

May 16th, 1:45 PM

A Novel Bromodomain and Extra-terminal Domain Inhibitors (BETi) that Reverses HIV-1 Latency

Shuai Liu

University of Massachusetts Boston

Maxime Jean


University of Rochester Medical Center

Wei Zhang

University of Rochester Medical Center

See next page for additional authors

Follow this and additional works at: http://escholarship.umassmed.edu/cts_retreat

 Part of the [Medicinal-Pharmaceutical Chemistry Commons](#), [Translational Medical Research Commons](#), and the [Virus Diseases Commons](#)

Liu, Shuai; Jean, Maxime; Zhang, Wei; and Zhu, Jian, "A Novel Bromodomain and Extra-terminal Domain Inhibitors (BETi) that Reverses HIV-1 Latency" (2017). *UMass Center for Clinical and Translational Science Research Retreat*. 47.
http://escholarship.umassmed.edu/cts_retreat/2017/posters/47

This material is brought to you by eScholarship@UMMS. It has been accepted for inclusion in UMass Center for Clinical and Translational Science Research Retreat by an authorized administrator of eScholarship@UMMS. For more information, please contact Lisa.Palmer@umassmed.edu.

Presenter Information

Shuai Liu, Maxime Jean, Wei Zhang, and Jian Zhu

Keywords

HIV-1 infection, AIDS, combinatory antiretroviral therapy

Creative Commons License

This work is licensed under a [Creative Commons Attribution-Noncommercial-Share Alike 3.0 License](https://creativecommons.org/licenses/by-nc-sa/3.0/).

A NOVEL BROMODOMAIN AND EXTRA-TERMINAL DOMAIN INHIBITORS (BETI) THAT REVERSES HIV-1 LATENCY

Shuai Liu¹, Huachao Huang², Maxime Jean², Wei Zhang¹, Jian Zhu²

¹Department of Chemistry, University of Massachusetts Boston; ²Department of Microbiology and Immunology, University of Rochester Medical Center, Rochester, NY

Although combinatory antiretroviral therapy (cART) is effective to reduce HIV-1 viremia, it does not eliminate HIV-1 infection. HIV-1 remains latent with the presence of cART, impeding the cure of AIDS. Recently, latency-reversing agents (LRAs) have been developed to purge latent HIV-1, providing an intriguing strategy for eradication of residual, latent viral reservoirs. Our earlier studies show that antagonism of HIV-1 competitive factor bromodomain containing 4 (BRD4) using bromodomain and extra-terminal domain inhibitor (BETi) JQ1 may facilitate the reversal of HIV-1 latency. BETis have recently emerged as a class of compounds that are promising for both the anticancer and HIV-1 latency-reversing uses. However, the current BETis, including JQ1, are modest to reverse HIV-1 latency as a single drug, which complicates the study of the underlining mechanisms. BETis, which are more potent and easier for synthesis, are currently under active development. UMB-32 is a novel BETi based on an imidazo[1,2-a]pyrazine scaffold. We screened 61 UMB-32 derivatives and identified that one BETi, UMB-136, reactivates HIV-1 in multiple cell models of HIV-1 latency with better efficiency than JQ1 and UMB-32. Furthermore, UMB-136 enhances the latency-reversing effect of PKC activators (Prostratin, Bryostatin) in CD8-depleted PBMCs containing HIV-1 latent reservoirs. Thus, our results illustrate that structurally improved BETis, such as UMB-136, could be use as promising LRAs for HIV-1 eradication.

Contact:

Shuai Liu

University of Massachusetts Boston

Shuai.Liu001@umb.edu