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In This Issue

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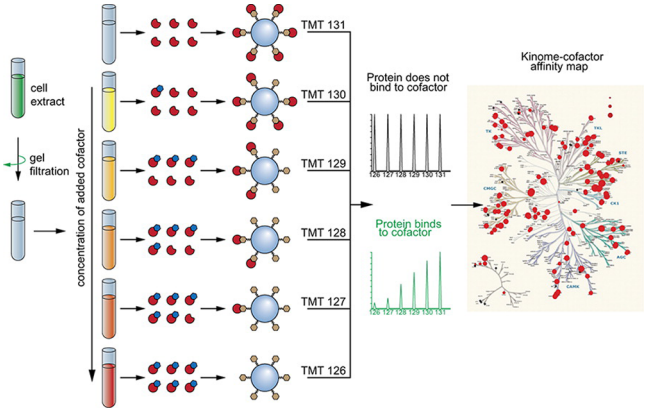
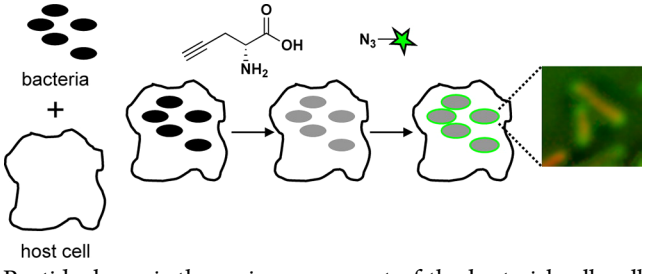
PROFILING KINASE NUCLEOTIDE BINDING



Over 500 protein kinases populate the human kinome, and these enzymes represent an important class of drug targets, especially for cancer. Most kinase inhibitors target the ATP binding site of the enzyme, making finding compounds that are selective for a given kinase an extraordinary challenge. Moreover, different kinases have different affinities for ATP, further complicating the cellular dynamics of kinase inhibition. Now, Becher *et al.* (DOI: 10.1021/cb3005879) use a chemoproteomic approach to gain new insight into these complex dynamics.

The authors use a variation of their "kinobeads" methodology, in which a kinase affinity matrix is used to enable determination of kinase ligand affinities, to characterize the ATP, ADP, and GTP binding profiles of over 200 kinases in two cancer cell lines. They also examine how these profiles impact inhibitor selectivity. The data acquired in this study is a valuable resource for kinase drug discovery efforts and will facilitate prediction of inhibitor efficacy.

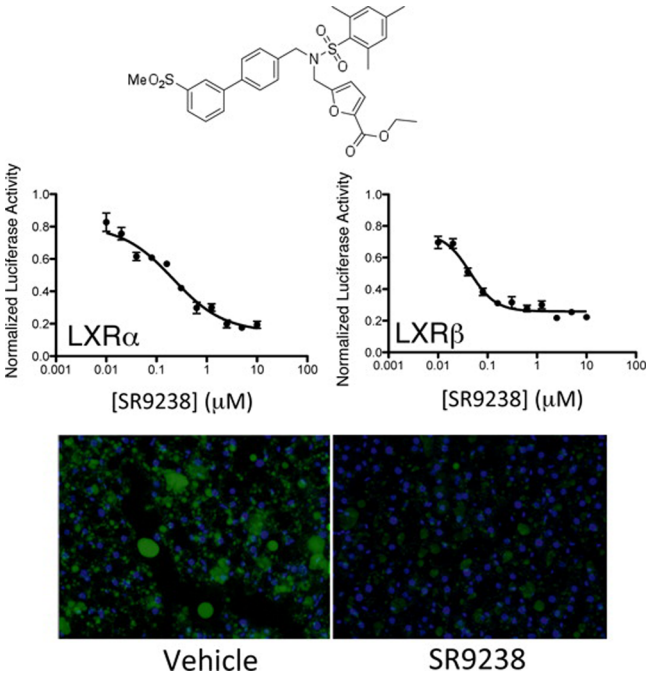
WATCHING THE BACTERIAL CELL WALL



Peptidoglycan is the main component of the bacterial cell wall and the target of numerous drugs against pathogenic bacteria. While there has been extensive investigation into the synthesis and function of peptidoglycan in bacterial cell culture, much less is known about peptidoglycan biology during the infection process. A unique feature of the network of cross-linked glycopeptides that make up peptidoglycan is the presence of D-amino acids, and Siegrist *et al.* (DOI: 10.1021/cb3004995) now report the use of various D-amino acid analogs to explore peptidoglycan biology during infection of mouse macrophage cells.

The authors use azide and alkyne containing D-amino acid derivatives in metabolic labeling experiments with the pathogenic bacteria *Listeria monocytogenes*. Like their natural counterparts, the D-amino acid derivatives are incorporated into peptidoglycan chains. They can then be selectively labeled with fluorescent probes, enabling visualization of the bacterial cell wall. This approach allows spatial and temporal monitoring of peptidoglycan dynamics during bacterial growth and infection and can be applied to the study of various bacterial species.

A DIET PILL FOR THE LIVER



Nonalcoholic fatty liver disease, in which various fats accumulate in liver cells, is associated with metabolic diseases such as obesity and type II diabetes and can lead to inflammation in the liver and even liver failure. The condition affects up to 30% of the population, but few therapeutic options are available to treat it. Now, Griffett *et al.* (DOI: 10.1021/cb300541g) report the activity of a new class of small molecules with potential to prevent the progression of fatty liver disease.

Building off the structure of a known small molecule antagonist of LXR, an enzyme that regulates lipogenesis (the biosynthesis of fat), the authors designed and synthesized a compound called SR9238 that exhibited potent inverse agonist activity against LXR in biochemical and cellular assays. The compound also suppressed inflammation and lipogenesis in the liver in a mouse model of fatty liver disease, providing an exciting new lead for the development of drugs to treat this increasingly prevalent condition.

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