Thomas Boehm – pushing back the frontiers of knowledge

Difficult to believe that the immune systems of animals as diverse as lampreys and humans have some basic functions in common. But they do. The comparison of different animal species enables us to understand the crucial principle of immune defence – on condition that the right investigative approach is chosen. Prof. Dr. Thomas Boehm, director of the Max Planck Institute of Immunobiology and Epigenetics in Freiburg has been doing just this for many years. Based on insights into fundamental immune system functions, Boehm's research is aimed at developing new strategies for the diagnosis and therapy of people whose immune system is not working correctly. He was recently awarded the Ernst Jung Prize for his achievements in the field of human medicine.

Prof. Dr. Thomas Boehm is a physician and natural scientist whose work involves the search for an organization principle of the immune system common to a large number of species.

Born in the city of Gelnhausen in the German state of Hesse in the summer of 1956, Prof. Dr. Thomas Boehm recalls his time as a high-school student and his many early interests that could have taken him down many different career paths. He eventually opted for medicine thanks to his aunt, a WW2 veteran and nurse who convinced him of the importance of a career where he could do good. "I have never really had a specific career plan," says Boehm, now the director of the Max Planck Institute of Immunology and Epigenetics (MPI-IE) in Freiburg. "I just grabbed at opportunities as and when they came up." He studied in Frankfurt, Germany, but also spent some short periods in New York and London. He was awarded his PhD in biochemistry in 1982 on the methylation of DNA.

During his six-year post-doc period, Boehm started looking into the cells of the haemotopoietic system, more specifically the development and genetics of leukaemia. From 1986 to 1991, Boehm conducted research at the Medical Research Council's Laboratory of Molecular Biology in Cambridge, before returning to Germany to become professor of molecular medicine at the University of Freiburg. After three years in Freiburg, he became professor of experimental therapy at the German Cancer Research Center in Heidelberg before returning to Freiburg in 1998 where he was offered the position of director of the Department of Immune System Development at the Max Planck Institute of Immunology and Epigenetics, which he still holds today.

Driven by the fate of the sick

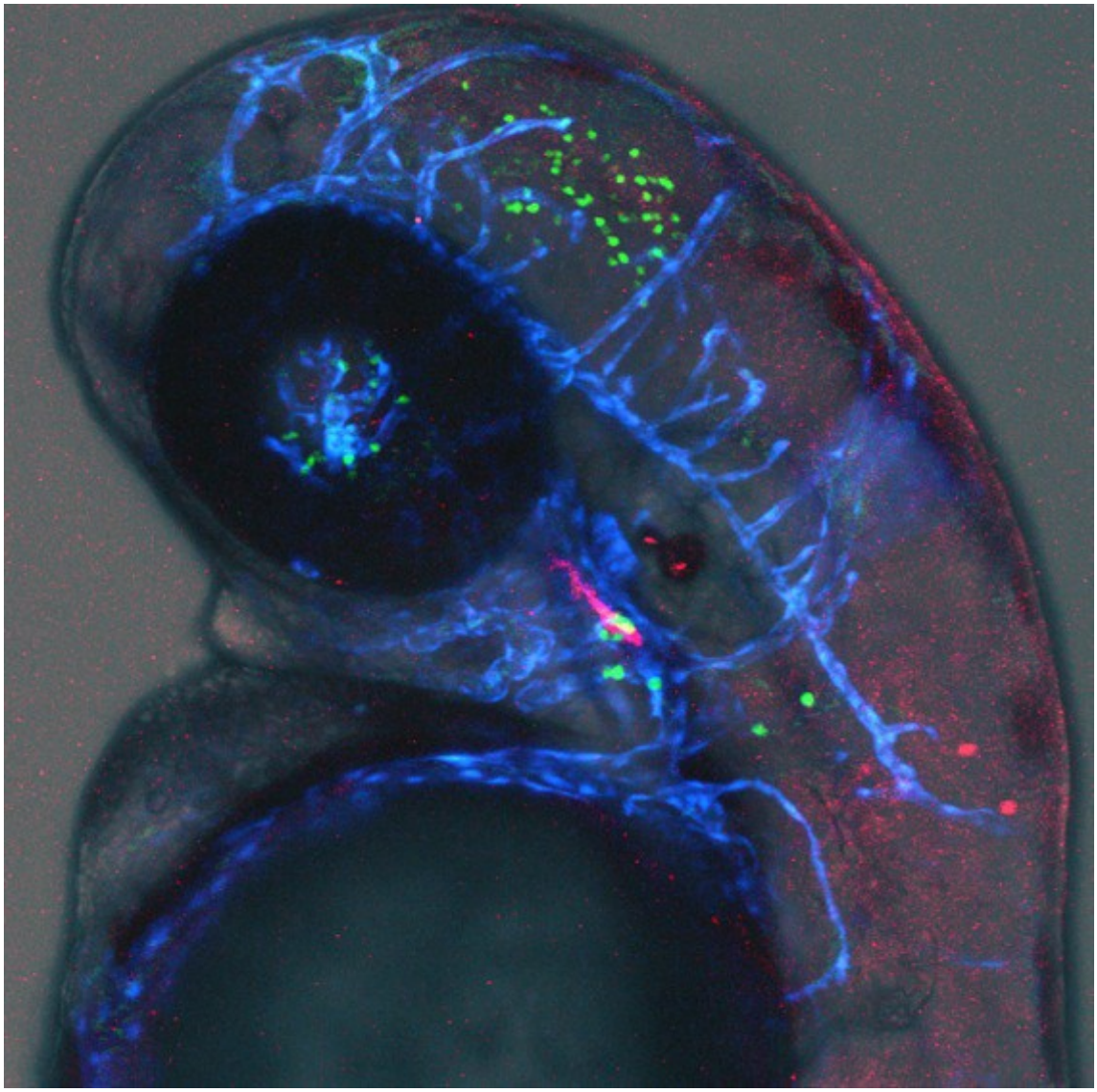
Working at the Children's University Hospital in Frankfurt am Main, Germany, Boehm often had seriously ill patients in his charge whom he was unable to help. This experience was one of his main motivations for wanting to look in more detail at the causes of diseases, in particular those of the haematopoietic system. In addition to relatively rare primary immunodeficiencies, Boehm was initially interested in the more common types of life-threatening leukaemias in children.

"Although leukaemias can be treated efficiently with chemotherapy and bone marrow transplants, we are still seeking to gain an in-depth understanding of how the haematopoietic and immune systems work," says Boehm. "And this requires more theoretical and experimental work in order to improve the chances of being able to help people. What some patients have to go through can really hit you hard," he says.

He regards basic research as a means pushing back the frontiers of knowledge. He is well aware that day-to-day work is often a series of tiny steps forward and that only in retrospect does one realize that one has covered more ground than one thought. Boehm's intention is to move knowledge forward in order to be able to help the next patient better than the last.

Thymus tinkering

Back in Freiburg, Boehm began to focus intensively on the thymus, a primary lymphoid organ that is often referred to as the control system of the immune system. In the thymus, T cells learn to differentiate sick cells from healthy ones and foreign cells from the body's own cells. They recognize and eliminate undesired structures. The thymus is where T cells develop correctly and where thymocytes that may cause autoimmunity are removed. Triggered by chemical signals, precursor



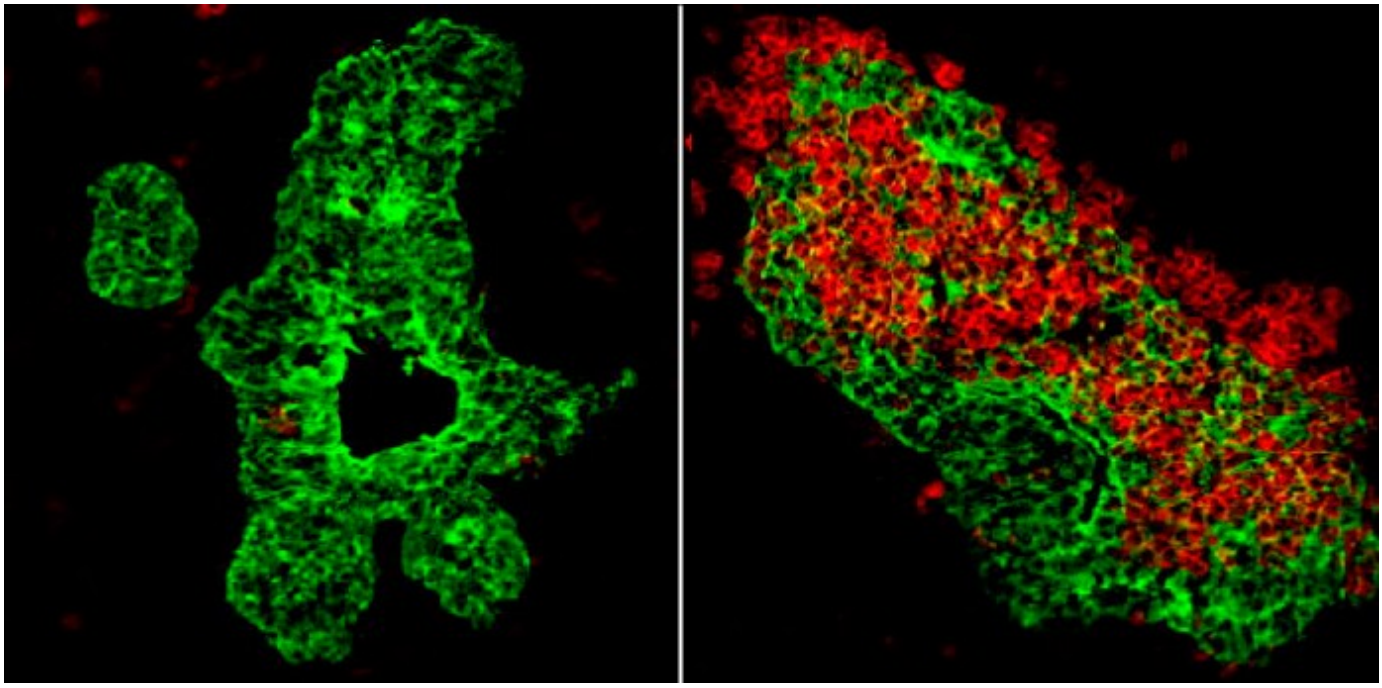
In zebrafish embryos, T cells (green, in the centre of the photo) enter the thymus (red, in the centre of the photo) where they mature. (Blue: blood vessels; the green and red stained cells originate from other tissues.)

cells migrate from the bone marrow into the thymus where they mature into T lymphocytes. The differentiation signal comes from the thymus epithelium. T cells then start to express T-cell receptors on their surface and these T-cell receptors pass a kind of ability test. Only cells that are able to recognize antigens presented by major histocompatiblity (MHC) proteins are released into the body in order to go about their work.

Boehm and his team have been able to elucidate important control mechanisms of T-cell development. "What are the factors required for the establishment of a functional vertebrate immune system?" is one of the central questions Boehm is attempting to answer. He was surprised to find that no more than two thymus factors were needed for T cells to mature into the decisive T-cell progenitors that are able to generate self-reactive receptors in a somatic and essentially random assembly process. From there, the cells quickly become mature T cells. The researchers found that the mechanisms were less complicated than originally presumed.

Deducing the importance of structures found in both lampreys and humans

Using a broad approach in which he and his team studied different animal species, Boehm was able



Thymus tissue (green) that releases the right attractant, attracts progenitor T cells (red) to the thymus where they mature.
© Prof. Dr. Thomas Boehm, MPI-IE Freiburg

to obtain important insights into the development and fundamental functions of the immune system. He used mice, zebrafish, sharks and lampreys for his investigations. The use of different animal models is an excellent approach. "When different species have something in common, it is highly likely to be something related to basic function," says Boehm. "This then helps us to study the fundamental organization of immune systems." Boehm is hoping to use the information to artificially restore the immune system functions.

Boehm believes that this information could be used to develop drugs that can correct faulty regulatory mechanisms that are the basis of diseases such as type I diabetes mellitus. These corrections might enable people to develop tolerance to their own tissue again. Another of Boehm's objectives with potentially far-reaching consequences is the construction of an artificial thymus. He and his team have already made good progress. They have been able to produce artificial thymus tissue in mouse embryos, where they succeeded in growing the basic lines of defence cells up to the stage where they start to express surface receptors. "This is still relatively easy. But things become more complicated when it comes to selection and self-tolerance," says the researcher, going on to add, "but this is exactly where the immunological interest and relevance lies." Yet another scientific nut that he will want to crack.

Basic researcher to the core

Boehm was recently awarded the Ernst Jung Prize for his fundamental contributions to our understanding of the development, differentiation and evolution of the immune system. Other projects are already underway and the award might help him to turn at least some of his projects into reality. Boehm's private life often suffers from his scientific obsession. He has several children and grandchildren, loves Haydn and Robert Gernhard, riding his bike and hiking. But he clearly lacks time to enjoy these hobbies. "Being a scientist is a full-time job and leaves little time for anything else," says Boehm torn between laughter and tears.

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