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Selective HAT inhibitors as mechanistic tools for protein acetylation.

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Streszczenie

This chapter introduces the use of selective Histone acetyltransferases (HATs) inhibitors as mechanistic tools to probe the catalytic features of HATs and their roles in various cellular pathways. The chapter describes the design, synthesis, and applications of these inhibitors in different biological contexts. HATs regulate gene expression by the targeted acetylation of histones and other proteins. It is a difficult challenge to identify the functional effects of protein acetylation in specific pathways. HATs catalyze the transfer of acetyl groups from acetyl-CoA to the ε-amino groups of lysine residues in protein and play a major role in the regulation of transcriptional machinery and the modulation of gene expression. While HATs were initially thought of as enzymes that catalyze the acetylation of histones on lysine residues, it is increasingly recognized that these inhibitors act on a wide variety of protein substrates. These acetylation events may in some cases affect protein-protein interactions. The use of small molecules to modulate cellular and *in vivo* systems, sometimes called ‘‘chemical genetics,’’ has received renewed interest in the biology community in part because of continuing improvements in synthetic chemistry as well as molecular design.

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