Tipo	Periódico
Título	Pharmacological Targeting of BET Bromodomain Proteins in Acute Myeloid Leukemia and Malignant Lymphomas: From Molecular Characterization to Clinical Applications
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Programa/Curso (s)	Programa de Pós-Graduação Stricto Sensu em Ciências da Saúde
DOI	10.3390/cancers11101483
Assunto (palavras chaves)	bromodomain and extra-terminal domain; BRD2; BRD4; super-enhancer; NF-κB; MYC; combination therapy; hematological malignancies; protein degraders
Idioma	Inglês
Fonte	Título do periódico: Cancers (Basel) ISSN: 2072-6694 Volume/Número/Paginação/Ano: v. 11, p. 1483, 2019
Data da publicação	2 October 2019
Formato da produção	Digital https://doi.org/10.3390/cancers11101483
Resumo	Alterations in protein-protein and DNA-protein interactions and abnormal chromatin remodeling are a major cause of uncontrolled gene transcription and constitutive activation of critical signaling pathways in cancer cells. Multiple epigenetic regulators are known to be deregulated in several hematologic neoplasms, by somatic mutation, amplification, or deletion, allowing the identification of specific epigenetic signatures, but at the same time providing new therapeutic opportunities. While these vulnerabilities have been traditionally addressed by hypomethylating agents or histone deacetylase inhibitors, pharmacological targeting of bromodomain-containing proteins has recently emerged as a promising approach in a number of lymphoid and myeloid malignancies. Indeed, preclinical and clinical studies highlight the relevance of targeting the bromodomain and extra-terminal (BET) family as an efficient strategy of target transcription irrespective of the presence of epigenetic mutations. Here we will summarize the main advances achieved in the last decade regarding the preclinical and clinical evaluation of BET bromodomain inhibitors in hematologic cancers, either as monotherapies or in combinations with standard and/or experimental agents. A mention will finally be given to the new concept of the protein degrader, and the perspective it holds for the design of bromodomain-based therapies.
Fomento	