

Title: *Small molecule inhibitors of transcription factors for treatment of HIV infections*
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Applications:

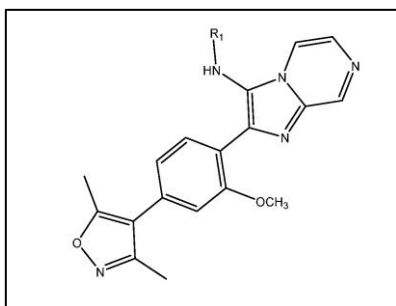
- Treatment of HIV-1 latency
- Treatment of immune deficiency disorders

Benefits:

- Novel mechanism for treating HIV-1 latency
- Novel, potent chemical entities with enhanced BET inhibition
- Compounds can be used in combination with PKC agonists or other drugs

Technology Description: Combinatory antiretroviral therapy (cART) is effective to reduce HIV-1 viremia, but it does not eliminate HIV-1 infection. The resulting HIV-1 latency has led to interest in identifying latency-reversing agents. Bromodomain-containing proteins have been widely studied in recent years, and in particular, the bromo and extra terminal protein (BET) family proteins have been implicated in diseases such as cancer and other inflammatory diseases. BRD4 is a bromodomain protein that can be a negative regulator of HIV-1 replication, so that antagonism of BRD4 with a bromodomain inhibitor can increase proviral transcriptional elongation and alleviate HIV-1 latency in cell-line models. The inventors have previously shown that BET inhibitors such as JQ1 may facilitate the reversal of HIV-1 latency. Although JQ1 is a strong BET inhibitor, this compound alone is inefficient to reverse HIV-1 latency in primary CD4+ T cells or CD8-depleted PBMCs isolated from cART-treated HIV-1 aviremic patients, and stronger inhibitors may be needed. Accordingly, this invention comprises the discovery and synthesis of several novel, potent small molecules that have been identified as acetyl-lysine mimetics for bromodomain inhibition. These compounds may offer novel potential methods of treating HIV-1 infections and related diseases.

Patent and Publication Status: UMass Boston and the University of Rochester are owners of a [pending PCT patent application](#) on this invention. The research underlying the invention has been published as Huang et al. [Front. Microbiol. 2017; 8: 1035](#).



Structure of the scaffold of the compounds of the invention.

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