BIOGRAPHICAL SKETCH

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NAME: Ulrich H. von Andrian

eRA COMMONS USER NAME: vonandrian

POSITION TITLE: Mallinckrodt Professor of Immunopathology

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Ludwig-Maximilians Univ. Munich, Germany	M.D.	1989	Medicine
Ludwig-Maximilians Univ. Munich, Germany	Ph.D.	1992	Neurology/Neurosurgery

A. Personal Statement

During the past 26+ years, I have been conducting basic research in immunology using a broad range of molecular, cellular and whole animal approaches. A major scientific focus has been on the molecular mechanisms of immune cell migration and homing in lymphoid and non-lymphoid tissues using intravital microscopy techniques.

B. Positions and Honors

Positions:

1988 – 1989 Internship, Dept. of Surgery, Zentralklinikum Augsburg, Germany; Dept. of Neurology, Univ. of Michigan, Ann Arbor, MI; and Medizinische Klinik I, Klinikum Großhadern, Munich, Germany
1989 – 1992 Postdoctoral Fellow, La Jolla Institute for Experimental Medicine, La Jolla, CA
1989 – 1992 Visiting Scholar, Dept. of Applied Mechanics and Engineering Sciences, UCSD, La Jolla, CA
1992 – 1993 Postdoctoral Fellow, Dept of Pathology, Stanford University Medical Center, Stanford, CA
1994 – 1999 Assistant Professor of Pathology, Harvard Medical School, and Junior Investigator, CBR Institute for Biomedical Research, Boston, MA
1999 – 2003 Associate Professor of Pathology, Harvard Medical School, and Investigator, CBRI
2003 – 2011 Professor of Pathology, Harvard Medical School, and Senior Investigator, CBRI
2006 – Edward Mallinckrodt Jr. Professor of Immunopathology, Harvard Medical School
2011 – Professor of Microbiology and Immunobiology, Harvard Medical School, Boston, MA
2013 - Program Leader, Basic Immunology and Member, Steering Committee, Ragon Institute at MGH, MIT and Harvard, Cambridge, MA

Awards:

1989 – 1991 Research stipend of the International Institute for Microcirculation
1992 – 1994 Research stipend (Forschungsstipendium) of the Deutsche Forschungsgemeinschaft
1997 Microcirculatory Society Wiederhielm Award
2004 – Amgen Outstanding Investigator Award (ASIP)
2004 – 2005 Iacocca Faculty Fellow, Joslin Diabetes Center, Boston, MA
2006 – Bowditch Award (APS)
2007 BD-Biosciences Award (AAI)
2010 – Landis Award (MCS)
2010 – Cox Program for Entrepreneurial Initiative Award, Harvard Medical School

Memberships:

1994 – Member, Microcirculatory Society (MCS)
1998 – Member, American Association of Immunologists (AAI)
1998 – Member, North American Vascular Biology Organization (NAVBO)
2000 – Elected Member, American Association of University Pathologists ("Pluto Society")

2002 – Member, American Society for Investigative Pathology (ASIP)
2002 – Elected Member, European Academy of Sciences
2004 – Member, The American Society for Cell Biology (ASCB)
2005 – Member, American Physiological Society (APS)

Editorial Boards:
1999 – 2004 *Microcirculation*
1999 – 2000 *American Journal of Physiology: Heart and Circulatory Physiology*
2002 – *Journal of Experimental Medicine*
2003 – Faculty of 1000
2004 – *Current Immunology Reviews*
2005 – Associate Editor, *Immunity*
2007 – *Journal of Vascular Research*
2007 – *The Open Microbiology Journal*
2007 – *The Year in Immunology* (NY Academy of Sciences)
2008 – 2010 Board of Reviewing Editors, *Science*
2009 – *Cell*

C. Contribution to Science

1. During my postdoctoral work, I performed intravital microscopy (IVM) in inflamed rabbit mesentery venules, which resulted in the first *in vivo* demonstration that intravascular neutrophil adhesion depends on the sequential engagement of selectins and integrins. This discovery provided an experimental foundation for the paradigm that leukocyte trafficking is orchestrated by multi-step adhesion cascades, a concept that has since become a standard component of every basic Immunology textbook. Building on this discovery during the past 20+ years, my laboratory has introduced many new IVM approaches and other experimental strategies to further investigate how the trafficking of specialized leukocyte subsets is regulated by multi-step adhesion cascades. This has resulted in a series of discoveries that have dissected the molecular underpinnings for subset- and tissue-specific leukocyte migration to a variety of lymphoid and non-lymphoid tissues at both steady-state and in pathological settings.
   a. von Andrian, U.H., Chambers, J.D., Mc Evoy, L., Bargatze, R.F., Arfors, K.E., and Butcher E.C. Two step model of leukocyte-endothelial cell interaction in inflammation: Distinct roles for LECAM-1 and the leukocyte ß2 integrins in vivo. *Proc. Natl. Acad. Sci. USA* 88: 7538-7542, 1991. PMID: 1715568
   b. Mazo, I.B., Guttierrez-Ramos, J.-C., Frenette, P., Wagner, D.D., Hynes, R.O. and von Andrian, U.H. Hematopoietic progenitor cell rolling in bone marrow microvessels: parallel contributions by endothelial selectins and VCAM-1. *J. Exp. Med.* 188: 465-474, 1998. PMID: 9687524
   c. Mora, J.R., Bono, M.R., Manjunath, M., Weninger, W., Cavanagh, L.L., Rosemblatt, M. and von Andrian, U.H. Selective imprinting of gut-homing T cells by Peyer's patch dendritic cells. *Nature*, 424:88-93, 2003. PMID: 12840763
   d. Massberg. S, Schaerli, P., Knezevic-Maramica, I., Köllnberger, M., Tubo, N., Moseman A.E., Huff, I.V., Junt, T., Wagers, A.J., Mazo, I.B. and von Andrian, U.H. Physiological recirculation of haematopoietic progenitor cells through blood, lymph and extramedullary tissues. *Cell* 131: 994-1008, 2007. PMID: 18045540
2. Upon establishing my first independent laboratory at the Center for Blood Research at Harvard Medical School, I developed a microsurgical approach to perform IVM in murine inguinal lymph nodes (LNs) to investigate lymphocyte homing via high endothelial venules (HEVs). This phenomenon was first documented by Gowans' classic studies in the 1960s, but was still poorly understood at the cellular and molecular level. This technical advance, which has since been adopted by multiple other laboratories, permitted us, for the first time, to analyze lymphocyte interactions with HEVs at the single-cell level and under precisely controlled (patho)physiological conditions.
   a. von Andrian, U.H. Intravital microscopy of the peripheral lymph node microcirculation in mice. *Microcirculation*, 3 (3): 287-300, 1996. PMID: 8930886
   b. Diacovo, T.G., Puri, K.D., Springer, T.A., and von Andrian, U.H. Platelet-mediated lymphocyte delivery to high endothelial venules. *Science*, 273: 252-255, 1996. PMID: 8662511

c. Warnock, R.A., Askari, S., Butcher, E.C., and von Andrian, U.H. Molecular mechanisms of lymphocyte homing to peripheral lymph nodes. *J. Exp. Med.* 187: 205-216, 1998. PMID: 9432978

d. Stein, J.V., Rot, A., Manjunath, N., Nakano, H., Luo, Y., Quackenbush, E.J., Gunn, M.D., Matsuzawa, A., Dorf, M.E., and von Andrian, U.H. The CC chemokine thymus-derived chemotactic agent 4 (TCA-4, secondary lymphoid tissue chemokine, 6Ckine, Exodus-2) triggers lymphocyte function-associated antigen-1-mediated arrest of rolling T lymphocytes in peripheral lymph node high endothelial venules. *J. Exp. Med.* 191: 61-75, 2000. PMID: 10620605

3. My group was among the first in the field of Immunology to employ multi-photon intravital microscopy (MP-IVM) to characterize the dynamics of T cell interactions with antigen-presenting cells in living animals. We developed a model for MP-IVM in murine popliteal lymph nodes to show that priming of naive T cells by antigen pulsed dendritic cells occurs in three sequential phases. We have since gone on to dissect the rules that govern the transition from one interactive phase to the next and the impact of each phase on T cell function and differentiation. This work has been widely cited and has changed immunologists' long-held views of how T cells communicate and function.

   a. Mempel, T.R., Henrickson, S.E. and von Andrian, U.H. T cell priming by dendritic cells in lymph nodes occurs in three distinct phases. *Nature* 427: 154-159, 2004. PMID: 14712275

   b. Mempel, T.R., Pittet, M.J., Khazaie, K., Weninger, W., Weissleder, R. von Boehmer, H. and von Andrian, U.H. Regulatory T cells reversibly suppress cytotoxic T cell function independent of effector differentiation. *Immunity*, 25(1):129-141, 2006. PMID: 16860762

   c. Henrickson, S.E., Mempel, T.R., Mazo, I.B., Liu, B., Flynn, M., Artomov, M., Junt, T., Wong, H.C., Chakraborty, A.K. and von Andrian, U.H. T cell sensing of antigen dose governs interactive behavior with dendritic cells and sets a threshold for T cell activation. *Nature Immunology* 9(3):282-291, 2008. PMID: 18204450

   d. Henrickson, S.E., Senman, B., Flynn, M.P., Mazo, I.B., Mempel, T.R., Iannacone, M. & von Andrian, U.H. Antigen availability determines CD8(+) T cell-dendritic cell interaction kinetics and memory fate decisions. *Immunity* 39:496-507, 2013. PMID: 24054328

4. Ten years ago, we made the surprising observation that recombination actiating gene (RAG) deficient mice, which lack all T and B cells, can develop antigen specific immunological memory to haptens and viral antigens. We showed that this unexpected capacity resided within a specific subset of natural killer (NK) cells that were highly concentrated in the animals' liver. Our first publication of this discovery was met with considerable skepticism by the scientific community as it called into question one of the central paradigms of classic immunology. In the meantime, NK cell memory has been independently confirmed by a number of groups and in a variety of experimental systems. This discovery has broad implications for basic immunology, infectious disease biology and autoimmunity. We are continuing to explore the molecular and cellular underpinnings of this phenomenon.

   a. O'Leary, J.G., Goodarzi, M., Drayton, D. and von Andrian, U.H. T and B cell-independent adaptive immunity mediated by natural killer cells. *Nature Immunology*, 7 (5):507-516, 2006. PMID: 16617337

   b. Paust, S., Singh Gill, H., Flynn, M., Moseman, E.A., Senman, B., Askenase, P., Compans, R. & von Andrian, U.H. Critical role for CXCR6 in NK cell mediated adaptive immunity. *Nature Immunology* 11(12):1127-1135, 2010. PMID: 20972432

5. In a series of recent studies, my group has analyzed the multi-facetted innate and adaptive immune responses to lymph-borne pathogens in LNs that drain infected tissues. Using several viral model pathogens, we demonstrated a critical role for subcapsular sinus macrophages in viral antigen presentation and as the gatekeepers that prevent neurotropic viruses from invading peripheral nerves. This work has important implications for our understanding of the sequelae of viral infections and the development of novel vaccine approaches. Building on this work, we have recently discovered a novel mucosal vaccination strategy that employs charge-switching synthetic vaccine particles (cSAP) to induce a potent TH1-biased memory cells that protect against infection with *C. trachomatis*. This discovery provides a rationale for our research strategy proposed here.

   a. Junt, T., Moseman, Iannacone, M., Massberg, S., Lang, P. A., E.A., Boes, M., Fink, K., Henrickson, S., Shayakhmetov, Di Paolo, N., D.M., van Rooijen, N., Mempel, T.R., Whelan, S.P. and von Andrian, U.H.

Subcapsular sinus macrophages in lymph nodes clear lymph-borne viruses and present them to antiviral B cells. *Nature* 450(7166):110-114, 2007. PMID: 17934446

b. Iannacone, M., Moseman, E.A., Tonti, E., Bosurgi, L., & von Andrian, U.H. Subcapsular sinus macrophages prevent CNS invasion on peripheral infection with a neurotropic virus. *Nature*, 465(7301): 1079-1083, 2010. PMID: 20577213

c. Sung JH, Zhang H, Moseman EA, Alvarez D, Iannacone M, Henrickson SE, de la Torre JC, Groom JR, Luster AD, von Andrian UH. Chemokine guidance of central memory T cells is critical for antiviral recall responses in lymph nodes. *Cell* 150(6):1249-63. PMID: 22980984

d. Stary G, Olive A, Radovic-Moreno AF, Gondek D, Alvarez D, Basto PA, Perro M, Vrbanac VD, Tager AM, Shi J, Yethon JA, Farokhzad OC, Langer R, Starnbach MN, von Andrian UH. A mucosal vaccine against Chlamydia trachomatis generates two waves of protective memory T cells. *Science* 348(6241): aaa8205, 2015. PMID: 26089520.

List of Published Work: http://www.ncbi.nlm.nih.gov/sites/myncbi/ulrich.von andrian.1/bibliography/40459024/public/?sort=date&direction=ascending
Citation Indices for published work: https://scholar.google.com/citations?user=9sIHNxEAAAAJ&hl=en