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In This Issue

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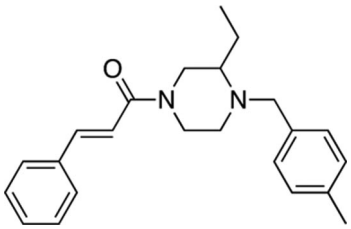
APPLIED BIOLOGICAL SCIENCES

Compounds against botulinum neurotoxin

Paralysis-inducing neurotoxins produced by the bacterium *Clostridium botulinum* are highly toxic proteins to humans and are classified as category A bioagents by the U.S. government. One subtype, botulinum neurotoxin A, is approximately 100 billion times more potent than cyanide. Currently available protein therapies against the toxin are inadequate because of limited availability, high production costs, and potential side effects. Using a multifaceted, high-throughput screening approach, Lisa Eubanks *et al.* identified eight compound "pools" of small molecules, isolated individual compounds, and tested their efficacy in cell-based assays and in mice exposed to botulinum neurotoxin. One compound, NA-A1B2C10, increased survival time in the mice by 36%, whereas 16% of animals treated with a second molecule (2,4-dichlorocinnaminic hydroxamic acid) survived with no obvious symptoms. The compounds showed little activity in the cell-based assays, suggesting that standard cell-based screening methods may miss potential inhibitors. Because of their complementary modes of actions, the two compounds could be used as a "cocktail therapy" against botulinum neurotoxin, the authors suggest. — M.M.



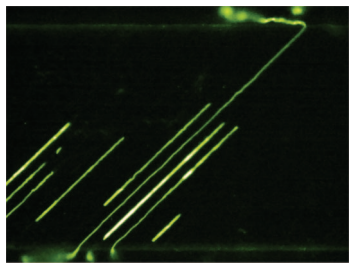
Chemical structure of candidate botulinum neurotoxin inhibitor.

"An in vitro *and* in vivo *disconnect uncovered through high-throughput identification of botulinum neurotoxin A antagonists" by Lisa M. Eubanks, Mark S. Hixon, Wei Jin, Sukwon Hong, Colin M. Clancy, William H. Tepp, Michael R. Baldwin, Carl J. Malizio, Michael C. Goodnough, Joseph T. Barbieri, Eric A. Johnson, Dale L. Boger, Tobin J. Dickerson, and Kim D. Janda* (see pages 2602–2607)

BIOPHYSICS

Barcoding DNA in nanoslits

Experimental techniques using single molecules are poised to dramatically change the way biological research is performed, especially in genome analysis. The mainstream use of single-molecule analytes for genomic investigation will require efficient, high-throughput nanoscale devices. Kyubong Jo *et al.* report the development of a technique for confining, elongating, and barcoding individual strands of DNA into nanoslits, which could lead to advanced methods of sequencing individual DNA molecules. The authors trapped DNA molecules in patterned silicone rubber chips with micro- and nanoscale channels and slits in various sizes and orientations. DNA stiffness and elongation in the channels were controlled by adjusting the concentration of the buffer solution, which eliminated the need to precisely control the sizes of the channels and slits. An enzymatic reaction added fluorescent tags to the DNA strands, and their sequence-dependent positions could then be determined by reading the fluorescent signals as a barcode. Jo *et al.* also developed a set of equations accounting for the DNA's elongation and stiffness in the channels. According to the authors, once this technique is fully automated, it will rapidly barcode single molecules of DNA, allowing large-scale genome analysis. — P.D.



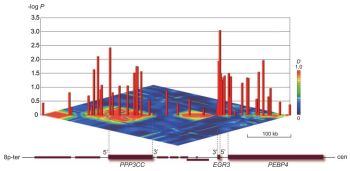
Nanoslits for single-molecule DNA analysis.

"A single-molecule barcoding system using nanoslits for DNA analysis" by Kyubong Jo, Dalia M. Dhingra, Theo Odijk, Juan J. de Pablo, Michael D. Graham, Rod Runnheim, Dan Forrest, and David C. Schwartz (see pages 2673–2678)

GENETICS

Schizophrenia candidate gene in calcineurin pathway

Eighty percent of schizophrenia cases show a pattern of heritability, but the genes responsible for development of this psychiatric disorder are unknown. Kazuo Yamada *et al.* report on a possible candidate gene in the calcineurin pathway. Calcineurin, an enzyme expressed heavily in the CNS, regulates signaling in both the dopamine and glutamate neurotransmitter systems. To investigate a link between calcineurin function and schizophrenia, Yamada *et al.* searched for polymorphisms



Genetic associations with schizophrenia.

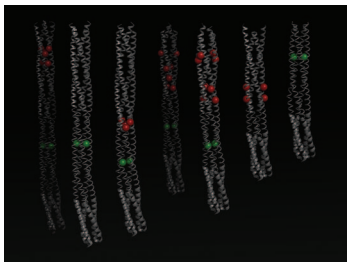
in 14 calcineurin-related genes in a population of Japanese individuals with schizophrenia. Four genes, including one coding for a calcineurin subunit, showed association with schizophrenia. Three of the genes belong to a family of transcription factors called EGR, with *EGR3* down-regulated in the brains of patients with schizophrenia. Looking for *EGR3* variants in >1,000 schizophrenia case-control samples revealed 15 variants, one of which was closely linked with the development of disease. The authors suspect that altered *EGR3* signaling in the calcineurin pathway could explain some of the hallmarks of schizophrenia, including impairments in attention and language. — T.H.D.

"Genetic analysis of the calcineurin pathway identifies members of the EGR *gene family, specifically* EGR3*, as potential susceptibility candidates in schizophrenia" by Kazuo Yamada, David J. Gerber, Yoshimi Iwayama, Tetsuo Ohnishi, Hisako Ohba, Tomoko Toyota, Jun Aruga, Yoshio Minabe, Susumu Tonegawa, and Takeo Yoshikawa* (see pages 2815–2820)

MICROBIOLOGY

Conserved characteristics of microbial chemoreceptors

Bacteria constantly sense their environment in an effort to travel toward nutrients or other favorable conditions and away from hostile environments. Methyl-accepting chemotaxis proteins (MCPs) are the bacterial cell's environmental sensors, able to detect minute concentrations of relevant compounds and relay signals inward. Little is known about how MCPs translate their exquisite detection abilities into signals. Using comparative genomic analysis, Roger Alexander and Igor Zhulin identified structural features of MCPs critical to their function. Because sequences that are unchanged over evolutionary time are likely to be important structural or functional elements of a protein, the authors compared the sequences of >2,100 different MCP domains to determine which areas have been conserved. In addition to identifying a previously unknown flexible signaling portion of the protein, Alexander and Zhulin found that changes in the signaling and adaptation domains in any MCP are tightly coupled. This coupling could explain the diversity of chemotaxis mechanisms, including how a positive signal for one species could be a negative signal for another. — T.H.D.



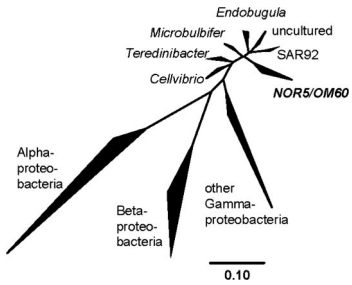
Characterizing microbial chemoreceptors.

"Evolutionary genomics reveals conserved structural determinants of signaling and adaptation in microbial chemoreceptors" by Roger P. Alexander and Igor B. Zhulin (see pages 2885–2890)

MICROBIOLOGY

Previously unknown marine photosynthetic bacteria

During the summer months, a large part (up to 11%) of the bacterioplankton composition of marine coastal systems is made up of a specific gammaproteobacterial lineage called NOR5/OM60. Bernhard Fuchs *et al.* sequenced the genome of *Congregibacter litoralis* KT71, a gammaproteobacterium isolated from the North Sea and representative of the NOR5/OM60 clade. The authors found that KT71 is capable of photosynthesis, indicating the existence of a sizable, previously unknown group of photosynthesizing bacteria in the oceans. The genome of KT71 was found to contain a complete photosynthesis superoperon, including genes coding for accessory pigments. Although the bacterium was only weakly colored, it expressed pigments typical of anoxygenic photosynthesis. Photosynthesis in KT71 also appears to be regulated by light and redox conditions. Because members of the NOR5/OM60 clade have been found worldwide, Fuchs *et al.* say these results will help illuminate the roles of KT71 and other gammaprotobacteria in the oceans. — P.D.



Parsimony tree of gammaproteobacterial clade NOR5/OM60.

"Characterization of a marine gammaproteobacterium capable of aerobic anoxygenic photosynthesis" by Bernhard M. Fuchs, Stefan Spring, Hanno Teeling, Christian Quast, Jörg Wulf, Martha Schattenhofer, Shi Yan, Steve Ferriera, Justin Johnson, Frank Oliver Glöckner, and Rudolf Amann (see pages 2891–2896)