

BIOGRAPHICAL SKETCH

NAME Markus Müschen Date of birth: June 2 nd , 1972; Bonn, Germany	POSITION TITLE Professor
eRA COMMONS USER NAME MMUSCHEN	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
University of Nantes, Nantes, France Institut Pasteur, Paris, France	B.Sc.	6/1996 12/1997	Immunology Immunology
Heinrich-Heine-Universität Düsseldorf University of Cologne, Germany Institute for Genetics, University of Cologne University of Chicago, IL University of Cologne, Germany	M.D./Ph.D. Intern/Res Postdoc Postdoc Postdoc	11/1999 12/1999 10/2000 10/2001 11/2002	Molecular Biology Hematology/Oncology Genetics Molecular Genetics Immunology

A. PERSONAL STATEMENT

Markus Müschen is interested in basic mechanisms of lymphocyte development and oncogenic signaling in acute leukemias. He completed his medical training in Hematology and Oncology under Volker Diehl (Cologne), his doctoral thesis in Biochemistry and postdoctoral training under Klaus Rajewsky, Ralf Küppers (Cologne) and Janet D Rowley (Chicago). Markus Müschen developed his primary research interest both in the field of immunology (B cell development) and oncology (oncogenes in leukemia). He started his independent laboratory in 2001 in Cologne, Germany and moved with his group to Los Angeles in 2006 to serve as the Director of the Leukemia Research Programs at Children's Hospital Los Angeles and the USC Norris Cancer Center. Since then, he has trained multiple PhD students and postdoctoral scholars and served as mentor for six junior faculty members. Mentoring of junior faculty member involved both formal roles as designated mentor as well as serving as informal advisor and collaborator for junior faculty starting off their own independent research programs. He is currently a Scholar of the Leukemia and Lymphoma Society and his laboratory is currently funded by four NIH/NCI grants (3 R01, 1 R21), the California Stem Cell Agency, the Leukemia and Lymphoma Society and AACR Stand Up to Cancer. His research involves multi-disciplinary approaches (immunology, hematology/oncology, signal transduction) and has a genuine translational focus.

B. POSITIONS AND HONORS**Positions and Employment**

1994-1999	Doctoral thesis in Biochemistry and Molecular Biology, <i>summa cum laude</i> (Mentor: Helmut Sies)
1997-1999	Internship and Residency in Hematology and Oncology (Mentor: Volker Diehl)
1999-2000	Postdoctoral fellow, Institute for Genetics, Cologne (Mentor: Klaus Rajewsky and Ralf Küppers)
2000-2001	Postdoctoral fellow, University of Chicago (Mentor: Janet D Rowley)
2001-2002	Postdoctoral fellow, Institute for Immunology, Cologne (Mentor: Martin Krönke)
2002-2004	Assistant Professor of Immunology (Privatdozent)
2004-2010	Associate Professor of Stem Cell Biology (C3; with tenure), Heinrich-Heine-Universität Düsseldorf, Germany
2006-2010	Associate Professor of Pediatrics, Biochemistry and Molecular Biology (Tenure-track); USC Keck School of Medicine and Children's Hospital Los Angeles.
2006-2010	Program Leader, Leukemia and Lymphoma Program, Norris Comprehensive Cancer Center, University of Southern California, Los Angeles, CA
2006-Present	Director, Leukemia Research Program, Children's Hospital Los Angeles, Los Angeles, CA
2010-Present	Professor of Pediatrics, Biochemistry and Molecular Biology, USC Keck School of Medicine and Children's Hospital Los Angeles.
2010-Present	Professor (with tenure), Department of Laboratory Medicine, Department of Pathology University of California San Francisco, San Francisco, CA

Honors

1999	Doctoral Thesis Award of the German Association for Hematology and Oncology (DGHO)
2000	Postdoctoral Fellowship Award of the Cancer Research Institute, New York, NY
2001	<i>Emmy-Noether</i> Young Investigator Award, The German Science Foundation (DFG)
2001	Stem Cell Research Investigator Award, The State of North-Rhine-Westphalia
2002	Best Habilitation Thesis of the Year, School of Medicine, University of Cologne, Germany
2003	Fritz Melchers Award for Immunology, the German Association for Immunology
2006	Leukemia Clinical Research Award, The German Association for Hematology and Oncology
2006-present	Honorary Professor of the Xinxiang Medical University, Xinxiang, P.R. China
2009-present	Section Editor for Acute Lymphoblastic Leukemia (ALL), <i>Leukemia</i>
2009-present	Study section member, Leukemia and Lymphoma Society, DOD Hematologic Malignancies Panel, NYStem (New York Stem Cell Research Agency)
2010-present	Editorial Board <i>Biological Chemistry</i> ; Associate Editor <i>Blood Cancer Journal</i>
2010	Scholar Award, <i>The Leukemia and Lymphoma Society</i>
2011	Abstract Reviewer, American Society of Hematology
2011	Ad hoc member; NIH Special Emphasis Panel Cancer Therapy (ZRG1) and Molecular and Cellular Hematology (MCH)

C. SELECTED PEER-REVIEWED PUBLICATIONS (OF 64 TOTAL)

- Müschen M**, Rajewsky K, Brauninger A, Baur AS, Oudejans JJ, Roers A, Hansmann ML, Kuppers R. Rare occurrence of classical Hodgkin's disease as a T cell lymphoma. *J Exp Med* 191:387-394 (2000).
- Müschen M**, Re D, Brauninger A, Wolf J, Hansmann ML, Diehl V, Kuppers R, Rajewsky K. Somatic mutations of the CD95 gene in Hodgkin and Reed-Sternberg cells. *Cancer Res* 60:5640-5643 (2000).
- Müschen M**, Re D, Jungnickel B, Diehl V, Rajewsky K, Kuppers R. Somatic mutation of the CD95 gene in human B cells as a side-effect of the germinal center reaction. *J Exp Med* 192:1833-1840 (2000).
- Re D, **Müschen M**, Ahmadi T, Wickenhauser C, Staratschek-Jox A, Holtick U, Diehl V, Wolf J. Oct-2 and Bob-1 deficiency in Hodgkin and Reed Sternberg cells. *Cancer Res* 61:2080-2084 (2001).
- Müschen M**, Rajewsky K, Krönke M, Küppers R. The origin of CD95-gene mutations in B-cell lymphoma. *Trends Immunol* 23:75-80 (2002).
- Müschen M**, Lee S, Zhou G, Feldhahn N, Barath VS, Chen J, Moers C, Krönke M, Rowley JD, Wang SM. Molecular portraits of B cell lineage commitment. *Proc Natl Acad Sci USA* 99:10014-10019 (2002).
- Klein F, Feldhahn N, Lee S, Wang H, Ciuffi F, von Elstermann M, Toribio ML, Sauer H, Wartenberg M, Barath VS, Kronke M, Wernet P, Rowley JD & **Müschen M**. T lymphoid differentiation in human bone marrow. *Proc Natl Acad Sci USA* 100:6747-6752 (2003).
- Klein F, Feldhahn N, Harder L, Wang H, Wartenberg M, Hofmann WK, Wernet P, Siebert R & **Müschen M**. The BCR-ABL1 kinase bypasses selection for the expression of a pre-B cell receptor in pre-B acute lymphoblastic leukemia cells. *J Exp Med* 199:673-685 (2004).
- Feldhahn N, Klein F, Mooster JL, Hadweh P, Sprangers M, Wartenberg M, Bekhite MM, Hofmann WK, Herzog S, Jumaa H, Rowley JD & **Müschen M**. Mimicry of a constitutively active pre-B cell receptor in acute lymphoblastic leukemia cells. *J Exp Med* 201:1837-1852 (2005).
- Feldhahn N, Rio P, Soh BN, Liedtke S, Sprangers M, Klein F, Wernet P, Jumaa H, Hofmann WK, Hanenberg H, Rowley JD & **Müschen M**. Deficiency of Bruton's tyrosine kinase in B cell precursor leukemia cells. *Proc Natl Acad Sci USA* 102:13266-13271, 2005.
- Feldhahn N, Henke N, Melchior K, Duy C, Soh BN, Klein F, von Levetzow G, Giebel B, Li A, Hofmann WK, Jumaa H & **Müschen M**. Activation-induced cytidine deaminase acts as a mutator in BCR-ABL1-transformed acute lymphoblastic leukemia cells. *J Exp Med* 204:1157-1166 (2007)
- Meixlsperger S, Kohler F, Wossning T, Reppel M, **Müschen M**, Jumaa H. Conventional light chains inhibit the autonomous signaling capacity of the B cell receptor. *Immunity* 26:323-333 (2007)
- Tsai A, Lu H, Raghavan SC, **Müschen M**, Hsieh CL & Lieber MR. Human Chromosomal translocations at CpG sites and a theoretical basis for their lineage- and stage-specificity. *Cell*, 135:1130-42 (2008)
- Trageser D, Duy C, Klemm L, Gruber TA, Kim YM, Hofmann WK, Groffen J, Jäck HM, Jumaa H, Heisterkamp N & **Müschen M**. Pre-B cell receptor-mediated cell cycle arrest in Ph⁺ acute lymphoblastic leukemia requires IKAROS function. *J Exp Med*, 206: 1739-1753 (2009)

Klemm L, Duy C, Iacobucci I, Li Z, Feldhahn N, Henke N, Park E, Hoffmann TK, Kim YM, Hofmann WK, Jumaa H, Groffen J, Lieber MR, Casellas R & **Müschen M**. The B cell mutator AID promotes drug-resistance and B lymphoid blast crisis in chronic myeloid leukemia. *Cancer Cell*, 16: 232-245 (2009)

Nowak D, Ogawa S, **Müschen M**, Kawamata N, Mossner M, Hofmann WK, Weiss T, Haferlach T, Haferlach C & Koeffler HP. SNP array analysis of tyrosine kinase inhibitor (TKI) resistant CML identifies heterogeneous secondary genomic alterations. *Blood* 115: 1049-1053 (2010)

Parameswaran R, **Müschen M**, Groffen J & Heisterkamp N. A functional receptor for B-cell activating factor is expressed on human acute lymphoblastic leukemia cells. *Cancer Res.* 70: 4346-4356 (2010)

Müschen M. Genetic relicts from the origin of ALL. *Blood* 115: 3424-3425 (2010)

Duy C, Yu J, Polo JM, Klemm L, Cerchiatti L, Melnick A, Ye BH & **Müschen M**. BCL6 is critical for the development of a diverse primary B cell repertoire. *J Exp Med*, 207: 1209-1221 (2010)

Gruber TA, Chang MS, Sposto R & **Müschen M**. Activation-induced cytidine deaminase accelerates clonal evolution in BCR-ABL1-driven acute lymphoblastic leukemia. *Cancer Res.* 70: 7411-7420 (2010)

Fang C, Y Wang, N Vu, WY Lin, YT Hsieh, L Rubbi, **Müschen M**, YM Kim, A Chatziioannou, HR Tseng & TG Graeber. Integrated microfluidic and imaging platform for a kinase activity radioassay to analyze minute patient cancer samples. *Cancer Res.* 70: 8299-8308 (2010)

Rubbi L, Titz B, Brown L, Galvan E, Komisopoulou E, Chen SS, Low T, Tahmasian M, Skaggs B, **Müschen M**, Pellegrini M & Graeber TG. Global phosphoproteomics reveals crosstalk between Bcr-Abl and negative feedback mechanisms controlling Src signaling. *Science Signaling* 4: ra18 (2011)

Park E, Gang EJ, Hsieh YT, Schaefer P, Klemm L, Huantes S, Loh M, Conway EM, Kang ES, Koo HH, Hofmann WK, Heisterkamp N, Pelus L, Crispino J, Kahn M, **Müschen M** & Kim YM. Targeting survivin overcomes drug resistance in acute lymphoblastic leukemia. *Blood*. 118: 2191-2199 (2011)

Nahar R, Ramezani-Rad P, Mossner M, Duy C, Cerchiatti L, Geng H, Dovat S, Jumaa H, Ye BH, Melnick A & **Müschen M**. Pre-B cell receptor-mediated activation of BCL6 induces pre-B cell quiescence through transcriptional repression of MYC. *Blood*. 118: 4174-4178 (2011).

Duy C, Hurtz C, Shojaee S, Cerchiatti L, Geng H, Klemm L, Kim YM, Jumaa H, Koeffler HP, Yu JJ, Heisterkamp N, Graeber TG, Wu H, Ye BH, Melnick A & **Müschen M**. BCL6 enables Ph⁺ acute lymphoblastic leukemia cells to survive BCR-ABL1 kinase inhibition. *Nature* 473: 384-388 (2011)

Hurtz C, Hatzi K, Cerchiatti L, Park E, Kim YM, Herzog S, Ramezani-Rad P, Jumaa H, Müller MC, Hofmann WK, Hochhaus A, Ye BH, Agarwal A, Druker BJ, Shah NP, Melnick AM & **Müschen M**. BCL6-mediated repression of p53 is critical for leukemia stem cell survival in chronic myeloid leukemia. *J Exp Med*. 208: 2163-2174 (2011)

Jiang XX, Nguyen Q, Chou YC, Wang T, Nandakumar V, Yates P, Jones L, Wang L, Won HJ, Lee HR, Jung JU, **Müschen M**, Huang XF & Chen SY. Control of B-cell development by the histone H2A deubiquitinase MYSM1. *Immunity*. In press (2011)

D. ACTIVE RESEARCH SUPPORT

R01CA137060-A1	Müschen (PI)	04/01/2008 - 03/31/2013
NCI/NIH		\$207,500
"Pre-B cell receptor signaling in acute lymphoblastic leukemia". The central goal of this project is to clarify the role of pre-B cell receptor signaling in acute lymphoblastic leukemia.		
R01CA139032	Müschen (PI)	04/01/2008 - 03/31/2013
NCI/NIH		\$207,500
"AID-mediated genetic instability in BCR-ABL1-transformed B cell lineage leukemia". The central goal is (1) to identify the regulatory mechanisms that lead to aberrant expression of AID and (2) to identify the consequences of aberrant AID-activity in leukemia cells.		
R01CA157644	Müschen (PI)	07/01/2011-06/30/2016
NIH/NCI		\$207,500
'Infectious origins of childhood leukemia'. The central goal of this proposal is to experimentally test the 'delayed infections hypothesis' in the etiology of childhood ALL and to delineate mechanisms of genetic vulnerability of human pre-B cells in the context of infection.		

R21CA152497	Müschen (PI)	06/01/2010 - 05/31/2012
NCI/NIH		\$138,500
"Mechanism of BCL6-dependent stem cell maintenance in B cell lineage leukemia". The central goals of this proposal are (1) to clarify the role of BCL6 in leukemia-initiation of Ph ⁺ ALL and (2) To determine the frequency and phenotype of BCL6-dependent leukemia stem cells.		
TR2-01816	Müschen (PI)	10/01/2010-09/30/2013
California Institute for Regenerative Medicine (CIRM)		\$575,500
Early Translation Award. Development of a BCL6 small molecule inhibitor for targeted eradication of leukemia stem cells. The main goals of this project are (1) computer aided drug-design of BCL6 lateral groove inhibitors, (2) PK/PD assays and SAR studies of identified lead compound series and (3) pre-clinical validation.		
AACR 138564	Müschen (PI)	12/01/2009 - 11/30/2012
AACR Stand Up To Cancer Innovation Award		\$225,000
Stand Up To Cancer Innovation Award: Role of BCL6 in leukemia stem cell self-renewal. The main goal of this project is to study the role of BCL6 in the maintenance of leukemia-initiating cells in ALL.		
LLS 1497-11	Müschen (PI)	10/01/2010-09/30/2015
The Leukemia and Lymphoma Society Scholar Award		\$110,000
Leukemia and Lymphoma Society Scholar Award, will cover salary expenses related to NIH grant R01CA137060 'Pre-B cell receptor signaling in acute lymphoblastic leukemia'.		
LLS 6132-09	Müschen (PI)	10/01/2008-09/30/2012
The Leukemia and Lymphoma Society		\$180,000
Translational Research Grant 'Targeting AID in BCR-ABL1-driven leukemia'. The main goal of this project is to study the role of AID in aberrant somatic hypermutation as a cause of genetic instability.		
LLS 6097-10	Müschen (PI)	07/01/2009-06/30/2013
The Leukemia and Lymphoma Society		\$100,000
Translational Research Grant 'BCL6 in oncogene-induced senescence'. The main goal of this project is to study the role of BCL6 in oncogene-induced senescence in MYC-driven B cell lymphoma.		
ALSF-2011-10	Müschen (PI)	7/01/2011-06/30/2013
Alex's Lemonade Stand Foundation for Pediatric Cancer Research		\$100,000
Innovative Research Grant 'Targeting PTEN-mediated feedback signaling in high-risk childhood ALL'. The main goal of this grant is to investigate the role of PTEN signaling in ALL cell survival.		
LLS 7005-11	Müschen (Project-PI)	10/01/2010-09/30/2015
Leukemia and Lymphoma Society SCOR		\$100,000
Project 2: Dual targeting of tyrosine kinase and feedback signaling in leukemia. Goals are identification of novel oncogenic tyrosine kinases and characterization of feedback mechanisms in response to tyrosine kinase inhibition. <u>Brian J Druker, Portland, OR is the PI of the SCOR.</u>		
LLS 7005-11	Müschen (Project-PI)	10/01/2010-09/30/2015
Leukemia and Lymphoma Society SCOR		\$75,000
Core E: (1) Generate and make xenografted samples available to SCOR projects, (2) Generate a centralized multidimensional database which links flow cytometry data, cytogenetics, gene expression, SNP chip analysis and clinical information. <u>Brian J Druker, Portland, OR is the PI of the SCOR.</u>		
LLS 6221-12	Müschen (PI)	07/01/2009-06/30/2013
The Leukemia and Lymphoma Society		\$180,000
Translational Research Grant 'Targeting inhibitory phosphatase signaling in Ph ⁺ ALL'. The main goal of this grant is to validate phosphatase inhibition as novel therapy approach in pre-clinical models for childhood ALL.		