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Cap Binding Complex 80/20 Binder ABX-464

National Cancer Institute

Source

National Cancer Institute. *Cap Binding Complex 80/20 Binder ABX-464*. NCI Thesaurus. Code C158506.

An orally available, small molecule binder of the cap binding complex (CBC) 80/20, with potential antiviral and anti-inflammatory activities. Upon oral administration, ABX464 binds to the CBC, a complex at the 5'-end of the pre-mRNA transcript that promotes the initial interaction with transcription and processing machinery. This leads to a conformational change in the CBC and enhanced splicing of viral RNA variants and upregulation of the anti-inflammatory microRNA, miR-124, via splicing of a long noncoding RNA at the miR-124-1 locus. In human immunodeficiency virus type 1 (HIV-1)-infected cells, ABX464 interacts with the CBC of HIV-1 mRNA and inhibits viral replication by preventing Rev-mediated export of unspliced HIV-1 transcripts to the cytoplasm. Rev facilitates the nuclear export of unspliced or incompletely spliced viral pre-mRNAs, an essential step in HIV-1 replication. In inflammatory conditions, miR-124 reduces the production of various inflammatory mediators, including interleukin 6 (IL-6), tumor necrosis factor alpha (TNF-alpha), and C-C motif chemokine 2 (CCL2; MCP-1.). miR-124 plays a critical role in innate and adaptive immune responses and is a critical mediator of cholinergic anti-inflammatory action.