Lars Hellman, professor of molecular and comparative immunology at the Department of Cell and Molecular Biology, Uppsala University, is fascinated by the allergic immune system. And above all, IgE-driven allergy. Allergies are one of the greatest medical challenges of our time. An understanding of the underlying causes might make it possible to intervene in and redirect the immune system, find new treatment strategies and, it is hoped, find a solution to one of our most widespread diseases.

Allergies have increased dramatically over the past 40-50 years, affecting an estimated 20-30 percent of the population in many countries in the West. In some school classes, 40-50 percent of children have allergies. Allergies are caused by an overreaction of our own immune systems, probably caused by a combination of hereditary and environmental factors. The most common are the atopic, or IgE-mediated allergies, caused by pollen, animal fur, foods, dust mites, insect stings and asthma.

Is it possible to vaccinate against allergies? Vaccination is one way to control many viral and bacterial diseases affecting us humans. Lars Hellman’s research team studies therapeutic vaccines as a possible way to cure or reduce the suffering of people with allergies. Therapeutic vaccines contain no antibodies as such, but rather stimulate the immune system to produce its own therapeutic antibodies. It is hoped that by marking the foreign antigen as dangerous, therapeutic vaccines will quickly kick-start the immune system. But first you have to know what to vaccinate against. The IgE molecule is an interesting candidate, because it is central in atopic allergies. Other interesting target molecules include regulatory proteins such as growth factors and other inflammatory signal molecules.

“We have been working for some years on a vaccine against IgE in particular, with promising results in rats and primates,” says Lars Hellman. “However, we have had problems with species with high IgE levels in the blood, such as dogs, because we see only a very weak effect from the vaccine. People with asthma and atopic eczema normally have relatively high IgE levels, which therefore makes it difficult to achieve good clinical efficacy. And unfortunately, it is precisely these patients that have the most severe symptoms and the greatest need for new therapies.”

That is why they have continued searching for new possible target molecules to improve efficacy. They have made several interesting discoveries in mice. They have been able to induce severe atopic dermatitis by overexpressing two of the immune system’s signal molecules, IL-18 and TSLP, in skin tissue. Lars Hellman says that these two cytokines, as well as a third signal molecule, IL-33, also appear to be involved in asthma, which makes them very hot candidates for the treatment of asthma and atopic dermatitis. In animal models, very promising results have been achieved with the vaccine against IL-33 for both allergic eczema and asthma. The efficacy of some combination vaccines targeting these cytokines will now be studied in dogs and, we hope, in humans later, too, says Lars Hellman, explaining that depending on the breed, dogs have similar problems to us humans’. Three to 15 percent of dogs get skin problems caused by allergies, and suffer from severe itching.

He goes on to say that they have been able to identify a new immune-stimulating adjuvant that is biodegradable, safe and very effective – a major breakthrough for all therapeutic vaccines. The unavailability of adjuvants has been one of the biggest problems in the development of therapeutic vaccines, and a tough challenge for the whole field. There are high hopes for therapeutic vaccines not only in the allergy area, but also as a way of treating cancer and infectious diseases. Adjuvants enhance the vaccine’s abilities, and are added to improve its efficacy. They are also an imperative in enabling clinical trials of the vaccine in dogs and humans to begin.

The research team is also interested in how the immune system has evolved over time. This includes the timing of the appearance of IgE and its receptors during the evolution of the vertebrates. Mast cells bind IgE to their surfaces by means of specific receptors for that particular type of antibody. Histamine, among other things, is stored within these cells. It is this histamine, along with several other mast cell products, that causes the symptoms we see in allergy. Most of the proteins stored inside mast cells are proteases, which may account for more than 35 percent of the cell’s total protein content. Lars Hellman’s research team has been studying the structure, function and evolution of these proteases for many years. Lars Hellman wonders how we can have a system – the mast cells and IgE – that is so powerful, but also so problematic when things go awry. And why do we have IgE at all, when it causes so much trouble? One way to approach the question is to look at how other species have solved this. Among other things, it becomes apparent that all mammals have IgE,
from the egg-laying platypus through marsupials to humans – but resulting from just one gene. That points to the system being essential to our survival, but also so powerful that it must be kept under very tight control. Lars Hellman’s fascination for biology was awakened at an early age. Even as a child he was very interested in animals and nature.

“My father was a biology teacher, so our house was crammed with all sorts of animals. I have explored the natural world widely ever since. Plants. Fungi. Animals. I am interested in everything, not least fossils,” says Lars Hellman, mentioning that he has a large collection of fossils at home.

He is very keen on his garden, too. He says they pick 100-150 kg grapes each year, which he is delighted to share with his research colleagues at Uppsala Biomedical Centre.