Ancient antibody molecule offers clues to how humans evolved allergies

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Scientists funded by the Biotechnology and Biological Sciences Research Council have discovered how evolution may have lumbered humans with allergy problems. The team from the Randall Division of Cell & Molecular Biophysics, King's College London are working on a molecule vital to a chicken's immune system which represents the evolutionary ancestor of the human antibodies that cause allergic reactions.

Crucially, they have discovered that the chicken molecule behaves quite differently from its human counterpart, which throws light on the origin and cause of allergic reactions in humans and gives hope for new strategies for treatment. The work is published today (13 June) in *The Journal of Biological Chemistry*.

Researcher, Dr Alex Taylor said: "This molecule is like a living fossil – finding out that it has an ancient past is like turning up a coelacanth in your garden pond. By studying this molecule, we can track the evolution of allergic reactions back to at least 160 million years ago and by looking at the differences between the ancient and the modern antibodies we can begin to understand how to design better drugs to stop allergic reactions in their tracks."

The chicken molecule, an antibody called IgY, looks remarkably similar to the human antibody IgE. IgE is known to be involved in allergic reactions and humans also have a counterpart antibody called IgG that helps to destroy invading viruses and bacteria. Scientists know that both IgE and IgG were present in mammals around 160 million years ago

because the corresponding genes are found in the recently published platypus genome. However, in chickens there is no equivalent to IgG and so IgY performs both functions.

Lead researcher, Dr. Rosy Calvert said: "Although these antibodies all started from a common ancestor, for some reason humans have ended up with two rather specialised antibodies, whereas chickens only have one that has a much more general function.

"We know that part of the problem with IgE in humans is that it binds extremely tightly to white blood cells causing an over-reaction of the immune system and so we wanted to find out whether IgY does the same thing."

By examining how tightly IgY binds to white blood cells the researchers have found that it behaves in a much more similar way to the human IgG, which is not involved in allergic reactions and binds much less tightly.

Professor Brian Sutton, head of the laboratory where the work was done said: "It might be that there was a nasty bug or parasite around at the time that meant that humans needed a really dramatic immune response and so there was pressure to evolve a tight binding antibody like IgE. The problem is that now we've ended up with an antibody that can tend to be a little over enthusiastic and causes us problems with apparently innocuous substances like pollen and peanuts, which can cause life-threatening allergic conditions."

The next stage of the work is to examine in very fine detail the interaction between the antibodies and the surface of the white blood cell. This is with a view to designing drugs that could alter this interaction and therefore 'loosen' the binding of IgE, making it more like its chicken counterpart.

Source: Biotechnology and Biological Sciences Research Council