Martin Zenke, PhD, Professor of Cell Biology

Biographical Sketch

Personal Data

Name and Academic Title	**Martin Zenke** – PhD, Professor 07.08.1953 in Korbach/Waldeck (Germany)
Current Position	Professor of Cell Biology, RWTH Aachen University
Wikipedia	https://en.wikipedia.org/wiki/Martin_Zenke

Affiliation

Institution	**RWTH Aachen University**
Institute/Department **Address**	Department of Hematology, Oncology and Stem Cell Transplantation Department of Medicine IV RWTH Aachen University Medical School Pauwelsstrasse 30 52074 Aachen, Germany martin.zenke@rwth-aachen.de www.molcell.de www.stemcellfactory.de

University Education

1979 - 1982	Graduate studies in Molecular and Cell Biology, Institute for Virus Research, German Cancer Research Center (DKFZ), Heidelberg, Germany
1972 – 1978	Studies in Chemistry/Biochemistry and Medicine, Philipps-University, Marburg, Germany

Academic Qualifications

1992	Lecture qualification (Habilitation) in Molecular Genetics, Faculty of Life Sciences, Vienna University, Vienna, Austria
1982	PhD, Faculty of Life Sciences, Ruprecht-Karls-University, Heidelberg, Germany
1978	Diplom (Master), Chemistry/Biochemistry, Philipps-University, Marburg, Germany

Scientific Career

Since 2022	Professor of Cell Biology, c/o Department of Hematology, Oncology and Stem Cell Transplantation, Department of Medicine IV, RWTH Aachen University Medical School, RWTH Aachen University, Aachen, Germany
2003 - 2022	Professor of Cell Biology (C4) and Chairman, Institute for Biomedical Engineering, Department of Cell Biology, RWTH Aachen University Medical School and Helmholtz Institute for Biomedical Engineering, RWTH, Aachen, Germany
2011 - 2014	Managing Director Helmholtz Institute for Biomedical Engineering (3 years legislative period), RWTH Aachen University, Aachen, Germany
1995 - 2003	Research Group Leader (C3), Max-Delbrück-Center for Molecular Medicine (MDC), Berlin, Germany
1988 - 1995	Junior Scientist and Group Leader, Institute of Molecular Pathology (IMP), Vienna, Austria
1985 - 1988	EMBL Fellow and Staff Scientist with Thomas Graf and Hartmut Beug, Differentiation Programme, European Molecular Biology Laboratory (EMBL), Heidelberg, Germany
1982 - 1985	Postdoctoral Fellow with Pierre Chambon, Université Louis Pasteur and Laboratoire de Genetique Moleculaire des Eucaryotes (LGME), Strasbourg, France

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Personal Statement

Martin Zenke's scientific work over the past several years focused on both curiosity-driven and discovery-oriented research and also on translational research. Emphasis is on hematopoietic cells, in particular on hematopoietic stem cells and antigen presenting dendritic cells, and on hematopoietic malignancies. In this context patient and disease specific induced pluripotent stem cells (iPS cells) are being studied for disease modelling and compound screening.

Martin Zenke is also committed to foster stem cell research and to communicate science to the public. He is member of the "Central Ethics Committee for Stem Cell Research" of the Federal Ministry of Education and Research (BMBF) and Federal Ministry of Health (BMG), Berlin, Germany and member of "Gene Technology Report", Berlin-Brandenburg Academy of Sciences and Humanities, BBAW, Berlin, Germany.

Contributions to Science

2005-today

Induced Pluripotent Stem Cells and Disease Modeling

Hematopoietic stem cells have been Martin Zenke's prime interest for many years and in the 2005s he broadened his interest to also include pluripotent stem cells, such as embryonic stem cells (ES cells) and induced pluripotent stem cells (iPS cells).

A particular focus is on disease and patient specific iPS cells for disease modeling and compound screening. Emphasis is put on studying hematopoietic malignancies, thereby building on the close collaboration with clinical and preclinical partners. This also includes developing animal models of diseases and laboratory automation for cell production.

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Meents, J. E., Bressan, E., Sontag, S., Foerster, A., Hautvast, P., Rösseler, C., Hampl, M., Schüler, H., Goetzke, R., Chi Le, T. K., Kleggetveit, I. P., Le Cann, K., Kerth, C., Rush, A. M., Rogers, M., Kohl, Z., Schmelz, M., Wagner, W., Jørum, E., Namer, B., Winner, B., Zenke, M., and Lampert, A. (2019). The role of Nav1.7 in human nociceptors: insights from human iPS cell-derived sensory neurons of erythromelalgia patients. *Pain* 160, 1327-1341.

Frobel, J., Hemeda, H., Lenz, M., Abagnale, G., Jousssen, S., Denecke, B., Saric, T., Zenke, M., and Wagner. W. (2014). Epigenetic rejuvenation of mesenchymal stromal cells derived from induced pluripotent stem cells. *Stem Cell Reports* 3, 414-422.

Ding, X., Wang, X., Sontag, S., Qin, J., Wanek, P., Lin, Q., and Zenke, M. (2014). The polycomb protein Ezh2 impacts on induced pluripotent stem cell generation. *Stem Cells Dev*. 23, 931-940.

Ko, K., Tapia, N., Wu, G., Kim, J. B., Araúzo Bravo, M. J., Sasse, P., Glaser, T., Ruau, D., Han. D. W., Greber, B., Hausdörfer, K., Sebastiano, V., Stehling, M., Fleischmann, B. K., Brüstle, O., Zenke, M., and Schöler, H. R. (2009). Induction of pluripotency in adult unipotent germline stem cells. *Cell Stem Cell* 5*,* 87-96.

Kim, J. B., Zaehres, H., Wu, G., Gentile, L., Ko, K., Sebastiano, V., Araúzo-Bravo, M. J., Ruau, D., Han, D. W., Zenke, M., and Schöler, H. R. (2008). Pluripotent stem cells derived from adult neural stem cells by reprogramming with two factors. *Nature* 454, 646-650.

Ruau, D., Ensenat-Waser, C., Dinger, T. C., Vallabhapurapu, D. S., Rolletschek, A., Hacker, C., Hieronymus, T., Wobus, A. M., Müller, A. M., and Zenke, M. (2008). Pluripotency associated genes are reactivated by chromatin modifying agents in neurophere cells. *Stem Cells* 26, 920-926.

Biographical Sketch

1995-today

Stem Cells and Antigen Presenting Dendritic Cells

In the beginning of the 1990s the studies on the v-rel oncogene led Martin Zenke to work on antigen presenting dendritic cells (DC), a specific immune cell, which is important for immunity and immune tolerance. DC biology was poorly understood those days and Martin Zenke was one of the first to apply gene expression profiling with DNA microarrays for gene mining. This led to the discovery of Id2 transcription factor in DC development. Of interest, the Id2 gene data sets received accession numbers 1 and 2 (E-MEXP-1 and E-MEXP-2) of the ArrayExpress database, which now contains several million entries.

The DC work is being followed mainly in the mouse system, to study gene circuitries of DC development and function using RNA-Seq, ChIP-seq, ATAC-seq, chromatin conformation capture (4C) and CRISPR/Cas9 gene editing, and more recently in the human system using induced pluripotent stem cells (iPS cells).

Sontag, S., Förster, M., Qin, J., Wanek, P., Mitzka, S., Schüler, H. M., Koschmieder, S., Rose-John, S., Seré, K., and Zenke, M. (2017). Modelling IRF8 deficient human hematopoiesis and dendritic cell development with engineered induced pluripotent stem cells. *Stem Cells* 35, 898-908.

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Seré, K., Baek, J.-H., Ober-Blöbaum, J., Müller-Newen, G., Tacke, F., Yokota, Y., Zenke, M., and Hieronymus, T. (2012). Two distinct types of Langerhans cells populate the skin during steady state and inflammation. *Immunity* 37, 905-919.
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Hacker, C., Kirsch, R. D., Ju, X.-S., Hieronymus, T., Gust, T. C., Kuhl, C., Jorgas, T., Kurz, S. M., Rose-John, S., Yokota, Y., and Zenke, M. (2003). (cover story). Transcriptional profiling identifies Id2 function in dendritic cell development. *Nature Immunol*. 4, 380-386.

Boehmelt, G., Madruga, J., Dörfler, P., Briegel, K., Schwarz, H., Enrietto, P., and Zenke, M. (1995). Dendritic cell progenitor is transformed by a conditional v-rel estrogen receptor fusion protein v-relER. *Cell* 80, 341-352.

1986-1998

The erbA Oncogene and Red Blood Cell Differentiation

In 1986 Martin Zenke started to work on retroviral oncogenes, in particular on the v-erbA and v-rel oncogenes. He found that the v-erbA oncogene is a loss of function version of the c-erbA/thyroid hormone receptor and acts as a dominant negative transcriptional repressor. This was the first description of oncogenic activity by loss-of-function mutation. This discovery was surprising, since oncogenic potential was believed to be solely due to activating mutations.

The erbA work led Martin Zenke to work on red blood cell differentiation, with a focus on the just discovered GATA transcription factors. He found that GATA-1 promotes red blood cell development whereas GATA-2 blocks red blood cell development. These findings were the first to suggest GATA-2 function in early blood cell development.

Panzenböck, B., Bartunek, P., Mapara, M., and Zenke, M. (1998). Growth and differentiation of human stem cell factor/erythropoietin-dependent erythroid progenitor cells in vitro. *Blood* 92, 3658-3668.

Briegel, K., Bartunek, P., Stengl, G., Lim, K.-C., Beug, H., Engel, J. D., and Zenke, M. (1996). Regulation and function of transcription factor GATA-1 during red blood cell differentiation. *Development* 122, 3839-3850.

Briegel, K., Lim, K.-C., Plank, C., Beug, H., Engel, J. D., and Zenke, M. (1993). Ectopic expression of a conditional GATA-2/estrogen receptor chimera arrests erythroid differentiation in a hormone-dependent manner. *Genes Dev.* 7, 1097-1109.

Disela, C., Glineur, C., Bugge, T., Sap, J., Stegl, G., Dodgson, J., Stunnenberg, H., Beug, H., and Zenke, M. (1991). v-*erb*A overexpression is required to extinguish c-*erb*A function in erythroid cell differentiation and regulation of the *erb*A target gene CAII. *Genes Dev.* 5, 2033-2047.

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1979-1986

SV40 Enhancer and SV40 Chromatin

In the 1980s Martin Zenke's research focused on gene transcription and chromatin. In 1986 he and his colleagues showed that transcriptional enhancers exhibit a modular structure and are composed of individual elements, which on their own are rather weak but act in synergy by binding specific proteins, and thereby build up enhancer activity. This is textbook knowledge nowadays but in the 1980s enhancers were initially thought to boost transcription by a unique and particular strong enhancer sequence and factor. Martin Zenke's seminal work is depicted and referenced in Lewin's Genes XII, the standard Molecular Biology textbook.

Davidson, I., Fromental, C., Augereau, P., Wildeman, A. G., Zenke, M., and Chambon, P. (1986). Cell-type specific protein binding to the enhancer of Simian Virus 40 in nuclear extracts. *Nature* 323, 544-548.

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Wildeman, A. G., Zenke, M., Schatz, C., Wintzerith, M., Grundström, T., Matthes, H., Takahashi, K., and Chambon, P. (1986). Specific protein binding to the Simian Virus 40 enhancer *in vitro*. *Mol. Cell. Biol.* 6, 2098-2105.

Zenke, M., Grundström, T., Matthes, H., Wintzerith, M., Schatz, C., Wildeman, A. G., and Chambon, P. (1986). Multiple sequence motifs are involved in SV40 enhancer function. *EMBO J.* 5, 387-397.

Zenke, M., and Sauer, G. (1982). Spliced and unspliced virus specific RNA sequences are associated with purified Simian Virus 40 chromatin. *Nucleic Acids Res.* 10, 4543-4550.

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https://scholar.google.de/scholar?hl=de&as_sdt=0%2C5&q=Martin+Zenke&btnG=