Relapse and progression continue to be the most common causes of death in MDS and many other cancers. Recent evidence has shown that a molecularly diverse pool of hematopoietic stem cells lead to the formation of pre-cancerous/pre-leukemic stem cells that play a pivotal role not only in disease origination but also in relapse. Recent work has demonstrated the existence and essentiality of such pre-cancerous cell states including pre-MDS-SC and pre-AML-SC in mice and humans. However, still very little is known about the molecular mechanisms driving their formation and progression. We and others have performed molecular studies of pre-leukemic cell states in mouse genetic models as well as primary cells from patients and discovered new molecular and stem cell biological mechanisms in pre-MDS-SC, challenging current paradigms of bulk cell-focused “precision” oncology. Such models and data sets at the stem cell level provide novel tools for mechanistic study of pre-cancerous stem cells and their progression to overt MDS and AML, and for the development and testing of pharmacological approaches to therapeutically interfere with these processes. Together, recent studies have started to shed light on pre-cancerous stem cell states as the earliest origin of MDS, and on cell-intrinsic as well as selection mechanisms driving their formation and progression. These advances provide a basis for the specific therapeutic targeting of pre-cancerous stem cells for the causative treatment and potential prevention of MDS and AML and other cancers developing from pre-cancerous conditions in the future.

Biography: Ulrich Steidl is a graduate of the University of Heidelberg Medical School and the German Cancer Research Center in Heidelberg. He trained as a postdoctoral researcher at Harvard Medical School and joined the Albert Einstein College of Medicine in 2008. He is currently appointed as a Professor of Cell Biology and of Medicine (Oncology), and is the Scientific Director of the Division of Hemato-Oncology, the Program Leader of the ‘Stem Cells, Differentiation and Cancer’ program of the Albert Einstein Cancer Center, and a member of the Gottesman Institute for Stem Cell Research and Regenerative Medicine. Ulrich Steidl has a long-standing interest and expertise in the stem cell origin of myeloid malignancies including MDS and AML. His laboratory has developed and refined unique experimental tools for functional and mechanistic studies at the stem cell level, as well as novel approaches for their specific therapeutic targeting.

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