has already managed to make green LEDs simply by adding a little indium to the gallium nitride mix. If the South Carolina team or their competitors can figure out a way to also get red gallium nitride LEDs, it would allow them to integrate both the light emitters and the electronics needed to drive them on the same silicon substrate, which would drastically drop their cost to produce. That promise is enough to keep the lights burning late into the night at semiconductor labs around the globe.

–ROBERT F. SERVICE

GEOLOGY

Discovering the Original Emerald Cities

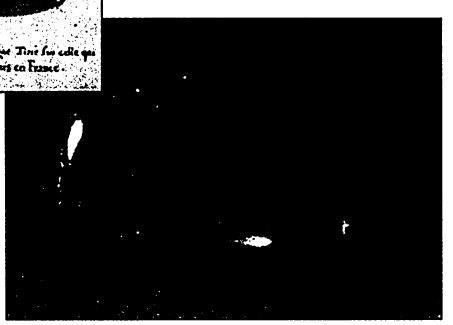
Emeralds have turned many an eye green with envy. The ancient Egyptians forced slaves to dig for the precious stones, prized as a symbol of immortality. Centuries later, Romans dominated the trade, setting the gems in gold jewelry. And when conquistadors in the 16th century captured mines in Colombia, they shipped back chests full of eye-popping emeralds that were snapped up by royalty, from Indian maharaji to Turkish sultans. Even today, dealers have no trouble spotting the exceptional clarity and intense color of the Colombian gems. But it's been notoriously difficult to track down the birthplaces of the murkier Old World emeralds.

Now on page 631, scientists describe a kind of atomic birth certificate that can peg where emeralds were grubbed from the ground. The technique might help dealers authenticate top-quality stones, and it could clear up the mysterious origins of Old World emeralds, including some famous gems. This new kind of detective work "is just the beginning," says Dietmar Schwarz, a mineralogist with Gübelin Gemmological Laboratory in Lucerne, Switzerland. Indeed, the approach is already providing information on ancient trade routes, and it might someday offer tantalizing hints of long-lost mines.

Emeralds are a kind of beryl, a mineral made when molten granite thrusts up into Earth's crust, cools, and hardens. Normally drab white or pale green, beryl can acquire a striking verdancy if the granite first muscles through rocks bearing chromium and vanadium. Hot water soaks up these and other elements, then crystallizes. Almost all the world's emerald deposits were formed this way.

Except in Colombia. There, hundreds of millions of years ago, black shale containing traces of chromium and vanadium washed off the west coast of South America. As the Caribbean Plate pushed eastward against the Brazilian Plate, it shoved the shale-covered sea floor onto the continent and twice created faults in the shale: first 65 million years ago, then again 38 million years ago. The squeezing and folding acted like a giant squeegee, forcing hot water into the black shales where the fluids picked up chromium, vanadium, and other ingredients of emerald. This brew percolated beneath impermeable shale layers until the pressure grew so great it ripped apart the rocks. The solution shot into the cracks, cooled, and gave birth to clear, blue-green emeralds, according to a scenario developed since the mid-1990s. But as researchers reconstructed this geologic history, they discovered more than a recipe for radiance: Colombian emeralds, it turns out, have unique oxygen isotope ratios that depend on where the stones were mined. So did emeralds from many mines elsewhere in the world.

Intrigued, Gaston Giuliani of the Petrographical and Geochemical Research Center (CRPG)–CNRS in Vandoeuvre-lès-Nancy, France—along with CRPG colleague Marc Chaussidon and Didier Giard and Daniel Piat of the French Association of Gemology—decided to see if they could use this isotopic tag to trace the origins of emeralds in artifacts. First they had to persuade the relics' wardens that they would do no harm. "No one wants you to touch [a precious specimen], no scratching, nothing," says Fred Ward, an independent gemologist in Bethesda, Maryland, and author of the book *Emeralds*. But the French group wasn't intending to hack off a piece. To measure oxygen isotopes, the researchers fire a beam of cesium atoms at the emerald, vaporizing a few atoms and leaving a hole a mere 20 micrometers wide and a few angstroms deep.



Crown jewel. The first isotopic analysis of this 13th century French crown suggests that its central emerald came from Austria—more than 500 years before the mine's documented discovery.

Reassured that samples weren't visibly marred in a test run, Henri-Jean Schubnel, the director of the National Museum of Natural History in Paris, and curators elsewhere let the team have a crack at a handful of gems spanning the history of emerald trading—from a Gallo-Roman earring to a thumb-sized emerald set on the Holy Crown of France to treasure from a Spanish galleon. "Gems with this pedigree are jealously guarded by museums, so to get access is quite an accomplishment," says Terri Ottaway, a geochemist and gemologist with the Royal Ontario Museum in Toronto, who has worked on Colombian emeralds. As expected, the emeralds from the wrecked galleon bore the isotopic signature of Colombian mines. But surprisingly, the stone in the earring turned out to come from the Swat River in Pakistan, demonstrating that the Romans had access to gems from much farther afield than Egypt. And the 13th century French crown, it turns out, is graced by an emerald from the Austrian alps—one that appears to have been unearthed more than 500 years before the first known description of these deposits.

For gem dealers, isotopes may help tell Colombian emeralds from top Afghani stones, which sometimes resemble each other, says Schwarz, who's working with Giuliani's team to see if oxygen isotopes can pinpoint the origins of rubies and sapphires. Customers care about an emerald's source, Schwarz says, because it helps determine value. Isotopes could also provide an additional tool for spotting synthetic emeralds, which are hard to distinguish from flawless gems. "We have big-time problems with fraud," says Ward.

The technique may offer an important new tool for archaeologists, too. They have a hard time tracing stony emeralds, the opacity of which tends to obscure microscopic drops of fluid or other telltale inclusions of a source region. Oxygen isotopes may lift this veil. "It's a great idea," says Ottaway, "but I'd like to see it tested with more samples." And who knows: If some ancient emerald turns out to be an isotopic orphan, it may point the way to a mine not found on any map.

–ERIK STOKSTAD

CELL BIOLOGY

Generating New Yeast Prions

For a controversy that many insist is settled, the long-running argument over whether abnormal proteins called prions act alone to cause disease has had amazing staying power. The stakes in the debate are high, because prions are implicated in several fatal neurodegenerative diseases, including human Creutzfeldt-Jakob disease and bovine spongiform encephalopathy, or "mad cow disease." But while most researchers now

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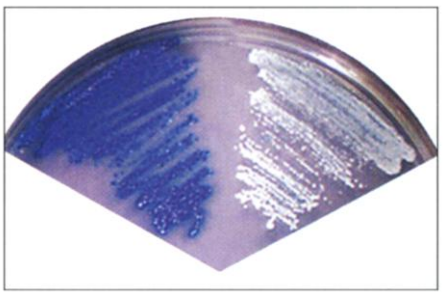
support the so-called "protein-only" hypothesis, a vocal minority insists that it is not yet proven—and that an as-yet-unidentified microbe, such as a virus, may team up with the prion protein to devastate the nervous system (*Science*, 22 October 1999, p. 660). New findings in yeast, reported in this issue and in the January issue of *Molecular Cell*, may now provide additional comfort for the prion proponents, although skeptics are unlikely to be convinced.

Prion doubters find the hypothesis hard to swallow because it holds that the proteins can infect tissues and reproduce themselves, thus violating long-standing dogma that a DNA- or RNA-based genome is necessary for such autonomous behavior. During the 1990s, geneticist Reed Wickner at the National Institutes of Health in Bethesda, Maryland, suggested that some bizarre patterns of yeast inheritance might be explained if these single-cell organisms also harbored prions. Soon afterward, University of Chicago geneticist Susan Lindquist's team showed that such so-called "yeast prions" do exist and that they appear to behave similarly to mammalian prions. They cause changes in the yeast's biochemical properties that can be passed on to daughter cells when the yeast cells divide, apparently independently of any infectious microbe or the yeast's own genome (*Science*, 2 August 1996, p. 580).

In the current work, reported on page 661, Lindquist and postdoc Liming Li created an artificial prion by fusing part of a yeast prion protein called Sup35 to a normal cellular protein from the rat. Like known yeast prions, this chimeric protein altered the biochemical properties of yeast cells in ways that could be inherited by progeny cells. "The astonishing thing is that the prion property can be transferred to a totally different protein," says neuropathologist Adriano Aguzzi of the University of Zurich, Switzerland. Indeed, this view is bolstered by a second paper, published in the current issue of *Molecular Cell*, in which the Lindquist lab has identified a new yeast prion, a protein called Rnq1, and shown that a segment of this protein also confers prionlike activity.

The new experiments build upon previous work showing that Sup35, like prion proteins that infect mammals, exists in two states: a normal, soluble form, and an abnormal, insoluble conformation. When the abnormal protein contacts its normal counterpart, it can trigger the structural change that converts it to the insoluble form, thus causing the prions to clump. In nerve cells, this causes permanent damage. In yeast, normal Sup35 helps control the yeast's genetic machinery, telling it when to stop translating messenger RNA into proteins. But when abnormal Sup35 dominates, this translational control is lost.

Researchers have found that a specific segment of Sup35 and Ure2, a yeast prion identified by Wickner, is needed for the proteins to act as prions. Lindquist and Li attached this "prion domain" from Sup35 to the rat glucocorticoid receptor, which controls the transcription of DNA into RNA—an entirely different function from Sup35's. In its soluble form, the new protein, called NMGR, could still induce transcription, as demonstrated by its ability to turn on a gene coding for the enzyme β-galactosidase. But when switched to its prion form, the hybrid protein was no longer capable of turning on the gene. Most importantly, this inactivated phenotype could be transmitted in a heritable fashion between mother and daughter yeast cells.



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Switcheroo. The artificial prion protein can exist in an active form in which it turns on the β-galactosidase gene (indicated by the blue color of the yeast) and an inactive form in which it doesn't (white yeast cells).

To find the new yeast prion, Lindquist and graduate student Neal Sondheimer searched gene databases for sequences sharing the characteristic features of the prion domains of Sup35 and Ure2, which both have large amounts of the amino acids glutamine and asparagine. They hit upon a protein they called Rnq1. Although Rnq1's function is as yet unknown, it can exist in normal and abnormal states like other prions. In addition, when the team substituted Rnq1's prion domain for that of Sup35 and introduced the altered protein into yeast, it had the same biochemical properties as Sup35, thus proving, the authors say, that the prion domains are alone responsible for perpetuating the prion behavior.

"The new experiments provide an almost incontrovertible argument in favor" of the protein-only hypothesis, at least in yeast, Lindquist says. "One has to come up with some very implausible scenarios to explain all of this with a virus." But some researchers argue that the new work may not be relevant to mammals. Yale University neuropathologist Laura Manuelidis, a leading prion skeptic, says Lindquist's work with yeast has put the prion within a "more acceptable, experimentally testable paradigm." But she notes that the yeast prion model "has nothing to do with infectious disease."

Despite these criticisms, researchers agree that genetically engineered prions might help resolve the debate over the protein-only hypothesis in mammals, particularly if pure prion preparations unassociated with any suspected virus or other microbe could re-create prion diseases in test animals. So far, attempts to do this with genetically engineered versions of the human prion protein PrP have failed, although this might be due to difficulties in coaxing the protein into the exact conformation necessary for infectivity.

But in work reported in the October 1999 issue of *Nature Cell Biology*, the Lindquist group did succeed in expressing mouse PrP in both yeast and cultured nerve tumor cells and getting it to convert to an abnormal form close to that adopted by naturally occurring mouse prions. The team is now testing whether these transgenically produced prions can infect mice. "If they can put in a pure or recombinant PrP protein, made in a virus-free cell, and get something that replicates infectivity in mammals, then I would be convinced [that the protein-only hypothesis] is correct," says Manuelidis. "I've been waiting 20 years to see that experiment."

–MICHAEL BALTER

SCIENTIFIC PUBLISHING

Publishers Discuss European E-Print Site

While U.S. organizers were putting the finishing touches on a new Web site known as PubMed Central, a group of scientists and publishers met in Heidelberg last week to plan a European counterpart called "E-Biosci." The U.S. project, due to go online within a week, is billed as a free archive of biomedical papers. It catalyzed the European initiative but will not be exactly the same. E-Biosci, according to organizers, is likely to require tougher peer reviewing for nonpublished articles and may allow publishers to charge some fees for access to their papers.

The prime mover behind E-Biosci, Frank Gannon, executive director of the European Molecular Biology Organization (EMBO), believes it is "quite feasible" for the European site to begin operating this year, but he acknowledges that no final plan has been agreed on, and long-term funding has not yet been secured.

The 30 key European players who met on 19 January in Heidelberg to discuss E-Biosci did not set its exact contours. Participants in the meeting included representatives of EMBO, European science publish-