyes to life-threatening airway inflammation. A team from King's College London decided to find out whether IgY also has a similar propensity for sticking to white blood cells, so they took IgY from a chicken and measured its binding affinity.

They found that the bird antibody does not behave like IgE but does act more like human IgG, an antibody that binds loosely to white blood cells and does not cause allergic reactions. "We thought with that structure, you would always have tight binding, but IgY tells us that is not always the case," says Brian Sutton, a professor at King's College and an author of the paper describing the research (*J. Biol. Chem.* **283**, 16384–16390; 2008).

The next step, says co-author Rosy Calvert, is figuring out why the bird antibody has such a low binding affinity, because this might help scientists design therapeutic agents aimed at curbing the activity of IgE.

"We already have a therapy that shows that it's useful to block IgE from docking [onto white blood cells]," says Sarbjit Saini, an allergy and immunology expert at the Johns Hopkins University School of Medicine in Baltimore. "Could we also interfere with something that that allows IgE to stay bound?" Saini says. "By studying the IgY structure, you might be able to gain some insight."

Coco Ballantyne, New York

To know or not to know

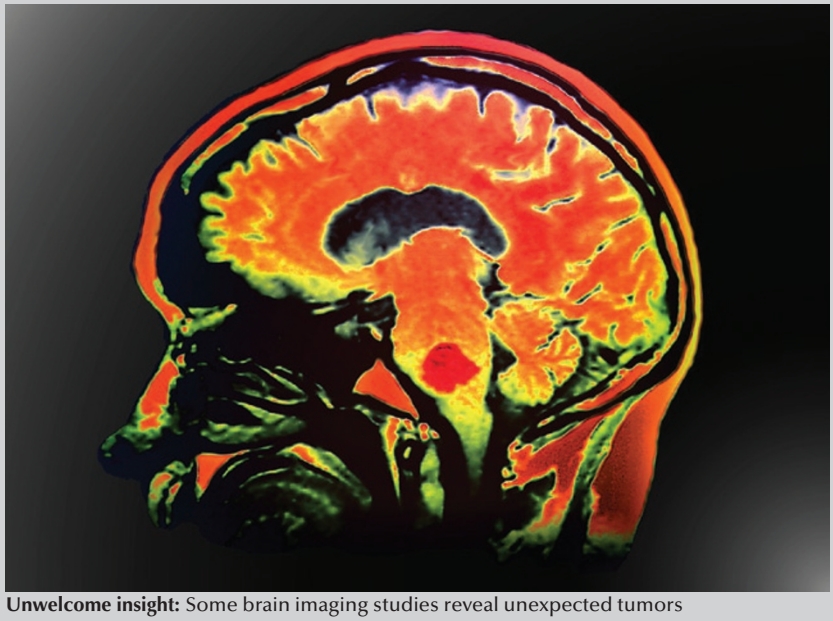
A young, apparently healthy college student enrolls in a memory study at her university. Scientists using magnetic resonance imaging (MRI) technology to map the woman's brain activity stumble across something unexpected: a bright spot on the brain scan that looks like a tumor. These types of incidental findings are becoming increasingly common, and the research community is in dire need of a standardized way to deal with them, says a team of US experts.

Studies on this subject vary, with most showing rates of clinically significant incidental findings in about two to eight percent of participants. But some researchers report a far higher rate of incidental findings, notes Judy Illes, neurology professor at the University of British Columbia in Vancouver, Canada.

"Many programs at top institutions receiving NIH [US National Institutes of Health] funding have done nothing about this," says University of Minnesota Law School professor Susan Wolf, who led a national two-year effort to draft the most exhaustive set of recommendations for managing incidental findings in imaging and genetics research. Wolf's team has designated three categories of incidental findings. The first category, for example, includes findings that clearly indicate a life-threatening condition or genetic abnormality that poses a grave health risk. The guidelines recommend disclosing information in this category to research participants, unless they have previously elected not to know (*J. Law Med. Ethics* **36**, 219–248; 2008).

David Magnus, director of the Stanford Center for Biomedical Ethics in Palo Alto, California, calls the guidelines "a comprehensive examination of the issues," but adds that many gray areas remain. He notes that studies sometimes produce incidental information that can mislead or cause undue alarm. For example, what if researchers find that a subject has a DNA sequence irregularity that could either be linked to a disease or mean nothing at all? Magnus points out, "I think we should be circumspect in giving away this type of information."

Coco Ballantyne, New York



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