Editorial: Making Science Fun – A Tribute to Our Colleague and Friend, Prof. Antonius G. Rolink (1953–2017)

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Editorial on the Research Topic

Making Science Fun – A Tribute to Our Colleague and Friend, Prof. Antonius G. Rolink (1953–2017)

RESEARCH TOPIC CONTENT

This Research Topic was organized to honor the memory of our dear friend Antonius “Ton” Rolink (April 19, 1953–August 06, 2017). The contributions are from his former students, colleagues, and collaborators. In the form of original research and review articles, these papers cover many of Ton’s scientific interests in different aspects of lymphocyte development in mouse and man. Thus, the majority of articles concern B cell biology, ranging from papers by Pang et al. and Kim and Schaniel on stem cells to Klein et al. and Winkler and Mårtensson on B cell precursors, Brennecke et al. and Hobeika et al. on inducible B cell development, Smulski and Eibel and Kowalczyk-Quintans et al. on B cell Activating Factor (BAFF) and the impact of BIM on B cell survival, Greaves et al. on tolerance and Song and Matthias on the formation of germinal centers. However, Ton’s research was also motivated by his continuous interest in T cells and graft-versus-host reactions, lymphoid tumours and in the application of antibody technology to develop novel therapeutic approaches. These subjects are covered by the contributions of Mori and Pieters on T cells, Calvo-Asensio et al. on T cell progenitors, by the article of Ghia on leukemia development, by Heiler et al. on GvH and by Hellmann et al. on human antibody libraries.

TON’S SCIENTIFIC CAREER

Ton Rolink began his scientific career as a PhD student in the group of Ernst Gleichman at the University of Amsterdam focussing on the mechanisms of T cell mediated immunopathology during Graft versus Host Disease (GvHD). This resulted in a remarkable output of 12 publications, including five in the Journal of Experimental Medicine (1–12).

In 1983, he moved to the Basel Institute of Immunology (BII) as a Scientific Member, joining the laboratory of Fritz Melchers. In the following years, the team developed the technologies and skills that led to the discovery of fundamental principles in B cell development (13–16), B cell tolerance (17) and autoimmunity (18–20). Over the years, Ton and his collaborators generated many monoclonal antibodies, some of which, including those to precursor B cells (21), the IL-5 receptor (22), CD40 (23), CD93 (24), and BAFF (25), resulted in numerous novel findings and publications.

One of the key technical advances in which Ton made a significant contribution was the establishment of stroma cell-based in vitro system allowing the cultivation of B cell precursors
starting with single hematopoietic stem cells (26). Since Ton
indeed had “green fingers” for growing cells, he was naturally
gifted at cell culture. Therefore, when Stephen Nutt in
Busslinger’s laboratory showed that the transcription factor Pax5
(or BSAP) was essential for B lymphopoiesis (27) the scientific
collaboration established with Ton’s laboratory continued. This
culminated in 1999 with two seminal articles in Nature describing
how Pax5-deficient pro B cell lines could proceed along different
developmental pathways to become antigen-presenting dendritic
cells, osteoclasts, granulocytes or natural killer cells in vitro
and to T cells following reconstitution of mice in vivo (28,
29). The realization that the transcription factor Pax5 was a
master regulator of B cell development had a profound influence
on the field of haematopoiesis and lymphopoiesis and opened
new research avenues allowing in depth analysis of the roles
of other transcription factors in the regulation of lymphocyte
development (30–36).

By refining the conditions of in vitro B cell development,
the roles of different chemokines and cytokines implicated in B
cell development and homeostasis were also investigated (37–
41) including the detailed dissection in mouse and man of
the role of the B cell Activating Factor (BAFF) (42, 43) in
normal B cell homeostasis and as well as in the development of
autoimmunity (44–47). Using emerging molecular technologies,
Ton and his group dissected B cell development at the single cel-
level, analysing their genotypic and transcriptomic profiles (48–
50). For this, techniques capable of identifying rearrangement
of D\(H\) and J\(H\) genes on one immunoglobulin heavy chain allele,
corresponding to one molecule of rearranged DNA, could be
detected (51). Without a doubt, Ton’s research contributions
were recognized world-wide and he became one of the leaders
in studies of mouse and human B cell development.

Having helped to show the multi-lineage differentiation
capacity of B220\(^+\)CD117\(^{low}\)CD19\(^−\) Pax 5 KO pro-B cell lines,
Ton became interested in trying to identify a cell type with
identical phenotype and equivalent differentiation capacity
in the bone marrow of normal mice. This progenitor was
indeed identified and referred to as an Early Progenitor with
Lymphocyte and Myeloid Potential, or EPLM (52). More recent
experiments using additional markers and taking advantage
of single cell RNA sequencing, has revealed that the original
EPLM population is both phenotypically and genotypically
heterogeneous with the earliest member being already committed
to either lymphoid or myeloid lineages (53, 54).

Seeing that mice could be reconstituted with genetically-
modified B cell progenitors grown in vitro and that Pax5 KO
(29) and EPLM (52) could reconstitute the T cell compartment
led Ton to expand his studies to T cell development (55).
Realising that therapeutic use of progenitors grown on stromal
cells would pose difficulties for clinical approval, he established
stromal cell-free culture conditions whereby mouse and human
T cell progenitors could be expanded and differentiated without
stromal cells. The system developed was affectionately called “the
plastic thymus” (56) allowing the dissection of signals involved
in T cell commitment (57–59). In recent years, this led to
a series of experiments investigating the possible instructive

![FIGURE 1](https://example.com/figure1)

**FIGURE 1** The cartoon has been painted and kindly provided by Professor Daniela Finke, who has been for many years Ton Rolink’s colleague at the Department of Biomedicine, University of Basel.
role of cytokines, in particular IL-7 and Flt3L, on lymphocyte development (53, 60–62). This T cell work set the foundation for Ton’s subsequent studies on T cell autoimmunity. Using T cell progenitors from genetically-modified mice, his group was able to expand and reconstitute the T cell compartment of immunodeficient recipients (63). However, the “plastic thymus” could not replace one of the key functions of the thymus, namely the generation of regulatory T cells (64). Without endogenous regulatory T cells, after a few weeks recipient mice reconstituted with in vitro generated T cell progenitors invariably developed immunopathology reminiscent of that seen in GVHD. Addition of regulatory T cells to the T progenitor inoculum was sufficient to prevent disease onset (64), providing Ton with a functional in vivo assay for regulatory T cell function.

Ton’s interest in autoimmunity associated with GVHD, initiated whilst a PhD student and continued at BIL and the University of Basel, interested him until the very end of his career. In his latest publications, he looked at this topic from a T-cell (Heiler et al.) and a B-cell perspective (65). In the first, Heiler et al. analyzed the contribution of the different T cell compartments at various stages of disease, the latter (65) showed the processes by which self-reactive antibodies might arise in aged mice.

Ton Rolink’s key findings in the field of lymphocyte biology as well as his talent for developing numerous monoclonal antibodies and cell culture systems now used as research tools in many laboratories world-wide, were always complemented by his open, friendly, and generous personality and his infectious good humor. Throughout his scientific career, Ton worked almost daily at the bench. He was always ready to share his ideas, tools and expertise with his colleagues and collaborators, which in times of a steadily growing number of Material Transfer Agreements (MTAs), research contracts and “highly confidential information,” was a rare phenomenon among scientists. Therefore, Ton will not only be remembered for his exceptional work ethic and output, but also, and maybe even more, for his exceptional way of making science fun. He will also be remembered by his colleagues and collaborators through their projects that live and thrive thanks to his reagents and spirit (Figure 1).

His complete bibliography can be found in the Appendix and the following is a link to Ton’s publications on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/?term=Rolink+A.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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**Conflicts of Interest Statement:** The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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APPENDIX

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