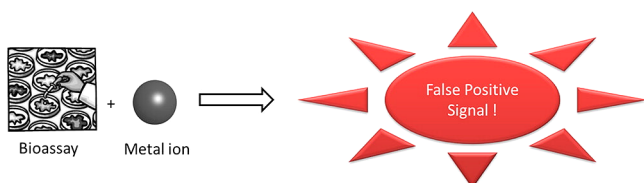


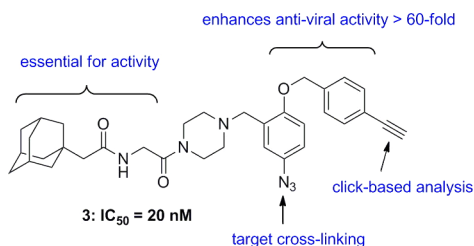
METAL IMPURITIES—CULPRITS IN HIGH-THROUGHPUT SCREENING FALSE HITS



A frequent problem in discovery campaigns using high-throughput screening is the false-positive signals often caused by organic impurities. However, in addition to organic compounds, interference and skewed results on many biochemical assays can also be largely caused by metal contaminations in the compound library.

In this issue, Hermann et al. (DOI: 10.1021/ml3003296) describe the impact of metal ions on biochemical and biosensor-based assays and describe how to identify metal-based inhibition. In particular, a counter screen to rule out inhibition caused by zinc contamination is proposed. Their research cautions against false hits in high-throughput screening and the continued pursuit of contaminated compounds that serves as positive hits in bioassays without thorough investigation of the mode of inhibition.

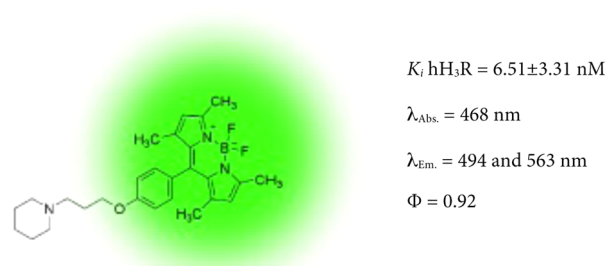
NEW TARGET FOR INHIBITORS AGAINST EBOLA VIRUS



Ebola virus causes outbreaks of rapidly fatal hemorrhagic fever in central Africa. Because there is no effective vaccine or antiviral therapy, there is a high level of public concern about the transmission of Ebola virus. Moreover, the massive production of proinflammatory cytokines in response to infection causes capillary leak and hypovolemic shock.

Here, Lee et al. (DOI: 10.1021/ml300370k) describe the structure–activity relationship and optimization of a small-molecule inhibitor against Ebola virus. The compound is evaluated for its antiviral activity, and its target was identified as the Niemann-Pick C1, a membrane protein expressed in lysosomes that mediates uptake of lipoprotein cholesterol and has been usurped by the virus as a portal for entry. The adamantane peptide inhibitor and its derivatives were found to prevent infection by interfering with the virus binding to Niemann-Pick C1, making this protein a promising target for antiviral therapy.

NEW FLUORESCENT DIAGNOSTIC TOOL FOR HISTAMINE H₃ RECEPTOR



Bodilisant – fluorescent hH₃R ligand

The human histamine H₃ receptor is one of the four human histamine receptor subtypes and is found to modulate the release of several neuronal neurotransmitters. There is still a great need for labeled receptor ligands as diagnostic tools in investigating neurological disorders due to varying results of known antagonists that are currently in preclinical and clinical trials.

In this issue, Tomasch et al. (DOI: 10.1021/ml300383n) describe the design, the synthesis, and the usage of novel small-molecule fluorescent G-protein-coupled receptor ligand, Bodilisant. This compound shows high affinity in the nanomolar range and good selectivity ratios, making it an excellent and novel pharmacological tool for the necessary receptor imaging on histamine H₃ receptor in life sciences, which is also applicable in human brain tissues.

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