Ribose-phosphate diphosphokinase is the main flux branching enzyme that shunts ribose phosphate from the CBB cycle into biomass production. Mapping the mutations in *prs* that were identified in the evolved strains onto the enzyme's crystal structure revealed that they were clustered in substrate-binding loop regions. The mutations were predicted to reduce the enzyme's reaction rate, which would decrease the shunting of ribose phosphate into biomass and increase flux through the CBB cycle. Overall, the mutations altered metabolite connections to favor carbon dioxide fixation.

This study marks a notable feat in metabolic engineering. Antonovsky *et al.*[2] succeeded in exploiting modularity and rational "tinkering"[7] to rewire enzymes into new modules. This is desirable because synthetic modules might be more orthogonal to native metabolic pathways. In the context of CO_2 fixation research, the authors have achieved the first hemi-autotrophic bacterium bearing a synthetic, fully operational carbon fixation module—albeit requiring a second module to generate the ATP and the reducing power to run it. This represents an important step toward realizing theoretical proposals to engineer autotrophy by co-opting parts from diverse pathways to form metabolic modules not found in nature[8,9].

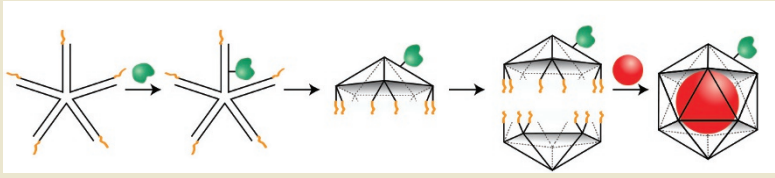
The remaining obstacle to fully autotrophic growth on CO_2 is to supply the hemi-autotropic *E. coli* with sufficient energy and reducing power. It is worth recalling that the ancestor of the chloroplast brought to its eukaryotic host not only the dark reactions of CO_2 fixation, but also the photochemical machinery needed to provide the requisite ATP and reducing power. One immediate application of the hemi-autotrophic *E. coli* will be as a platform technology to test synthetic modules that could energize the synthetic CBB cycle. Once the energetics problem is solved, the goal of a fully autotrophic *E. coli* will be attainable. Such an organism could be engineered into microbial cell factories to make biofuels, bioplastics or biopharmaceuticals using only CO_2 and water.

COMPETI\NG FINANCIAL INTERESTS
The author declares no competing financial interests.

1. Yoon, H.S., Hackett, J.D., Ciniglia, C., Pinto, G. & Bhattacharya, D. *Mol. Biol. Evol.* **21**, 809–818 (2004).
2. Antonovsky, N. *et al. Cell* **166**, 115–125 (2016).
3. Hartwell, L.H., Hopfield, J.J., Leibler, S. & Murray, A.W. *Nature* **402** (Suppl.), C47–C52 (1999).
4. Kerfeld, C.A. & Erbilgin, O. *Trends Microbiol.* **23**, 22–34 (2015).
5. Sharkey, T.D. & Weise, S.E. *Photosynthesis: Plastid Biology, Energy Conversion and Carbon Assimilation* (eds. Eaton-Rye, J.J., Tripathy, B. & Sharkey, T.D.) 649–672 (Springer, 2012).
6. Berg, I.A. *Appl. Environ. Microbiol.* **77**, 1925–1936 (2011).
7. Jacob, F. *Science* **196**, 1161–1166 (1977).
8. Erb, T.J. & Zarzycki, J. *Curr. Opin. Chem. Biol.* **34**, 72–79 (2016).
9. Bar-Even, A., Noor, E., Lewis, N.E. & Milo, R. *Proc. Natl. Acad. Sci. USA* **107**, 8889–8894 (2010).

DNA cages target quantum dots

Quantum dots (QDs) have high photostability and brightness that allow single-particle tracking in cells and tissues by fluorescence microscopy. But over a decade after they were first introduced in biology, it remains challenging to use QDs to label specific biomolecules because of their tendency to aggregate and technical difficulties in functionalizing them. To overcome this limitation, Bhatia *et al.*[1] encapsulated QDs in DNA icosahedra, artificial 20-faced DNA 3D structures that can be functionalized in a uniform, stable fashion. The combination of QDs with targetable DNA icosahedra allows detailed live imaging of endocytosis and in-depth characterization of endosome dynamics along different endocytic routes.



DNA polyhedra have notable advantages as small-molecule carriers. They can be readily loaded with nanoscale particles, such as QDs, without compromising the properties of the cargo. Previous work from the same laboratory showed that DNA polyhedra can be loaded with fluorescent molecules for imaging studies[2]. In their new paper, the authors encapsulated one CdSe/CdS/ZnS QD per DNA icosahedron by incubating QDs with a mix of two half-icosahedra in solution. The QDs were 5 nm in diameter, but the internal space of the icosahedra can potentially hold QDs up to 11 nm in diameter.

To identify the best residues in the DNA shell for displaying targeting molecules, the authors used AMBER (a software package for molecular dynamics simulations) to assess the stability of DNA icosahedra following monofunctionalization with folic acid at different positions of the scaffold. The simulations revealed icosahedra residues that exposed folate to the outside, and one of the seven conformations tested *in vitro* showed efficient uptake by cells in a folate-dependent fashion.

The ability to functionalize QDs with small molecules enabled real-time tracking of subcellular endocytic pathways. Using different endocytic ligands, such as folic acid, galectin-3 (Gal3) and Shiga toxin B-subunit (STxB), the authors could follow QDs along endocytic pathways specific for each ligand. As a first example, icosahedra functionalized with folate were seen to colocalize with the folic-acid endocytosis pathway, and their uptake was inhibited by adding excess folate, suggesting that uptake was folate-specific. The authors also showed that Gal3-functionalized icosahedra revealed the morphology of endosomal compartments at different stages along the Gal-3 endocytic pathway, including early and late endosome-like structures.

Finally, QDs tagged with STxB were used to image the dynamics of endosomal trafficking. Particle diffusion behavior on the extracellular face of the plasma membrane of HeLa cells was quantified by internal reflection fluorescence microscopy—an observation made possible thanks to the photostability of QDs. The results suggested a picket-fence-type compartmentalization of the underlying actin meshwork. The STxB QDs also enabled detailed study of the dynamics of endosome trafficking along the microtubule network. Internalized particles actively moved and fused with early endosomes, and individual endosomes carrying the nanoparticles alternated between active movement and diffusive behavior.

This innovative approach to target QDs could in principle be adapted to image dynamic biological processes other than endocytosis. "The cellular imaging and tracking results are very impressive," says Shuming Nie, a researcher at Emory University and the Georgia Institute of Technology, who was not involved in the study. Nevertheless, he says, "one major limitation is that this class of QD probes is still fairly bulky (about 10 nm in diameter), which could restrict diffusion and binding inside the highly crowded cytoplasm." In addition to reducing particle size, functionalization with multiple ligands may offer another approach to optimize the technology.

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1. Bhatia, D. *et al. Nat. Nanotechnol.* http://dx.doi.org/10.1038/nnano.2016.150 (2016).
2. Bhatia, D., Surana, S., Chakraborty, S., Koushika, S.P. & Krishnan, Y. *Nat. Commun.* **2**, 339 (2011).