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Synthesis of NVS-BPTF-1 and evaluation of its biological activity

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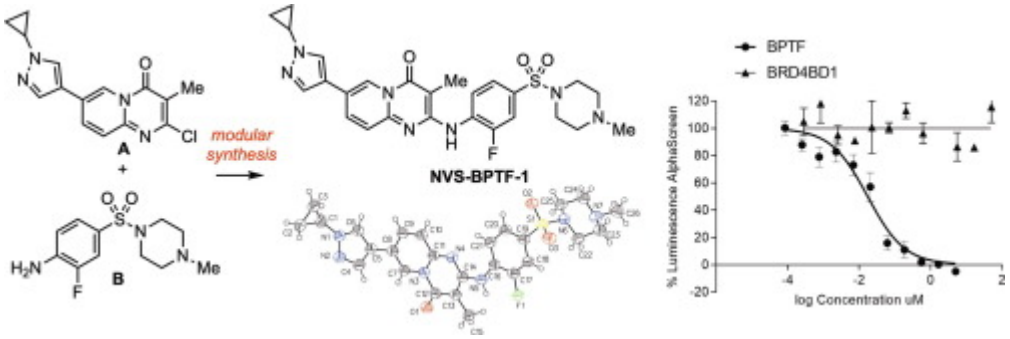
Abstract

BPTF (bromodomain and PHD finger containing transcription factor) is a multidomain protein that plays essential roles in transcriptional regulation, *T*-cell homeostasis and stem cell pluripotency. As part of the chromatin remodeling complex hNURF (nucleosome remodeling factor), BPTF epigenetic reader subunits are particularly important for BPTF cellular function. Here we report the synthesis of NVS-BPTF-1, a previously reported highly potent and selective BPTF-bromodomain inhibito

the impact of the inhibition of BPTF-bromodomain using NVS-BPTF-1 on selected proteins involved in the antigen processing pathway revealed that exclusively targeting BPTF-bromodomain is insufficient to observe an increase of PSMB8, PSMB9, TAP1 and TAP2 proteins.

Graphical abstract

The synthesis of NVS-BPTF-1, a chemical probe targeting the bromodomain and PHD finger containing transcription factor BPTF, was accomplished through palladium-catalyzed *N*-arylation of aniline **B** with chloropyridopyrimidinone **A**. The structure of synthetic NVS-BPTF-1 was confirmed through X-ray crystallography. NVS-BPTF-1 showed strong and selective inhibition of BPTF over BRD4(BD1) in an AlphaScreen assay, but no impact on cell proliferation in B16F10 mouse melanoma cells and no upregulation of PSMB8, PSMB9, TAP1 or TAP2.



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Keywords

NVS-BPTF-1; BPTF; NURF; Synthesis

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