ACS Medicinal Chemistry Letters

In This Issue

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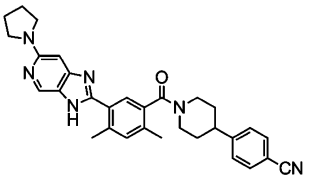
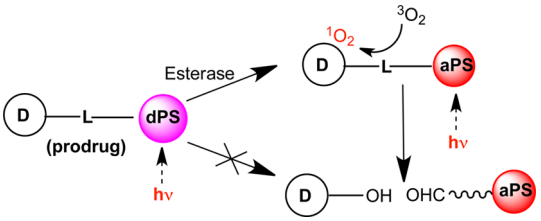
INVESTIGATING FATTY ACID SYNTHASE INHIBITOR AS ANTI-HCV DRUG



Fatty acid synthase, an enzyme synthesized by the liver, plays a key role in lipogenesis. Expression of this enzyme has also been shown to increase upon HCV infection. Thus, inhibition factors such as fatty acid synthase could result in new HCV treatments.

In this issue, Oslob et al. (DOI: 10.1021/ml300335r) describe the development of a novel and potent series of reversible small-molecule inhibitors of fatty acid synthase. One compound is found to have potent antiviral activity and to inhibit FASN inside the cell as well as in vivo. The inhibition of fatty acid synthase by this compound also further confirms that this enzyme is necessary for HCV infection. With its reversible binding mode of inhibition, this small-molecule drug could serve as a useful tool for conducting cellular or in vivo studies in the fields of oncology and metabolic diseases where FASN plays an important role.

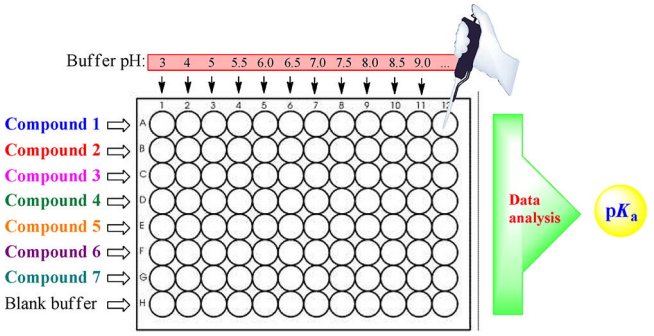
TURNING ON THE THERAPEUTIC BY LIGHT



Systemic side effects of chemotherapeutic agents are limiting factors for the improved therapeutic outcome. Thus, to avoid these systemic side effects, it is critical to minimize the concentration of drugs in the whole body while maximizing the drug concentration at the tumor site. The use of prodrugs, drugs that are administered in an inactive form and successively converted to an active agent, is one approach to achieve this goal. Tissue-penetrable light is a very attractive tool to switch the activation of prodrugs, by which active drug release can be controlled by the external light in a spatiotemporal manner.

Here, Hossion et al. (DOI: 10.1021/ml3003617) demonstrate the application of the photo-unclick chemistry, where the active form of drugs can be released by tissue-penetrable light via singlet oxygen, for the first time in the tissue culture model. This novel strategy of double activatable prodrugs could be applicable for other drug delivery systems.

RAPID PLATE ASSAY FOR pK_A DETERMINATION



Ionization constants are physicochemical parameters that govern the fate of ionizable drugs in the body. Administration, distribution, metabolism, and excretion of drugs as well as binding to their target are deeply influenced by their acidity constant (pK_a). Measuring pK_a values experimentally is an essential but time-consuming task in a drug discovery program. Thus, a new tool for measuring the pK_a of organic compounds by UV−spectrophotometry in a rapid throughput manner is highly desirable.

In this issue, Ríos Martínez and Dardonville (DOI: 10.1021/ml300326v) describe a method that enables the swift measurement of pK_a values of a series of compounds using UV−spectrophotometry. This protocol is straightforward to set up, takes advantage of the sensitivity of UV−spectroscopy, and can potentially be adapted to a more highly automated process.

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