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Positions:

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Research interests:

Recent work including from our own group has shown that myelodysplastic syndromes (MDS) and acute myeloid leukemias (AML) arise from an unexpectedly diverse pool of pre-leukemic stem cells (pre-LSC), preceding the formation of fully transformed leukemia stem cells (LSC). These highly polyclonal pre-LSC and LSC populations are relatively resistant to chemotherapy and thereby contribute to treatment failure. As a consequence, polyclonally driven progression and relapse continue to be the most common causes of death in MDS and AML.

The goal of our research is to delineate critical mechanisms in HSC that drive their heterogeneity and formation and function of pre-LSC and LSC, including key transcriptional/epigenetic regulators as well as mediators of aberrant signaling. We are studying murine genetic models as well as primary human samples from patients. Our studies aim at the development of targeted, pre-LSC- and LSC-directed therapies, which could ultimately also be employed for precision prevention of relapse/progression, or "cancer interception".

Current grant funding:

R35CA253127 (Steidl, PI) (NIH/NCI)	09/01/21 – 08/31/28 Molecular and Cellular Regulation of Pre-Leukemic Stem Cells and their Therapeutic Targeting
R01CA217092 (Steidl, PI) (NIH/NCI)	04/01/17 – 03/31/22 Mechanisms of formation and progression of preleukemic stem cells
R01HL139487 (Verma/Steidl, MPI) (NIH/NHLBI)	08/20/18 – 06/30/22 Therapeutic Targeting of MDS stem cells
R01HL105832 (Verma/Steidl, MPI) (NIH/NHLBI)	07/01/19 – 06/30/24 STAT3 inhibition as a therapeutic strategy against MDS stem cells
U01CA241981 (Buelow/Steidl, MPI) (NIH/NCI)	09/01/19 – 08/31/22 A Fluorescence-Based High-Throughput Platform for Glycotyping the Hematopoietic Cell Lineage
T2019-001 (Steidl/Verma, MPI) V Foundation	11/01/2019 – 11/01/22 Role of Stem Cell Subclones in MDS and Leukemic Progression

Recent publications (selected):

Ueda K et al. MDMX Acts as a Pervasive Preleukemic-to-Acute Myeloid Leukemia Transition Mechanism. *Cancer Cell*. 2021; 39:529-547

Wheat JC et al. Single Molecule Imaging of Transcription Dynamics in Somatic Stem Cells. *Nature*. 2020; 583:431-436

Chen J et al. Myelodysplastic Syndrome Progression to Acute Myeloid Leukemia at the Stem Cell Level. *Nat Med*. 2019; 25:103-110

Mitchell K et al. IL1RAP Potentiates Multiple Oncogenic Signaling Pathways in AML. *J Exp Med*. 2018; 215:1709-1727

Carvajal LA et al. Dual Inhibition of MDMX and MDM2 as a Therapeutic Strategy in Leukemia. *Science Transl Med*. 2018 Apr 11; 10:eao3003

Antony-Debré I et al. Pharmacological Inhibition of the Transcription Factor PU.1 in Leukemia. *J Clin Invest*. 2017; 127:4297-4313

Stanley RF, Piszczatowski RT, et al. A Myeloid Tumor Suppressor Role for NOL3. *J Exp Med*. 2017; 214:753-771

Okoye-Okafor UC et al. New IDH1 Mutant Inhibitors for Treatment of Acute Myeloid Leukemia. *Nat Chem Biol*. 2015; 11:878-886

Will B, Vogler TO et al. Minimal PU.1 Reduction Induces a Preleukemic State and Promotes Development of Acute Myeloid Leukemia. *Nat Med*. 2015; 21:1172-1181