Scientists move closer to developing a new class of asthma and allergy drugs

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A team of Biotechnology and Biological Sciences Research Council (BBSRC) funded scientists has moved a step closer to developing a new class of effective asthma and allergy drugs. With new research published today in *The Journal of Immunology*, the team from Barts and The London School of Medicine and Dentistry has found an important target that holds significant promise for millions of people suffering from allergies, asthma, rheumatoid arthritis and a range of other inflammatory diseases. This work confirms that a key component of the body's own response to allergy-causing agents (allergens) can be targeted to reduce allergic reactions in mice.

At present, the majority of treatments for asthma and allergies focus on reducing symptoms such as an inflamed airway or runny nose and itchy eyes. Because allergies are essentially an over-the-top immune response to allergens (such as dust, peanuts, or insect bites), it is possible to give a treatment that dampens down the immune system.

However this is very risky, leaving the person vulnerable to infection, and so is only used in the most extreme cases - for most people treatments that manage the symptoms of allergy are the best option. The BBSRC team led by Professor Bart Vanhaesebroeck has shown that by targeting a molecule called p110delta it is possible to interfere in the allergic reaction before symptoms occur, but without shutting down the immune system.

p110delta is a member of a family of eight proteins called PI3Ks, which

control important biological functions. Their activity is implicated in many different diseases including cancer and they are an important target for drugs. However, drugs that act on all PI3K family members tend to be toxic in the body. For this reason Professor Vanhaesebroeck's team uses genetic techniques to find out which PI3K family members are linked to specific diseases. By gaining a better understanding of each PI3K they hope to target drugs more specifically and reduce the potential for side effects.

The p110gamma member of the PI3K family had previously been implicated in allergic reactions and was thought to be more important than p110delta. However, in the current study, Prof Vanhaesebroeck's team has confirmed that p110delta, but not p110gamma, is important for allergic reactions in a mouse model. These results will help to inform and drive decisions in industry to prioritise which PI3K family members should be targeted for further investment and development. The next step to develop p110delta blockers is now ongoing in industry, and is expected to proceed into the preclinical arena in humans in the near future.

Lead author of the study, Dr Khaled Ali said: "p110delta was first identified in 1997 and, and although we had our suspicions, at that time we had no idea how important it would turn out to be. This work shows that we have the potential to take control of the body's reaction to an allergen and prevent symptoms from occurring."

Professor Vanhaesebroeck added: "This work confirms our previous findings and shows once and for all that in an allergic reaction it is p110delta that is the key player among the PI3K molecules. We are very hopeful that a drug for human patients can be developed in the very near future. This approach offers the potential for therapies for asthma and allergies that target the real causes, not just symptoms."

Professor Nigel Brown, BBSRC Director of Science and Technology, said: “Allergies alone cause misery for millions every year and is of significant cost the UK due to lost productivity. This research, basic bioscience funded by BBSRC, together with industry collaboration could mean an entirely new way of dealing with asthma and allergies.”

Source: Biotechnology and Biological Sciences Research Council

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