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In This Issue

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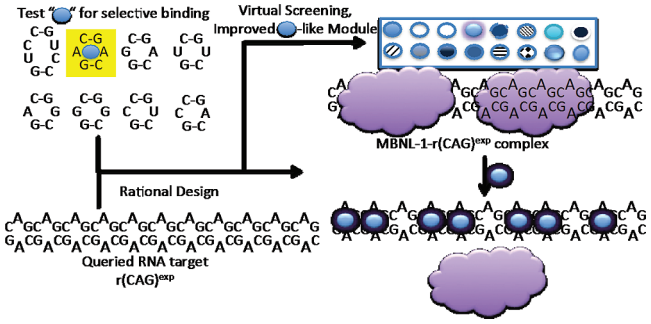
ANOTHER WAY TO SPLICE IT

As our understanding of the many functions of RNA, such as gene transcription, catalysis, and regulation of gene expression, increases, the biomolecule is emerging as an attractive drug target for numerous diseases. For example, the 5′CAG/3′GAC RNA motif is present as expanded triplet repeats in various neurological disorders including Huntington's disease, where it is thought to sequester a protein involved in mRNA splicing. Kumar *et al.* (DOI: 10.1021/cb200413a) now describe a new strategy for identifying compounds that bind to specific RNA motifs, cleverly using known DNA-binding agents as a jumping off point.

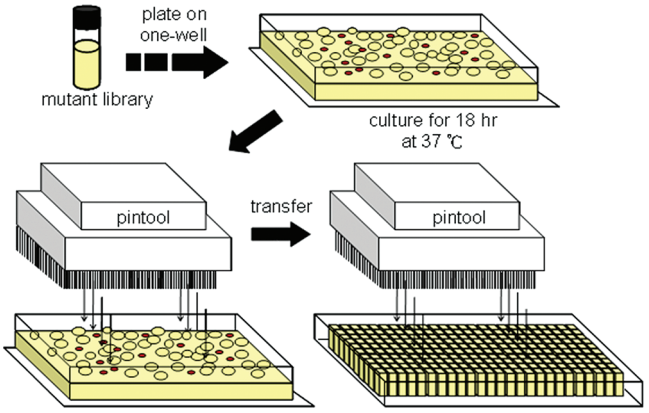


Initially, competition dialysis and fluorescence anisotropy were used to screen the DNA-binding agents for their ability to bind to the 5′CAG/3′GAC motif. The common DNA stain 4′,6-diamidino-2-phenyl-indole, known as DAPI, was identified and used as for a virtual screen to identify additional compounds with improved binding properties. The most potent compound discovered, 4-guanidinophenyl 4-guanidinobenzoate, improved splicing defects in cellular models of Huntington's disease as well as in cells derived directly from a patient with Huntington's disease.

ENGINEERING A FUNGAL ALCOHOL FACTORY

Conversion of biomass to ethanol by capable microorganisms offers a path for creation of renewable biofuels and reduction of carbon dioxide emissions. The plant material lignocellulose, which is made of cellulose, hemicellulose, and lignin, is an abundant source for ethanol production, though conversion of hemicellulose is less efficient than cellulose. The yeast *Pichia stipitis* is a relatively proficient converter of xylose, the most abundant sugar in hemicellulose, to ethanol and is thus a candidate for biofuel production from lignocellulose. Chen *et al.* (DOI: 10.1021/cb200396b) now report how protein engineering in *P. stipitis* can lead to improved conversion of xylose to ethanol.

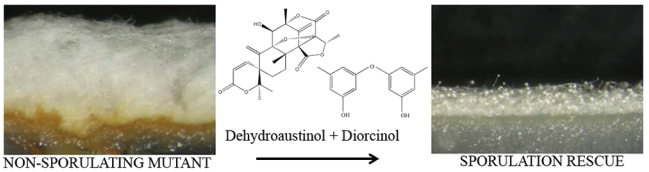
Careful examination of RNA expression, enzyme kinetics, and individual enzyme activities led to the identification of the enzyme transaldolase as the bottleneck in the conversion of xylose to ethanol in *P. stipites.* Using directed evolution, in which mutants of transaldose were screened to identify variants exhibiting enhanced activity over the wild-type enzyme, a transaldolase with a single point mutation was found that, when



stably expressed in *P. stipites*, increased both the rate and yield of xylose conversion to ethanol.

SIGNALING FOR SPORES

Filamentous fungi comprise a diverse group of microorganisms; they are the mold on your bread, produce life-saving medicines and environmentally friendly agricultural chemicals, and cause human disease. The thread-like structures that characterize these microbes are called hyphae, and when hyphae are exposed to the atmosphere, they produce spores which allow the fungi to reproduce. Studies using genetic mutants of the filamentous fungi *Aspergillus nidulans* that are unable to form spores have suggested that a factor secreted by wild-type *A. nidulans* is responsible for signaling for sporulation. Rodríguez-Urra *et al.* (DOI: 10.1021/cb200455u) now report that this factor is actually two small molecules, the meroterpenoid dehydroaustinol and the orsellinic acid derivative diorcinol.



Using an assay measuring sporulation activity, dehydroaustinol and diorcinol were purified from extracts of wild-type *A. nidulans* cultures. It was found that the compounds form an adduct that prevents crystal formation on the surface of the hyphae and increases the lipophilicity of the signal, properties that may contribute to sporulation.

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