ACS Medicinal Chemistry Letters

In This Issue

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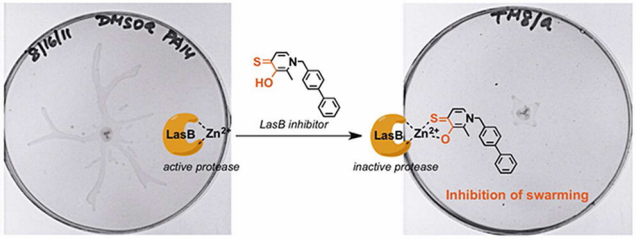
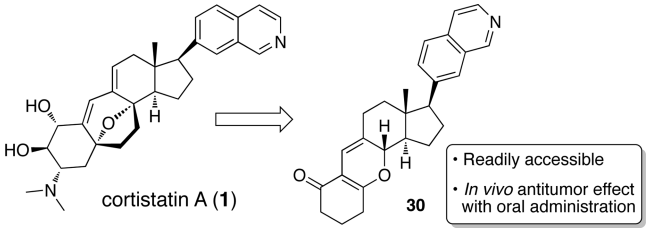
TARGETING THE BACTERIA VIRULENCE FACTOR LASB



The development of bacterial resistance is an ever-growing threat to public health. Thus, recent research has focused on targeting virulence factors. *P. aeruginosa* elastase, LasB, is a bacterial enzyme that has been implicated in the development of keratitis, pneumonia, and burn infection. In addition, this enzyme also plays a critical role in swarming and biofilm formation, which are processes that have been linked to antibiotic resistance.

Here, Garner et al. (DOI: 10.1021/ml300128f) describe the discovery of nonpeptidic small molecule inhibitors of LasB, which is different from previously reported peptide-based inhibitors. More importantly, the authors identified the first targeted compounds to inhibit swarming, a behavior linked to antibiotic-resistant phenotypes, and could aid in elucidating the role of this metalloprotease in *P. aeruginosa*-related infections and its ability to resist antibiotics.

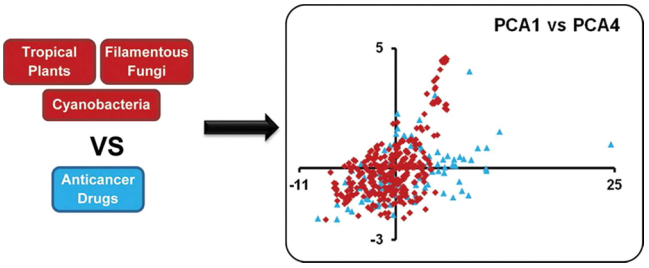
INHIBITING ANGIOGENESIS BY CORTISTATIN ANALOGUE



Angiogenesis, the formation of new from preexisting blood vessels, is a vital process in growth and development but is also a critical phase in the transition of tumors from dormant to malignant stage. This makes angiogenesis a desirable target for cancer treatment.

In this issue, Kotoku et al. (DOI: 10.1021/ml300143d) discuss the design, synthesis, and biological evaluation of analogue compounds of cortistatin A, a characteristic antiangiogenic steroidal alkaloid isolated from Indonesian marine sponge, exhibiting an in vivo antitumor effect. The analogues were designed by considering the 3D structure of cortistatin A. One analogue showed potent antiproliferative activity with high selectivity and also showed in vivo antiangiogenic activity and a significant antitumor effect by oral administration. This serves as a first example of the cortistatin-related compound exhibiting a potent in vivo antitumor effect through the inhibition of angiogenesis.

FOCUS ON CHEMICAL DIVERSITY OF NATURAL PRODUCTS ANTICANCER AGENTS



How diverse is our chemical diversity? How can chemical diversity be quantified and related to the diversity of FDA-approved anticancer drugs? While most studies probe chemical diversity of natural products and compare them to combinatorial libraries, very little, if any, have reported on the comparison of natural products from different sources and then related them to FDA-approved anticancer agents.

Here, El-Elimat et al. (DOI: 10.1021/ml300105s) studied the differences and similarities between the structures of compounds that have been found in three different natural sources: fungi, blue-green algae, and plants. These structures were then compared to the structures of compounds that are used to treat cancer. The goal of the study was to understand if the compounds from nature probe the structural space occupied by anticancer drugs. The authors found that the structural space explored by compounds from these three natural sources indeed probe the chemical space of anticancer drugs, which present a unique complementary way to search for new anticancer drug leads.

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