



Prof. Dr. Jan Klein (1936–2023)

Ronald Bontrop¹ · Martin Flajnik² · Colm S. O’Huigin³ · Masanori Kasahara⁴

Published online: 1 August 2023

© The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2023



Jan Klein was born in 1936 in Stemplovec, a small town in the Czech Republic. Quite fittingly, it was also the year that Peter Gorer discovered the Major Histocompatibility Complex (MHC). Jan graduated from the Charles University in Prague in 1955 and earned his Ph.D. in 1965 at the Czechoslovak Academy of Sciences. In 1968 he moved to the USA and held postdoctoral and then independent positions at Stanford, Michigan, Texas, and Miami (FL). From 1977 to 2004 he was the director of the Max-Planck-Institut für Biologie in Tübingen, Germany. Upon his retirement he moved back to the USA as the Frances R. and Helen S. Pentz Visiting Professor of Science and adjunct professor of biology at The Pennsylvania State University.

Initially Jan was trained as a botanist, but he is most famous for his work in the field of immunogenetics. His scientific legacy is enormous. His interest in immunogenetics, in particular the mouse MHC (*H2* complex), was cultivated at the Czechoslovak Academy of Sciences where he started his Ph.D. work in the laboratory of Milan Hašek, who independently discovered the phenomenon of immunological tolerance in birds. There, Jan obtained evidence for two class I regions separable by recombination in the *H2* complex. This work developed into the proposal of the two-locus model in 1972 by Jan and his postdoctoral mentor Donald C. Shreffler. This model formulated that the complexity of *H2* serology that plagued immunologists could be accounted for by postulating only two class I loci, *H2-K* and *H2-D*, thus eliminating considerable confusion over class I genetics. Jan also made important contributions to our understanding of class II loci. First, *H2* recombinant mice generated by him and by others played an essential role in mapping the immune response (*Ir-1*) locus within the *H2* complex. This collaborative work with Hugh O. McDevitt, who discovered the *Ir-1* locus and its role in humoral adaptive immunity, dramatically increased the interest of the immunological community in the *H2* complex. Jan supported the free availability of mouse strains that characterized the work of the *H2* pioneers. Second, Jan’s group was the first to serologically identify I-region associated (Ia) antigens, now known as class II molecules. From these seminal accomplishments, Jan was recognized as an innovator

✉ Martin Flajnik
mflajnik@som.umaryland.edu

Ronald Bontrop
bontrop@bprc.nl

Colm S. O’Huigin
ohuiginc@mail.nih.gov

Masanori Kasahara
mkasaha@med.hokudai.ac.jp

¹ Biomedical Primate Research Centre (BPRC), Department of Comparative Genetics & Refinement, Lange Kleiweg 161, Rijswijk 2288GJ, Netherlands

² Department of Microbiology and Immunology, University of Maryland School of Medicine, Bressler Research Building, Room 3-056, Baltimore, MD 21201, USA

³ Laboratory of Integrative Cancer Immunology, Center for Cancer Research, National Cancer Institute, Building 37, Room 4140B, Bethesda, MD 20852, USA

⁴ Hokkaido University, 5 Chome Kita 8 Jonishi, Kita Ward, Sapporo, Hokkaido 060-0808, Japan

by the entire immunological community. Most notable was his ability to digest and synthesize rapidly expanding, often confusing data and provide the proper interpretation. This is epitomized in his acclaimed review entitled “The traditional and a new version of the mouse *H-2* complex” published in 1981, which emphasized that a single *H2* locus is pleiomorphic and controls several functions such as allograft rejection, cell-mediated lymphocytotoxicity, mixed lymphocyte reaction, immune response, immune suppression, and restriction of T-cell specificity. His foresight is also evident in introducing the widely used terms, MHC class I and class II, which turned out to be compatible with their similarities in both structure and function.

Jan was also keen on introducing evolutionary biology into immunology. In the latter half of his career, he put considerable effort into understanding the evolution of the MHC and generally the origins of the adaptive immune system. He was particularly interested in the generation and maintenance of MHC polymorphism. In this regard, he fathered the concept of trans-species evolution of MHC alleles, initially from the study of rodent MHC and then from the comparison of nonhuman primate MHC alleles. This theory proposed that certain MHC class I and II alleles emerged prior to the divergence of species. Now we understand that the sharing of alleles in a strict sense is only observed between highly related species that are often subject to introgression, but the selectively driven maintenance of MHC class I and II allelic lineages between related species is a well-established phenomenon. Such ancient origins of alleles or allelic lineages called his attention to the problem of speciation and enabled him to estimate the size of founding populations in the process of speciation and adaptive radiation in collaboration with Naoyuki Takahata. The collaboration also provided insights into the relative strengths of mutation and selection during MHC evolution. A synthesis of Jan’s evolutionary work was published in the book “*Where do we come from?*” (Springer-Verlag, 2002) co-authored with Takahata. To understand the long-term evolution of the MHC, he studied the MHCs of various non-mammalian species, with a particular focus on bony fishes. He discovered that class I and class II genes are not linked in bony fish, indicating that they need not be on the same chromosome to carry out their distinct functions. By the mid-1990s, it became clear that all jawed vertebrates have an MHC along with immunoglobulins and T-cell receptors, but it was not known whether jawless vertebrates have an MHC. In collaboration with Max D. Cooper, Jan conducted comprehensive transcriptome analysis of lamprey lymphocytes and came to the conclusion that the MHC most likely exists only in jawed vertebrates, which subsequently turned out to be the case. He also initiated the introduction of a nomenclature system for MHCs in different species. This communication was published in

Immunogenetics, and is one of the most frequently cited papers of its kind.

Jan was a very productive scientist who authored more than 500 peer-reviewed papers and was awarded many international prizes. He was also an incredibly talented and prolific writer, authoring books which were highly appreciated among members of the community. Among them are three immunology textbooks: “*Immunology: The Science of Self-nonsel Self Discrimination*” (Wiley-Interscience, 1982), “*Immunology*” (Blackwell, 1990), and “*Immunology, 2nd edition*” coauthored with Václav Hořejší (Blackwell, 1997); and monographs on the MHC “*Biology of the Mouse Hictocompatibility-2 Complex. Principles of Immunogenetics Applied to a Single System*” (Springer-Verlag, 1975) and “*Natural History of the Major Histocompatibility Complex*” (Wiley, 1986). Some forty years after its publication, “*Natural History of the Major Histocompatibility Complex*” has become a classic and is still highly relevant. In particular, the MHC discovery section presents a captivating and thorough description of the key events and pioneering work of the godfathers that paved the way for the establishment of immunogenetics. Some of its sections also illustrate that Jan had a great sense of humour.

At the start of his career, Jan was trained as a teacher, and he became a great one. Under his mentorship in the USA and in Europe, countless scientists were trained and educated. Many of Jan’s proteges have become reputed professors in the fields of immunology or immunogenetics. Jan was a hard worker who strived for excellence and expected nothing less from his co-workers. In that regard, Jan was not easy-going and often willing to “stir things up” and generate controversy. All of us who worked with him or knew him well will remember those fierce debates at conferences. When Jan was convinced of something, he would passionately stand his ground during the exchange of arguments. However, no one is perfect, and Jan was sometimes wrong in his judgments. One example is the antigen presentation pathway that was put forward by Emil Unanue, which Jan accepted only after many years, when the evidence for antigen processing became unassailable. Jan probably never realized that his opinions were sometimes so strongly expressed that he inspired many colleagues in the field to prove that he was wrong! In retrospect, in this way he clearly also helped to advance scientific knowledge. As mentioned earlier, Jan had a very strong character and was not averse to voicing his opinion. For those who never met him, we recommend reading the article “Hegemony of mediocrity in contemporary sciences, especially in immunology,” which was published in *Lymphology*. A copy can readily be found on the internet.

If one knew Jan personally, however, one would sooner or later realize that he could also be a gentle giant. The three

of us remember those moments when we sat, in his garden for instance, and discussed topics outside of science. He was interested in the social aspects of life, and always asked about one's family or colleagues that he had not seen for a while. His scientific education occurred during the Lysenkoist hegemony, prompting him to read widely and hone his autodidactic skills. He became a walking encyclopaedia, conversant in music, history (and the history of science), culture, architecture, and many other non-scientific aspects of life. He could be a real joy with whom to share ideas and to spend quality time.

The scientific journal *Immunogenetics* was inaugurated in 1974. The first editor-in-chief was one of Jan's heroes, George D. Snell, who received a Nobel Prize for the discovery of the MHC. Jan became managing editor in 1974, and in 1978 he was made editor-in-chief, a position he held until 1998. In 2024, *Immunogenetics* will be celebrating its 50th

anniversary. This would not have been possible if Jan had not provided the underpinning for the journal with his critical discoveries as well as supplied a solid foundation for the future of the journal itself. The past and present (co)editors are grateful to Jan Klein for being a teacher, an inspirational leader, and a mentor. We have fond, indelible memories of our association with Jan, and are grateful for the opportunities that he offered us over the past four decades. In our opinion, the *Immunogenetics* society lost one of its most iconic characters with the death of Jan Klein on May 7, 2023. We wish his family and colleagues strength in this difficult time.

We are indebted to Dr Akie Sato for providing the photograph of Prof. Dr Jan Klein.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.