ACS Medicinal Chemistry Letters

In This Issue

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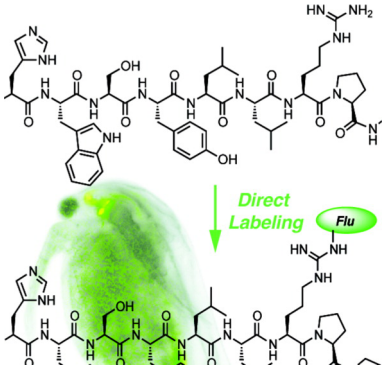
## REPORTER PEPTIDE DEVELOPMENT

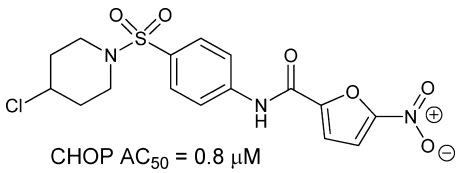
Peptides play an important role in all major processes of life. Studying their distribution is a difficult task as they do not naturally contain reporter groups. This study by Grundler and Gademann (DOI: 10.1021/ml5003508) presents an operationally simple method for the introduction of such reporter groups to biologically relevant peptides by labeling unprotected peptides at the guanidinium group of arginine residues. Two applications of this method are reported in this issue: labeling of the clinically used drug leuprolide and animal tissue distribution studies, and chemical tagging of the environmental toxic microcystin. This method could find applications in biochemical, toxicological, pharmacological, and environmental studies of Arg-labeled peptides.




## ACTIVATORS OF APOPTOSIS

Improperly folded cellular proteins can have toxic functions in the cell. These misfolded proteins are dealt with by the unfolded protein response (UPR). However, when the pathway that facilitates the clearance is overwhelmed, cells trigger apoptosis by upregulating transcription factors such as C/EBP-homologous protein (CHOP).

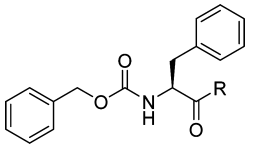
Here, Flaherty et al. (DOI: 10.1021/ml5003234) describe the identification of a sulfonamidebenzamide-based hit compound from a cell-based, high throughput screening method that selectively induced an apoptotic cellular pathway with initial low micromolar activity. Optimization of the scaffold was accomplished through strategic structure−activity relationships to afford several active compounds with improved potency.




## SP1−7 MIMICS FOR NEUROPATHIC PAIN TREATMENT

Chronic neuropathic pain is an underrecognized ailment, which posts a vast economic burden to society. Neuropathic pain is very difficult to treat as there are no specific treatments at this time, and favored treatments are antiepileptic and antidepressant medications. Thus, there is a strong need for new therapies.

Substance P 1−7 ($SP_{1-7}$) is a naturally occurring degradation product within the nervous system, which has been shown to reduce pain of neuropathic origin in relevant model systems. It is of interest to see if compound mimics of SP1−7 could serve as future bioavailable research tools and therapies. Here, Fransson et al. (DOI: 10.1021/ml5002954) describe a new series of small compounds with good binding affinity for the SP1−7 binding site. These compounds could guide further development of first-in-class drugs for treatment of neuropathic pain.



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