ACS SyntheticBiology

In This Issue

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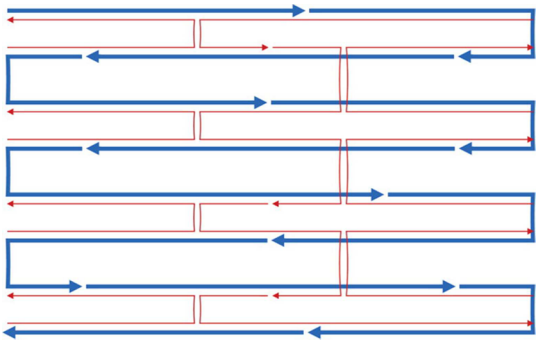
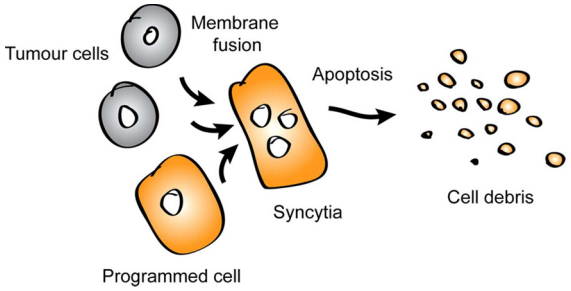
COMPLEX DNA NANOSTRUCTURES FROM OLIGONUCLEOTIDES



DNA nanotechnology is a powerful tool for building self-assembling nanostructures and devices with applications in diverse areas such as protein crystallization (lattice formation), electronics (nanotube and nanowire device integration), molecular programming, drug delivery, DNA computation, and general algorithmic self-assembly. The prevailing method of manufacturing large and complex DNA nanodevices, DNA origami, requires the use of a biologically derived single-stranded scaffold. Here, Mathur and Henderson (DOI: 10.1021/sb3000518) describe a novel methodology for creating nanostructures using entirely synthetic DNA oligonucleotides.

Using DNA's inherent genetic code and its specific property of Watson–Crick base pairing, the authors describe a way to build architectural structures and devices of the size of a couple hundred nanometers. This new method also allows the simultaneous formation of multiple nanostructures in a single reaction and represents a substantial advance in the field of nanotechnology, with a potential to expand the scope and utility of DNA nanostructures and devices.

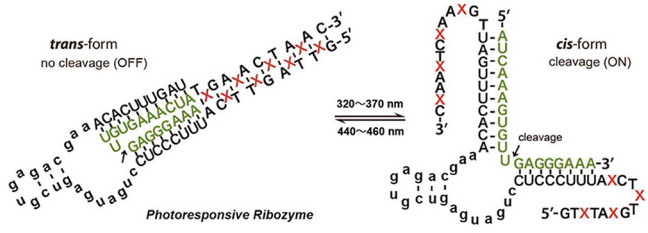
PROGRAMMING MEMBRANE FUSION AND APOPTOSIS



Cells can be programmed to perform a diverse array of functions through the delivery of natural or engineered proteins. Here, Nagaraj et al. (DOI: 10.1021/sb3000468) introduce a set of proteins that has the potential ability to program a cell for therapeutic intervention against tumor cells.

Using vesicular stomatitis virus glycoprotein (VSV-G), a common envelope protein employed in lentivirus generation, the authors confirmed membrane fusion between cells at a low pH. They then showed that fused cells (syncytia) lose their ability to dynamically bleb, a mode of migration preferred during tumor metastasis. Finally, it was reported that co-expression of VSV-G with L57R (a previously engineered caspase-7 protein) allowed cells to first fuse at low pH and then undergo apoptosis via a light stimulation. This study suggests that membrane fusion combined with apoptosis has a potential application in the clearing of unwanted cells in cell-based therapies.

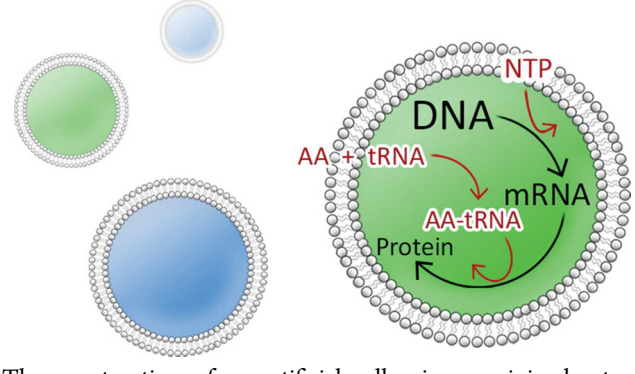
PHOTOSWITCHING NUCLEIC ACID CATALYTIC ACTIVITY



The ability to photoregulate biological molecules is an efficient way to investigate their functions. Additionally, *in vivo* applications of photoactive systems might facilitate the development of new therapies that use photoresponsive molecules. Here, Liang et al. (DOI: 10.1021/sb300120n) demonstrate the generality and mechanism of a strategy for photoswitching the activity of functional nucleic acids by modulating their topological structure.

Ribozymes and DNAzymes have two binding arms and a catalytic loop used for the efficient photoregulation of RNA cleavage. The authors attached an artificial double helix, regulatable by light, to each arm and found that RNA cleavage is suppressed in the duplex state and rescued in the single-stranded state. This analysis showed that topological constraints can suppress RNA cleavage by causing both the unfavorable structural change of the catalytic site and the decreased binding affinity of the RNA substrate.

LINKING GENOTYPE AND PHENOTYPE IN PROTEIN SYNTHESIZING LIPOSOMES



The construction of an artificial cell using a minimal set of purified components assembled in well-defined conditions is

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certainly one of the biggest challenges in synthetic biology. The ability to control the expression of multiple genes and to generate predictable output proteins relies on the link between genotype and phenotype. Here, Nourian and Danelon (DOI: 10.1021/sb300125z) provide the first report on this relationship in protein synthesizing lipid vesicles using a bottom-up synthetic biology approach.

The authors encapsulated an elementary gene expression system inside semipermeable lipid vesicles, fueling the internal mRNA and protein synthesis machinery with an external supply of nutrients. The amounts of DNA molecules and synthesized proteins were visualized by fluorescence confocal microscopy in individual surface-tethered vesicles. The results presented in this study are of primary importance in the building of multigene artificial cells and next generation drug delivery systems.

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