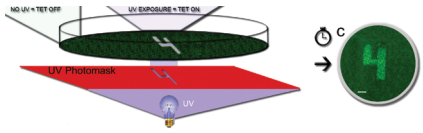
In this ISSUE

Lighting Up Gene Expression

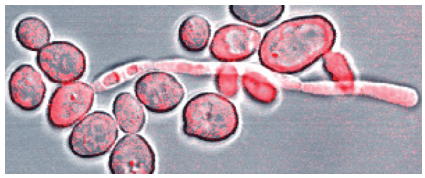
Tissue formation relies on a cell's ability to precisely control the expression of its genes. Use of small molecules to manipulate such gene expression has potential applications in diverse areas including cancer therapies and artificial tissue creation. A promising approach toward this goal is the use of photocaged molecules that regulate gene expression upon activation with light. However, current methods have various limitations, such as cell permeability issues, poor spatial resolution, and weak gene expression levels. Sauers *et al.* (DOI: 10.1021/cb9002305) now demonstrate a highly efficient, photoinducible gene patterning system using the tetracycline-dependent transactivator/transrepressor system (RetroTET-ART) and a photocaged form of doxycycline (NvOC-Dox).



With the RetroTET-ART system, cells are engineered to express a protein of interest only upon induction with doxycycline, which is liberated from a photocaged form upon exposure to ultraviolet light. Use of this system in cell monolayers enabled direct visualization of photolithographic patterns of green fluorescent protein. In addition, patterned expression of the cell adhesion ligand ephrin A5 enabled the directed adhesion of cells expressing the appropriate ephrin A5 receptor.

Saponifying Fungal Pathogens

The prowess of certain fungal organisms, such as *Candida albicans,* as human pathogens has led to a pressing need for new antifungal drugs. The ability of *C. albicans* to form biofilms and produce filaments contributes to its resistance to current antifungal therapeutics, and thus compounds that can combat these behaviors are particularly intriguing. To this end, Coleman *et al.* (DOI: 10.1021/cb900243b) report the discovery of novel antifungal activity found in the plant natural products saponins.

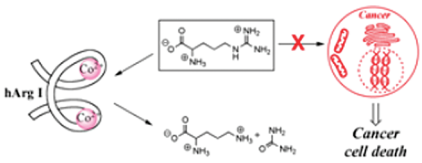


A high-throughput, whole animal screen of over 2500 natural products for their ability to increase the survival of the nematode *C. elegans* infected with *C. albicans* led to the identification of a dozen saponins. Some of these polycyclic, carbohydrate-bearing compounds exhibited antifungal activity as good as that of amphotericin B, the current drug of choice against *C. albicans.* The saponins, which are known to increase cell permeability, also disrupted biofilm and filament production in *C. albicans*. These characteristics may position them well as agents that can, either alone or in combination with other antifungal drugs such as those with limited cell permeability, overcome drug-resistant fungal strains.

Exploiting an Arginase Addiction

Certain prostate, kidney, liver, and skin cancer cells possess a dysfunctioning urea cycle. In order to thrive, these carcinomas require the nonessential amino acid L-arginine. Strategies to target these L-arginine auxotrophs with enzymes that degrade arginine, such as arginine deiminase and human Arginase I, are promising but thus far have encountered various stumbling blocks that have limited their utility. Stone *et al.* (DOI: 10.1021/cb900267j) go back to the basics to devise a new strategy for enhancing the therapeutic potential of human Arginase I.

Arginase I relies on a Mn^{2+} cofactor to facilitate production of the hydroxide ion involved in degrading arginine, but the enzyme works best at a pH of ~9.5. On the basis of several lines of evidence hinting that replacement of Mn^{2+} with Co^{2+} might decrease the pH optimum of the enzyme, a Co^{2+}-substituted Arginase I, referred to as Co-hArgI, was created and characterized. Indeed, Co-hArgI was an order of magnitude more active at physiological pH, exhibited increased stability in human serum (an important feature for a potential therapeutic agent), and was more effective at killing human liver and skin cancer cell lines than its Mn^{2+}-containing counterpart.



Published online March 19, 2010 • 10.1021/cb100047y