

Christof von Kalle

Director, National Center of Tumor Diseases (NCT) at the University Hospital Heidelberg and the German Cancer Center (DKFZ), Heidelberg;
Tenured Full Professor and Chairman, Division of Translational Oncology, NCT and Department of Translation Oncology, DKFZ Heidelberg

Current Research

Over the last decade we have specifically been interested in the clonal composition of post-transplant hematopoiesis and genotoxicity in connection with retroviral vector integration both in preclinical animal models as well as clinical gene therapy studies. By means of a highly innovative methodology for the identification of individual integration sites of viral vectors which we developed it is now possible to thoroughly investigate retroviral integration in numerous gene therapy studies. In clinical as well as preclinical gene transfer studies the clonal composition of early and late hematopoiesis after transplantation could be elucidated. We will intensify our research aiming at an improved biosafety by evaluating related assays for onco and retroviral gene transfer.

Another area of interest of our group is the structure of the transplantable human hematopoietic stem cell compartment. We have extensive experience with various syngeneic and xenogeneic mouse stem cell transplantation models. We were able to establish a xenotransplantation model that for the first time revealed functional heterogeneity of human hematopoietic stem cells and the role of human short-term repopulating cells (STRC). Moreover, using techniques that allow the isolation of viable hematopoietic cells in specific stages of the cell cycles or in accordance with their cell cycle history in culture we were able to directly prove the self-renewal activity of human repopulating cells in culture and demonstrate cell cycle-related changes in the transplantability of stem cells.

Contact:

National Center for Tumor Diseases
and Department of Translational Oncology,
German Cancer Research Center
Im Neuenheimer Feld 350
69120 Heidelberg

+49 6221 56 6991 (phone)
+49 6221 56 6930 (fax)
christof.kalle@nct-heidelberg.de



Future Projects and Goals

For the future, we aim to prospectively monitor insertional mutagenic events in real-time. Another main focus will be the extension of mathematical and bioinformatic tools to improve data mining and to establish a retro- and lentiviral integration site database. Another project will examine the cell cycle, chemosensitivity and self-renewal activity of individual colon cancer-initiating cell clones as well as their role in tumor and metastasis formation.

Selected Publications

- Deichmann A, Hacein-Bey Abina S, Schmidt M, et al. Vector Integration is Non-Random, Clustered and Influences the Fate of Lymphopoiesis in SCID-X1 Gene Therapy. *J Clin Invest*. 2007 Aug;117(8).
- Ball CR, Pilz IH, Schmidt M, et al. Stable differentiation and clonality of murine long-term hematopoiesis after extended reduced intensity selection for MGMT P140K transgene expression. *Blood*. 2007 May 11;
- Woods NB, Bottero V; Schmidt M, **von Kalle C**, Verma IM. Gene therapy: therapeutic gene causing lymphoma. *Nature*. 2006; 440(7088):1123.
- Ott M, Schmidt M, Schwarzwaelder K et al. Correction of X-linked chronic granulomatous disease by gene therapy, augmented by insertional activation of MDS1/EVI1, PRDM16 or SETBP1. *Nature Medicine*. 2006; 12(4):401-9.
- Montini E, Cesana D, Schmidt M, et al. (2006) Hematopoietic stem cell gene transfer in a tumor-prone mouse model uncovers low genotoxicity of lentiviral vector integration. *Nature Biotechnology* 24(6):687-96.
- Glimm H, Schmidt M, Fischer M, et al. Efficient marking of human cells with rapid but transient repopulating activity in autografted recipients. *Blood*. 2005; 106(3):893-8.
- Hacein-Bey-Abina S*, **Von Kalle C***, (cofirst author*) Schmidt M*, et al. LMO2-associated clonal T cell proliferation in two patients after gene therapy for SCID-X1. *Science*. 2003; 302(5644):415-9.