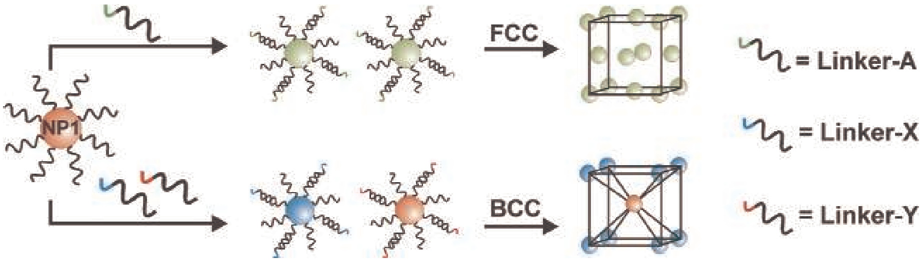
CHEMISTRY

DNA Assembles Materials From the Ground Up

For sheer utility, it's hard to beat DNA. It's the molecule of life, of course. And manipulating it is the crux of the entire field of biotechnology, not to mention a novel form of computing. Now, researchers in the United States and Germany report in a trio of papers this week that DNA could also hold the future to building materials from the bottom up.

In two papers in *Nature*, two separate groups in the United States report that they have linked DNA to gold nanoparticles and used it to assemble the particles into extended crystals. Such crystals may prove useful in creating distortion-free lenses and other sought-after byproducts of optical materials known as metamaterials. Down the road, they could also lead to new ways to construct everything from electronic materials to protein crystals coveted by drug developers. The third paper, which appears on page 594 of this issue of *Science*, uses DNA as tweezers to pick up compounds and place them where they're wanted. Although probably too slow for assembling large amounts of materials, the technique could help researchers put chains of molecules together to answer questions such as how different enzymes work together in a series, each handing off its product to become the starting material of the next enzyme.

Taken together, the results show that nanotechnologists are beginning to look at DNA in a whole new light. "This is a watershed in using DNA to assemble objects other than DNA," says John Crocker, a physicist at the University of Pennsylvania.



Shape shifter. Nanoparticles coated with different DNA sequences can form different crystalline lattices, depending on whether the DNAs bind to themselves (*top*) or to sequences on other particles (*bottom*).

DNA's power lies in the way chains of its four nucleotide bases pair up, with A's binding selectively to T's and C's binding to G's. As a result, researchers can synthesize single strands of DNA with a particular sequence of bases, knowing that if the strand encounters its complement the two will bind. More than 10 years ago, teams led by Chad Mirkin at Northwestern University in Evanston, Illinois, and Paul Alivisatos at the University of California, Berkeley, took advantage of this affinity to make DNA sensors. They linked DNA to gold nanoparticles and then added complementary DNA strands to a solution containing the DNA-coated particles. As the DNA partners came together, they drew the particles into an extended network that changed the way light propagated through ▸

DEVELOPMENTAL BIOLOGY

Aging of the Ovary Linked to PTEN Pathway

When a woman is born, her ovaries already contain a full supply of the immature eggs she will need in her reproductive lifetime. Normally, these eggs begin ripening at about age 13 and are gradually released, usually at the rate of one per month, until she is about 50 years old. But in a small minority of women, perhaps 1 in 100, the ovaries stop releasing eggs much earlier in life, thus causing infertility and premature aging. Exactly why that happens isn't understood, but new results may help provide an explanation.

On page 611, a team led by Kui Liu of Umeå University in Sweden, reports that a gene called *Pten*, which is best known as a suppressor of tumor growth, is needed to keep egg development in check. In its absence, the researchers found, the egg-containing follicles of mice were activated rapidly at an early age, thus causing depletion of the animals' eggs much sooner than is normal—a situation similar to that of premature ovarian failure (POF) in humans.

"It is a very nice piece of work that shows the importance of the PTEN pathway" in controlling follicle maturation in mice, says reproductive geneticist Aleksandar Rajkovic of Baylor College of Medicine in Houston, Texas. If *PTEN* also controls human egg maturation, the finding may aid the design of improved infertility treatments.

Liu and his colleagues came to their conclusion by genetically engineering a mouse strain in which *Pten* expression was inactivated specifically in the animals' oocytes. The results showed that a functional *Pten* in oocytes is needed to keep egg follicles from maturing. Without it, Liu says, "all the primordial follicles were activated prematurely."

Once a follicle is activated, there's no going back. Its egg either matures and is released for fertilization or dies. As a result, the animals had one litter but were infertile by about 3 months of age, which is early adulthood for mice. By that same age, their ovaries had lost essentially all their follicles.

The result is consistent with previous findings from Diego Castrillon, Ronald DePinho, and their colleagues at Harvard Medical School in Boston. About 5 years ago, they showed that knocking out the gene for the Foxo3a protein produced essentially identical effects (*Science*, 11 July 2003, p. 215). As it happens, *Pten* negatively regulates two other enzymes, PI3 kinase and Akt, which suppress Foxo3a. So with *Pten* gone, Foxo3a can't function.

Castrillon's team, now at the University of Texas Southwestern Medical Center in Dallas, reported in the January issue of *Human Reproduction* that Foxo3a mutations are not a common cause of POF in humans. Still to be determined is whether mutations in PTEN or in other proteins that cooperate with PTEN in producing its cellular effects are involved with human ovarian problems.

Even with that uncertainty, researchers think that the PTEN pathway is a good target for potential fertility treatments. Foxo3a and a number of other proteins shown to affect egg development in

CREDIT: S. Y. PARK *ET AL.*, *NATURE* (JANUARY 2008)

the solution and produced a color change (*Science*, 22 August 1997, p. 1036). Today, the technique is at the heart of DNA sensors now on the market.

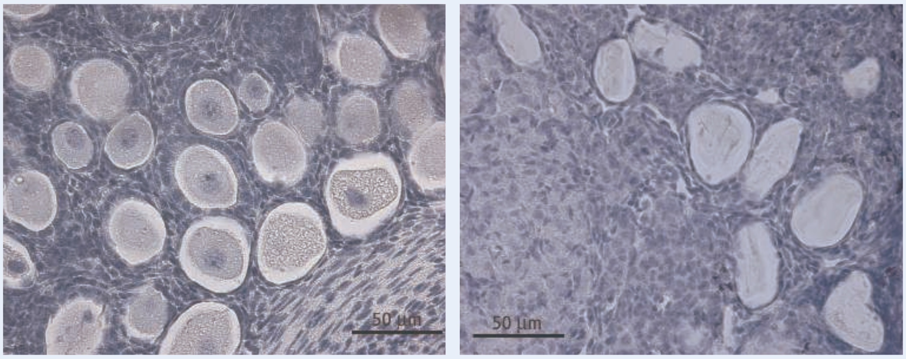
But although the early effort showed it was possible to make clumps of DNA-linked particles, it couldn't organize those particles into regular crystalline arrays. Crocker and Mirkin say they think numerous groups tried and failed to find the magic recipe.

In *Nature*, Mirkin and colleagues, as well as a second group led by Oleg Gang at Brookhaven National Laboratory in Upton, New York, report hitting on a similar solution: longer DNAs. The trouble with previous efforts, Gang says, is that the DNA linkers they used between nanoparticles were likely too short and thus relatively rigid. By substituting longer, floppier DNA molecules, Mirkin's and Gang's groups gave the particles room to move around and settle into a conformation that maximized the number of links they could make with their neighbors. The result was that both groups were able to program their materials to form what is known as a body-centered cubic arrangement, a crystalline lattice in which two particle types alternate their positions at the corners and the center of the cube (see figure, p. 558). And both Gang and Mirkin expect this is only the beginning. "There is a hope that many more structures will be possible," Gang says.

That hope is echoed by Hermann Gaub, whose team at the University of Munich, Germany, also pushed the limits on using DNA to organize other materials. Gaub's team used DNA as a tool to assemble materials molecule by molecule. A version of this experiment was first reported in 1990, when Donald Eigler and colleagues at IBM used the tip of a scanning tunneling microscope to assemble xenon atoms on a surface to spell "IBM." But that required a vacuum chamber and a temperature near absolute zero.

Gaub and colleagues essentially repeated the feat at room temperature and in water, using as building blocks light-emitting molecules known as fluorophores. First, they linked the fluorophores to DNA strands; then, using complementary strands attached to the tip of an atomic force microscope, they moved them one by one onto a surface where other DNA molecules held them in place. Gaub says he hopes the technique will help engineers further miniaturize biomedical devices by allowing biomolecules to be spotted down with exquisite control. Such specificity is DNA's forte and could help the biomolecule gain a new job as a construction tool for the nanoworld.

–ROBERT F. SERVICE



Running out. Mouse ovarian tissue in which *Pten* was inactivated in oocytes (*left*) shows many activated follicles just 8 days after birth. But by 12 weeks (*right*), the mouse ovaries are depleted of follicles.

CREDIT: P. REDDY *ET AL., SCIENCE*

animals are transcription factors that regulate gene expression. But PTEN is an enzyme, and developing compounds that inhibit it, thus promoting egg development and maturation, should be easier. An enzyme "has the advantage of being easily manipulated," says Aaron Hsueh, an ovarian physiologist at Stanford University School of Medicine in Palo Alto, California.

He notes that although most women with POF are diagnosed after all their eggs are depleted, some still have follicles in their ovaries. It's impossible to tell when they will mature and release an egg, but treatment with a PTEN inhibitor could allow physicians to control that and perhaps help a woman become pregnant. Another possibility is to use a PTEN pathway inhibitor to aid follicle maturation in ovarian tissue in lab dishes, as may be needed for women who have had their ovaries removed prior to chemotherapy that would render them sterile.

–JEAN MARX

SCIENCE**SCOPE**

Tissues Case Over

Participants who have donated tissue for research shouldn't get their hopes up that they can ever take it back. That issue was largely settled last week when the U.S. Supreme Court declined to intervene in a fight between a medical researcher and his former university over who owns tissue donated by patients. William Catalona, a prostate cancer researcher at Washington University in St. Louis, Missouri, sued the school after it blocked him from taking his patients' tissue samples to a new job at Northwestern University in Evanston, Illinois.

The university argued successfully in federal district and appellate courts that institutions own the biological samples their researchers collect because patients have donated them as gifts (*Science*, 29 June 2007, p. 1829). Law professor and bioethicist R. Alta Charo of the University of Wisconsin, Madison, says that although the district court's ruling in favor of the school may not apply in every case—it depends on a particular state's gift law and the details of the patient consent form—"the opinion is likely to be highly influential nationwide." Catalona says that the legal rulings have made "a travesty "of federal regulations protecting research subjects.

–JOCELYN KAISER

EPA Wants Data: If You Please

How risky are nanomaterials? Last week, the U.S. Environmental Protection Agency (EPA) launched a voluntary nanomaterials toxicity reporting program to help find out. The new program encourages—although it does not mandate—companies that make, use, or import nanomaterials to submit characterization and risk data to help the agency figure out which nanomaterials are worrisome.

The agency has also affirmed its previous decision that it will not consider nanoparticles new chemicals if they are made of the same chemicals as materials currently registered under toxicity databases. The rule would apply, for example, to nanoparticles of zinc oxide because larger clumps of the stuff are a component of skin creams.

That's a mistake, says Andrew Maynard, chief science adviser to the Woodrow Wilson International Center for Scholars Project on Emerging Nanotechnologies. "EPA's approach ignores the existing scientific research that suggests different nanostructures with the same molecular identity present different hazards," Maynard says.

–ROBERT F. SERVICE

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