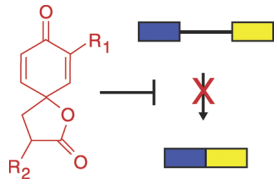
In this ISSUE

Any Way You Splice It

In the complex world of eukaryotic gene expression, splicing of precursor-mRNA (pre-mRNA) to excise non-protein-coding introns is an important and highly regulated step in the process. The spliceosome, composed of five small nuclear RNAs and over 100 proteins, is responsible for carrying out the multistep splicing reaction, but its catalytic and regulatory mechanisms remain largely unknown. In a search for tools to facilitate investigation of the spliceosome, Aukema *et al.* DOI: 10.1021/cb900090z) discover 10 small molecule inhibitors of yeast splicing.

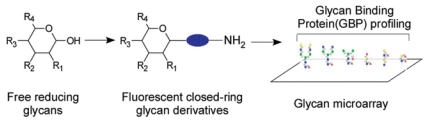
Of 26 molecules tested for their ability to inhibit splicing of yeast pre-mRNA in an *in vitro* splicing reaction, four antibiotics, one kinase inhibitor, and five oxaspiro compounds were identified. Further characterization revealed that two of the antibiotics were selective for yeast splicing over human splicing and four of the oxaspiro derivatives specifically prevent the first cleavage reaction in the splicing process. Just as small molecule ribosome inhibitors have provided invaluable information about protein translation, these compounds promise to be effective tools for exploring spliceosome function.



Glycan Microarrays, Naturally

Glycoconjugates are integral in numerous biological processes, including immune function, tissue development, and disease pathogenesis. The inherent structural complexity of glycoconjugates has made investigation of their function challenging to say the least. Glycan microarrays offer a convenient platform to explore binding properties of carbohydrate-containing biomolecules, but most methods to generate such microarrays result in modification to the glycan structure at its reducing end. Song *et al.* (DOI: 10.1021/) now report a method for generating glycan microarrays that retains the closed ring structure at the reducing end that is present in natural glycans.

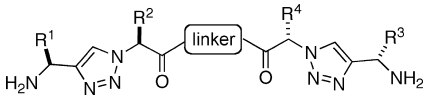
Central to this strategy for glycan microarray preparation were the creation of a stabilized, activatable glycosylamide and the use of a fluorescent bifunctional linker. Reaction of the activated glycosylamide with the linker results in the generation of a glycan that can easily be conjugated to a microarray surface, but whose reducing end closely resembles that of the natural compound. In addition, the presence of the fluorescent group in the linker facilitates characterization and purification of the glycans prior to microarray attachment.



Neurotrophin Mimics: Life or Death?

Neurotrophins are growth factors that help nerve cells decide whether to live or die. Two types of neurotrophins receptors, Trk and p75, exist to mediate neurotrophin activity, complicating our ability to decipher cellular responses to neurotrophins and neurotrophin receptor agonists and antagonists. Small molecule ligands selective for specific neurotrophin receptors would be valuable tools for investigating neurotrophin biology, and to this end, Chen *et al.* (DOI: 10.1021/cb9001415) report the design, synthesis, and activity of compounds selective for the TrkC receptor.

Building on design elements from previous work, a library of fluorescently labeled, triazole-based, bivalent β-turn mimics was synthesized and tested for binding to cells expressing neurotrophin receptors. Active compounds were resynthesized as biotin conjugates and tested for their ability to promote cell survival, differentiation, and signal transduction. In addition to finding inhibitors selective for TrkC, sets of compounds capable of inducing either survival or differentiation, but not both, were identified. Such compounds are particularly intriguing, as their ability to trigger distinct signaling pathways may give them a therapeutic edge.



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