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Derepression of an endogenous long terminal repeat activates the CSF1R proto-oncogene in human lymphoma.

Lamprecht B, Walter K, Kreher S, Kumar R, Hummel M, Lenze D, Köchert K, Bouhlel MA, Richter J, Soler E, Stadhouders R, Jöhrens K, Wurster KD, Callen DF, Harte MF, Giefing M, Barlow R, Stein H, Anagnostopoulos I, Janz M, Cockerill PN, Siebert R, Dörken B, Bonifer C, Mathas S.

Source

[Max-Delbrück-Center for Molecular Medicine, Berlin, Germany.

Abstract

Mammalian genomes contain many repetitive elements, including long terminal repeats (LTRs), which have long been suspected to have a role in tumorigenesis. Here we present evidence that aberrant LTR activation contributes to lineage-inappropriate gene expression in transformed human cells and that such gene expression is central for tumor cell survival. We show that B cell-derived Hodgkin's lymphoma cells depend on the activity of the non-B, myeloid-specific proto-oncogene colony-stimulating factor 1 receptor (CSF1R). In these cells, CSF1R transcription initiates at an aberrantly activated endogenous LTR of the MaLR family (THE1B). Derepression of the THE1 subfamily of MaLR LTRs is widespread in the genome of Hodgkin's lymphoma cells and is associated with impaired epigenetic control due to loss of expression of the corepressor CBFA2T3. Furthermore, we detect LTR-driven CSF1R transcripts in anaplastic large cell lymphoma, in which CSF1R is known to be expressed aberrantly. We conclude that LTR derepression is involved in the pathogenesis of human lymphomas, a finding that might have diagnostic, prognostic and therapeutic implications.

Comment in

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