



# **Cancer Immunotherapy: Chapter 22. Epigenetic Approaches: Emerging Role of Histone Deacetylase Inhibitors in Cancer Immunotherapy**

*Eva Sahakian, Karrune Woan, Alejandro Villagra, Eduardo M. Sotomayor*

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Histone deacetylase inhibitors (HDI) have been largely known for their ability to induce cell cycle arrest and apoptosis of tumor cells, effects that have translated into clinically significant antitumor activity against certain malignancies. In addition, there is now increasing evidence that HDIs are also endowed with immunoregulatory properties. Interestingly, while some reports have highlighted the anti-inflammatory effects of these compounds, others have shown pro-inflammatory effects triggered by HDIs in in vitro and in vivo studies. Known targets for HDIs are histone deacetylases (HDACs), enzymes that are recruited to gene promoters where they regulate transcription through histone modifications. Some HDACs, however, can also deacetylate nonhistone proteins, indicating that the role of HDACs in cell biology goes beyond their initial described effects on histones and encompasses now more complex regulatory functions. This complexity, along with the fact that most of the HDI currently in use are pan-HDI (multiple HDAC targets), might explain the divergent immunoregulatory effects of these compounds. Given this conundrum, in this chapter we have summarized the current understanding of the expression/function of specific HDACs in immune cells, knowledge that is providing important insights into their role in immunobiology and also paving the way for the development of more selective and potentially less toxic epigenetic-based approaches to effectively harness antitumor immune responses.

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