Histone deacetylase inhibitors (HDAC-Is) are agents that have demonstrated anticancer activity in vivo and in vitro, leading to clinical trials evaluating their efficacy in multiple cancer types. Only two HDAC-Is are currently approved by the U.S. Food and Drug Administration, vorinostat and romidepsin, both with indications for cutaneous T-cell lymphoma. Romidepsin has an additional approval in peripheral T-cell lymphoma. Promising clinical trial results in other cancer types will likely lead to expanded use of these and other HDAC-Is. To provide care for patients receiving these agents, oncology nurses should be knowledgeable about the emerging role of HDAC-Is. This article reviews the mechanism of action of HDAC-Is, currently approved therapies, and nursing management of cutaneous T-cell lymphoma.

Histone Deacetylase Inhibitors: Novel Agents in Cancer Treatment

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Histone deacetylases (HDACs) are enzymes involved in the regulation of gene transcription in the human body. Genes, the basic units of inheritance and the instructions by which all cell processes occur, are held in cells in tightly wound structures called chromatin. Chromatin is composed of nucleosomes, which are made of DNA wrapped tightly around core histones (Thiagalingam et al., 2003). Histone acetyltransferases (HATs) and HDACs are enzymes that acetylate and deacetylate histones, respectively. Acetylation of histones is a key modification that regulates gene transcription. The acetyl group is removed from histones by HDACs, leading to the unwinding of DNA for transcription to occur (Pons et al., 2003). Conversely, when HDAC interacts with a histone, the acetyl group is removed, and the DNA is once again wound tightly to block transcription (see Figure 1). Inhibiting histone deacetylation, then, allows acetylation to occur, therefore allowing transcription to occur (Johnstone, 2002). Several other functions of HDACs in the body are hypothesized that also involve cell cycle regulation and cell survival. In addition to their interaction with histones, HDACs interact with non-histone proteins, many of which are involved in regulation of cell proliferation. Proteins such as c-MYC, pRb, and p53 (a tumor suppressor gene) are involved in cell cycle regulation and, when interacting with HDACs, can upregulate or downregulate cell replication (Marks & Xu, 2009).

Eighteen known HDACs exist, each with a unique function and location within the cell. These HDACs are divided into four classes (class I-IV) and are organized by their homology to yeast proteins (Lane & Chabner, 2009). Classes I (HDACs 1, 2, 3, and 8), II (HDACs 4, 5, 7 and 9), and IV (HDAC 11) are the zinc-dependent classes, so named because of a zinc molecule...