

Olli Mäkelä

* 31.8.1929 † 27.5.2022



Professor Emeritus of Serology and Bacteriology at the University of Helsinki Valto Eero Olavi (Olli) Mäkelä died in Helsinki on 27 May 2022. He was born in Voikkaa, Kuusankoski, on 31 August 1929. He graduated as a Licentiate of Medicine from the University of Helsinki in 1955 and earned his PhD in 1957. He became Docent in Medical Genetics (the first in Finland) in 1962. Olli Mäkelä was Director of the State Serum Institute 1965–1968, Personal Extraordinary Professor of Immunology at the University of Helsinki 1968–1970 and Research Professor at the Academy of Finland 1970–1977. His main post was his professorship in bacteriology and serology from 1972 to 1995.

The main area of research in Olli Mäkelä's early career was blood groups and blood group immunity, or serology, where blood group antibodies were studied from serum samples. With his wife Pirjo Mäkelä, he studied bacterial genetics and bacteriophages, which he later also used as models in his immunological work. Blood groups were initially identified using lectins extracted from the seeds of various plants. Lectins have specificity to recognize various sugar structures. Many seeds had already been collected in a large trunk at

the department by Mäkelä's predecessors, particularly Professor Werner Oswald Streng. Mäkelä later turned his interest towards antibodies, the genetic determination and properties of their structure and function. He continued to pursue this line of research throughout his career. This is no wonder, as antibodies are some of the most complex molecules found in humans. They can be used to identify millions of different structures. How antibodies can be made highly specific for identifying certain structures and, on the other hand, maintain an extremely wide repertoire, without destroying their structures, are some of the key questions in immunology.

Olli Mäkelä made a research visit to the laboratory of Nobel laureate Joshua Lederberg at Stanford University in the early 1960s. There, he conducted research with the Australian (Austria-born) immunologist Gustav Nossal on the genetics underlying the multiplicity of antibodies and the ability of single cells and cell clones to produce antibodies. After this (1963–1965), Mäkelä moved to London (Mill Hill) to work in the laboratory of Nicholas Avriani Mitchison, studying the ability of lymphocytes to produce antibodies. One of Olli Mäkelä's most significant findings was that

one cell only produces one type of antibody. This has proven to be an extremely important immunological feature. Mäkelä's work paved the way for later research on monoclonal antibodies and the generation of antibody genes through somatic recombination and somatic mutations. This "gene roulette" can produce tens of millions of different antibodies. Research on these topics brought the Nobel Prize to Georges Köhler from Germany and César Milstein from Argentina (1984) and Susumu Tonegawa from Japan (1987). A researcher on Mäkelä's team, Matti Kaartinen, even completed his post-doc in César Milstein's laboratory in Cambridge, England. Some of this work was based on the oxazolone antibody model, developed in Mäkelä's laboratory, which Kaartinen transferred to Milstein's laboratory (Kaartinen et al., *J Immunol*, 1983). César Milstein was appointed Honorary Professor of the University of Helsinki at a conferment ceremony in 2000.

Olli Mäkelä's research was classic basic immunology, but with a focus on fundamental questions and scientific principles. He had an eye for detail, which often gave rise to broader principles. In addition to the antibody specificities mentioned above, he also studied their other properties, the subclasses of IgG antibodies, genetically determined allotypic markers (such as Gm allotypes) and affinity. From England, the Department of Serobacteriology received a traditional, manual DNA sequencing method, developed by Fred Sanger, which was used to read the sequences of antibody genes. One person would read them out loud (ACCGGTT...), while another would write them down. Mäkelä was interested in immune reactions against small model molecules, so-called haptens (oxazolone, DNP,

NIP). Complex phenomena, such as somatic hypermutations, could thus be studied using models that were as simple as possible. This eventually led to one of Olli Mäkelä's own scientific discoveries, so-called heteroclitic antibodies. These are antibodies that react better with a related immunizing antigen than the antigen itself (Mäkelä, *J Immunol*, 1965). The immunogenetic structures are cross-reactive, but probably due to genetic influence or structural reasons, the immune reaction is stronger towards a similar structure. This showed that the immune reaction does not match the immunizing structure one-to-one.

Mäkelä considered the reliability of immunological research to be important. He helped develop multiple methods for measuring the content and bond strength of various substances and antibodies generated by infections. The antibody avidity research conducted on the initiative of Klaus Hedman has led to many diagnostic applications for distinguishing new infections from old immunity. The demand for accuracy and precision also led Mäkelä to review other people's research, and competitive comparisons were made especially with the immunologists in Turku regarding *Yersinia* and *Legionella* bacteria findings and their serology.

Olli Mäkelä's manner of presenting results was exact, albeit somewhat difficult to understand at times. The topics were complex, and Mäkelä did not want to distort reality by simplifying things. For example, one publication included an image of a gel run and a slightly apologetic caption stating that the researcher had forgotten to mark the application points of the samples. The reader should have understood that in isoelectric focusing it does not matter where the samples are

originally placed, because the strong electric field will in any case move the molecules to their own isoelectric points. Mäkelä's subtle humour would sometimes emerge in various situations. The title of an early publication concerning blood groups was "A weak B containing anti-B" (Mäkelä & Mäkelä, *Ann Med Exp Biol Fenn.* 1955). Another memorable incident happened during a lecture when Olli Mäkelä, for lack of a spoon, calmly used a pointer to stir sugar in his coffee in front of the audience so that the thicker end of the stick, 3 metres up in the air, hardly wobbled at all.

Olli Mäkelä had a large network of international contacts. He knew the world's leading figures in immunology and was held in great esteem by basic immunologists. He helped establish the Finnish Society for Immunology (FSI) in 1974 and make it a member of the Scandinavian Society for Immunology (SSI). He was also involved in organising the European Congress of Immunology in Helsinki in 1975 when, due to the OSCE Summit held at short notice at the same time, many of the hotel bookings made by visitors were cancelled. Mäkelä did not hesitate, but welcomed as many guests as he could to his home and left them with many positive memories. The story goes that they tested if you could cook an egg by placing it at head height in the sauna. At work, Olli Mäkelä was a somewhat intimidating figure due to his uncompromising attitude. If you found a note on your desk saying "See Olli", you could never be sure what kind of consultation you were going to get.

Sharing knowledge was important to Olli Mäkelä. His immunology lectures were easy to follow. He initiated and co-authored

the first microbiology textbook in Finnish, which also covered immunology (published by *Duodecim*). He published more than 200 scientific articles in international journals and many articles in Finnish in the *Duodecim* journal to educate medical professionals. The topic of one such article was immunological tolerance, or "accustomization", as he called it (*Duodecim* 1968).

Olli Mäkelä received recognition for his merits. He was appointed a member of the Finnish Academy of Science and Letters already in 1973. The year before (1972), he received the Matti Äyräpää Prize and gave a lecture on the topic "Regulation of the Immune Response". He received the Medical Society of Finland (*Finska Läkaresällskapet*) Jubilee Prize in 1985. Olli Mäkelä served as Dean of the Faculty of Medicine at the University of Helsinki 1987–1995.

As is typical for a scientist, Olli Mäkelä was intelligent, honest and a critical thinker, but humble as a person. Before making decisions, he would listen to what others had to say and gather enough information to understand all the different viewpoints and be fair. After retirement, he no longer wanted to be involved in the matters of the department or the faculty, but eagerly cared for, mentored and entertained his children, grandchildren and great-grandchildren together with Pirjo. In terms of work, he dedicated himself to forest management and enjoyed opening the doors of his outbuildings to guests, revealing tractors, each one bigger than the last. Olli Mäkelä had a strong, original personality that is remembered by many. His scientific legacy has been fundamental to the development of vaccines, biological medicines and cancer therapies based on antibodies.

*Seppo Meri, Jukka Pelkonen
and Tomi Mäkelä*