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Titel des Beitrags:
An RNAi-based system for loss-of-function analysis identifies Raf1 as a crucial mediator of BCR-ABL-driven leukemogenesis.

Abstract:
Genetic loss-of-function studies in murine tumor models have been essential in the analysis of downstream mediators of oncogenic transformation. Unfortunately, these studies are frequently limited by the availability of genetically modified mouse strains. Here we describe a versatile method allowing the efficient expression of an oncogene and simultaneous knockdown of targets of interest (TOI) from a single retroviral vector. Both oncogene and TOI-specific miR30-based shRNA are under the control of the strong viral long terminal repeat promoter, resulting in a single shared RNA transcript. Using this vector in a murine syngeneic BM transplantation model for BCR-ABL-induced chronic myeloid leukemia, we find that oncogene expression and target knockdown in primary hematopoietic cells with this vector is efficient both in vitro and in vivo, and demonstrate that Raf1, but not BRAF, modulates BCR-ABL-dependent ERK activation and transformation of hematopoietic cells. This expression system could facilitate genetic loss-of-function studies and allow the rapid validation of potential drug targets in a broad range of oncogene-driven murine tumor models.

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