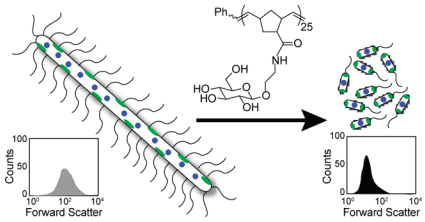
In this ISSUE

(Chemo)Attractive Insight into Swarmer Cells

Some bacteria can differentiate into highly motile cells called swarmer cells, which are particularly interesting because of their increased antibiotic resistance, elevated expression of virulence genes, and rapid colonization of new environments. Chemotaxis proteins, which help cells sense their environment, are required for swarmer differentiation, but the relationship between chemoattractants and swarmer differentiation is not well understood. Lamanna and Kiessling (DOI: 10.1021/cb900132e) have developed a flow cytometry assay to monitor the differentiation state of swarmer cells.

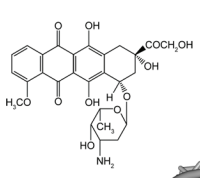


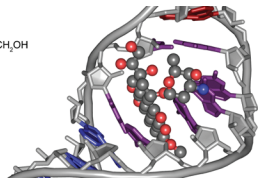
Swarmer cells are elongated relative to their undifferentiated counterparts, and they are also multinuclear. Since both differences in size and DNA content can be evaluated using flow cytometry, it was first demonstrated that this technique could be used to distinguish differentiated and dedifferentiated swarmer cells. Next, it was shown that multivalent glucose derivatives, which are potent chemoattractants, induced swarmer cells to undergo dedifferentiation. This suggests that molecules that target chemotaxis pathways are potential dedifferentiation agents. In addition, the assay described here will facilitate the discovery of new molecular tools to probe the link between chemotaxis and swarmer cell differentiation.

Shifting Targets for HIV

Despite tremendous progress in our understanding and development of treatments for human immunodeficiency virus type 1 (HIV-1), the high mutation rate of the virus enables it to escape drugs designed against its traditional targets, HIV protease and reverse transcriptase, almost as fast as we can develop them. Recently, a new target has emerged: the −1 programmed translational frameshift site RNA. The frameshift enables the translation of critical enzymes, including protease and reverse transcriptase, and is managed in part by a highly conserved stem-loop structure. Compounds that interact at this site could detrimentally affect viral replication, and Marcheschi *et al.* (DOI: 10.1021/cb900167m) describe their search for and the activity of small molecules that bind the stem-loop.

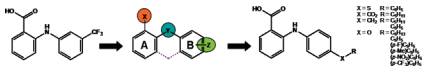
Replacing the middle guanine of the conserved GGA bulge at the base of the stem-loop with a fluorescent analogue enabled development of a high throughput screen, where small molecules that bind the bulge could be detected simply through monitoring changes in the fluorescence of the analogue. Of approximately 35,000 compounds screened, over 200 structurally diverse compounds were identified, including the cancer drug doxorubicin.





Anti-inflammatories Join the Fight Against Cancer

The androgen receptor (AR), a transcription factor that is a member of the nuclear receptor family, plays important roles in normal processes, such as the development and maintenance of male sexual characteristics, and also in diseases, most prominently prostate cancer. The AR is activated by its natural ligand androgen, and though antiandrogens have found some success in the treatment of prostate cancer, undesirable side effects and the development of resistant tumors has fueled the search for alternate treatment options. Building on the recent discovery that the nonsteroidal anti-inflammatory drug flufenamic acid is an AR antagonist, Féau *et al.* (DOI: 10.1021/cb900143a) report the synthesis and promising activity of flufenamic acid analogues.



Careful structure–activity analysis and focused library construction led to the identification of several compounds capable of binding to the androgen binding site and inhibiting AR-mediated gene transcription with potencies similar to those of antiandrogens used to treat prostate cancer. Compounds of this class have few side effects, suggesting their potential as improved prostate cancer drugs.

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