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ACCEPTED MANUSCRIPT

HDAC inhibitors as epigenetic regulators for cancer immunotherapy

HDACi in cancer immunotherapy

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ABSTRACT

In recent years, anti-tumor immunotherapy has shown promising results, and immuneoncology is now emerging as the fourth major wave in the treatment of tumors after
radiotherapy, chemotherapy and molecular targeted therapy. Understanding the impact of
the immune system on neoplastic cells is crucial to improve its effectiveness against
cancer. The stratification of patients who might benefit from immunotherapy as well as the
personalization of medicine have contributed to the discovery of new immunotherapeutic
targets and molecules. In the present review, we discuss the mechanistic role of histone
deacetylase inhibitors (HDACi) as potential immunomodulating agents to treat cancer. Our
current understanding of the use of HDACi in combination with various immunotherapeutic
approaches, such as immunomodulating agents and cancer vaccines, is also addressed.
The potential clinical applications of the growing number of novel epigenetic drugs for
cancer immunotherapy are widening, and some of these therapies are already in clinical

trials.

Abbreviations:

AICD: activation-induced cell death

AML: acute myeloid leukemia

APC: antigen-presenting cells

CAR: coxsackie- and adenovirus receptor

CDKs: cyclin-dependent kinases

CG: cancer germline

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