ACS Medicinal Chemistry Letters

In This Issue

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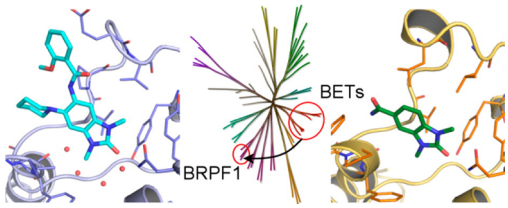
SELECTIVE INHIBITORS OF THE BRPF1 BROMODOMAIN

BRPF1 is a member of the bromodomain and PHD finger family, a multidomain protein that acts as a scaffold for assembly of the monocytic leukemia zinc finger protein MOZ and the related factor MORF histone acetyltransferase complexes. Abnormalities of these complexes have been associated with diseases such as leukemia and aberrant skeletal development. The bromodomain of BRPF1 is an epigenetic reader module, which recognizes acetyl-lysine modifications of histone proteins, although the contribution toward the treatment of disease that disrupts this interaction could make it so far unknown.

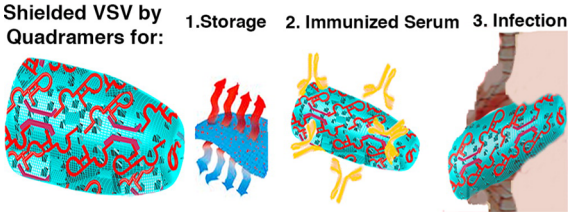
In this issue, Demont et al. (DOI: 10.1021/ml5002932) show the tractability of this target to small molecules by describing the discovery of potent leads that selectively bind to the BRPF1 bromodomain. This featured letter also reports the discovery, binding mode, and structure–activity relationship (SAR) of the first potent, selective series of inhibitors of the BRPF1 bromodomain, with one potent inhibitor exhibiting excellent selectivity and cell permeability.



APTAMER-FACILITATED CRYOPROTECTION OF VIRUSES

Cryoprotection of viral vectors is important for vaccine and therapeutic development due to temperature sensitivity of many viruses. However, the required system presents economic and logistical burden. Vesicular stomatitis virus (VSV) is a suitable choice for vaccine vectors but suffers from limited stability under different handling and storage conditions.

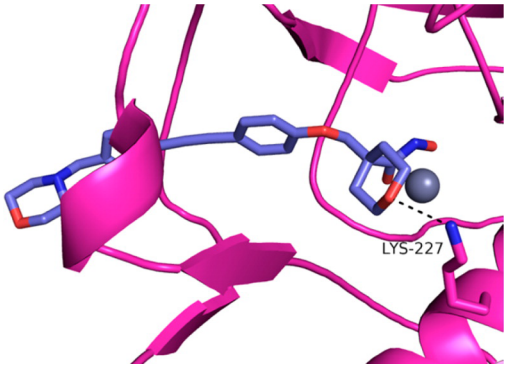
In this issue, Ghobadloo et al. (DOI: 10.1021/ml500322h) report on the use of a tetravalent antivirus DNA aptamers as a viral cryoprotectant by preventing virus aggregation during multiple freeze–thaw cycles. These types of aptamers could be applied in vivo to prevent clearance of the oncolytic virus and increase its efficiency.



NEW LPS-PENETRATING INHIBITORS

There is a critical need for new Gram-negative antibacterial agents due to rising complications with antibacterial resistance with current available therapies. Furthermore, the presence of a lipopolysaccharide (LPS) layer prevents effective compounds from penetrating the Gram-negative cellular envelope.

Here, Murphy-Benenato et al. (DOI: 10.1021/ml500210x) describe the identification, synthesis, and SAR of a new series of bacterial inhibitors for the treatment of Gram-negative infections. The lead compound was derived from a known matrix metalloprotease inhibitor, and the group employed crystallography and structure-based drug design to improve the series. These compounds demonstrate good penetration of the Gram-negative bacterial cell membrane and could lead to new avenues for inhibitor design.



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