Harald von Boehmer 1942–2018

Today, few topics in immunology receive more attention than efforts to detect, induce or reinvigorate the immune response to tumors. Although many types of immune cells affect and contribute to anti-tumor immune responses, the initial clinical findings that electrified the field focused on the T cell. Cancer biologists who grabbed the nearest immunology textbook in an effort to fully comprehend and build upon those initial clinical successes will have quickly realized that at their core, such approaches rely on understanding how T cells recognize and respond to antigen. What they may not have realized is how important Harald von Boehmer's work was in laying the foundation for this understanding.

Long before translational research was all the rage, Harald charged a segment of his lab with investigating how fundamental immunological principles might influence the onset of autoimmunity and tumor-specific immune responses. Early on he saw that breaking tolerance could result in an attack on healthy tissue or a tumor, and that suppressing the former and inducing the latter would require the study of two sides of a single coin.

Over the course of his scientific career Harald worked in or ran labs in four countries on three continents. After earning his M.D. from the Ludwig Maximilian University in Munich, Harald moved to Melbourne, Australia, where he obtained his Ph.D. under the supervision of Ken Shortman. During these early years he characterized the functions of the various cell types in the mixed-lymphocyte reaction, an assay essential for the understanding of donor–recipient compatibility in transplantation.

Shortly after receiving his Ph.D., Harald was recruited by Niels K. Jerne to the (now-defunct) Basel Institute of Immunology in Switzerland. There he worked closely with superb visiting and resident immunologists. Aided by the recent identification of genes encoding T cell antigen receptors (TCRs) and breakthroughs in transgenic technology, Harald generated mouse models that laid the foundation for understanding of the positive and negative selection of T cells, as well as T cell lineage commitment in the thymus. Through the use of these mice, he delineated the effect of major histocompatibility complex molecules and TCR cognate antigen on various stages of thymocyte development. For example, Harald demonstrated that the interaction

between the TCR and peptide–major histocompatibility complex determined whether a thymocyte would differentiate along the $CD4^+CD8^-$ T cell lineage or the $CD4^-CD8^+$ T cell lineage. A few years later, Harald's lab identified a previously unknown TCR, which he called the 'pre-TCR'.

In 1996, Harald left the Basel Institute of Immunology to join the Institut National de la Santé et de la Recherche Médicale and Institut Necker (Rene Descartes University) in Paris. At the Institut Necker, Harald found phenomenal immunologists, as well as direct exposure to a hospital with a tradition of the study of immunological conditions, including immunodeficiency and autoimmunity. This environment prompted him to expand the focus of his work to include more translational questions, such as those related to diabetes, T cell anergy and regulatory T cell function. However, during the same period, Harald continued to add substantial basic insights to the understanding of early T cell development; these included the identification of roles for the pre-TCR in thymocyte survival, allelic exclusion and commitment to the αβ or γδ T cell lineage.

Always fascinated by the USA, Harald had many good colleagues and friends there, and on several occasions he considered moving to a US university. In the final days of the 20th century he did, and he remained at Harvard Medical School until his retirement in 2013. Influenced by his new environment in the Smith Building of the Dana Farber Cancer Institute, Harald focused his work even more heavily on human disease. His lab made substantial contributions to the understanding of T cell leukemia, in particular the role of the Notch family of signaling receptors in this malignancy. With colleagues in the lab, Harald also published important insights into the mechanisms through which different T cell populations respond to tumors and destroy pancreatic β-cells. At the same time, he never stopped pursuing knowledge of the basic mechanisms that affect T cell development. While in Boston, his lab described mechanisms that affect the development of regulatory T cells in the thymus and the periphery and continued to publish insights into the structure and function of the pre-TCR.

After closing his Boston lab, Harald returned to his alma mater as a guest professor at the Institute for Immunology of the Ludwig Maximilian University in Munich. In his writings during this period, Harald expressed optimism about the future of immunological research. In one of his final Reviews, he mused that "The curiosity in T cell development is still very much alive even after retirement but I trust that the remaining issues are in good hands of younger scientific colleagues who identify the outstanding questions and think of clever experiments to address them" (von Boehmer, H. *Front. Immunol.* **5**, 424 (2014)).

The immunology community would have enough to thank Harald for if the only thing he left was the enormous body of immunological knowledge he revealed. But he left more than that—he left a global network of trainees, colleagues and friends who benefited from his relentless insistence on rigor, thoroughness, preparedness and creative thinking. As two of Harald's doctoral trainees, we can attest that thanks to his directness, it might not have always felt like we were benefiting while he conveyed his opinion of our work during Monday morning lab meeting. But we can also say with conviction that at the end of the day, it was always obvious that Harald's comments were made with our best interests in mind.

Harald passed away on 24 June 2018 at age of 75. His piercing intelligence, candor and unwavering support will be sorely missed. ❐

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