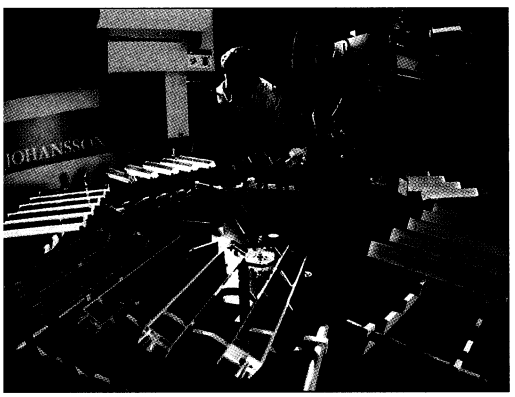
(Minatom) to inform it about visits from foreign researchers no less than 45 days prior to their arrival. Although the rules were put in place 3 years ago, Minatom had enforced them only at sensitive facilities such as the nuclear weapons design centers in Sarov and Snezhinsk. Now, purely civilian outfits like the Institute for Theoretical and Experimental Physics (ITEP) in Moscow are under pressure to toe the line, says ITEP physicist Boris Ioffe.



**Imperiled?** Russia's contribution to the LHC includes top minds and materials such as these lead tungstate crystals.

In the increasingly tense atmosphere last week ITEP director Mikhail Danilov, a key figure in Russia's delegation to CERN, tendered his resignation. When contacted by *Science*, Danilov declined to comment. However, some ITEP staff members assert that the resignation stems from Danilov's frustration over Minatom's recent restrictions on foreign contacts. Besides bleeding off some of Danilov's authority, the rules could put a chill on foreign collaboration, Ioffe predicts. Others insist that the administrative burden of the directorship, rather than any increased pressure from Minatom bosses, spurred Danilov's resignation. Either way, Ioffe says, "the situation is very difficult."

That's alarming news to CERN, which is relying heavily on Russian researchers to help build the $1.5 billion Large Hadron Collider (LHC), a machine that will explore fundamental questions such as why particles have mass. Roughly 600 Russian physicists are working on the LHC, providing an invaluable contribution to the collider and its associated experiments (*Science*, 13 October 2000, p. 250). About one-quarter of the Russian contingent comes from ITEP. "If, as I suspect, the security pressure will increase," Ioffe warns, "then ITEP's contacts with CERN will shrink, and consequently ITEP's participation in CERN projects will shrink." Others have a less dire take. "I don't see any danger for the time being," says ITEP deputy director Vitali Kaftanov. The most important wildcard, he argues, is whether Danilov's successor will be able to convince Minatom that the CERN collaboration is worth supporting.

–VLADIMIR POKROVSKY AND ANDREY ALLAKHVERDOV

Vladimir Pokrovsky and Andrey Allakhverdov are writers in Moscow. With reporting by Richard Stone.

CREDITS: (TOP TO BOTTOM) CERN GENEVA; ILLUSTRATION BY C. SLAYDEN

CELL CYCLE RESEARCH

## DNA: Once Copied, Thrice Blocked

When it comes to cell division, nature demands close tolerances. A dividing cell must keep a tight rein on DNA replication to ensure that each daughter receives exactly one copy. Indeed, failure of that control and the genetic instability that results can lead to cell death or even cancer. Although more than a decade ago cell biologists identified the master protein that guarantees that DNA replication occurs only once, they don't understand how it exerts its power. Now, part of that puzzle has been solved.

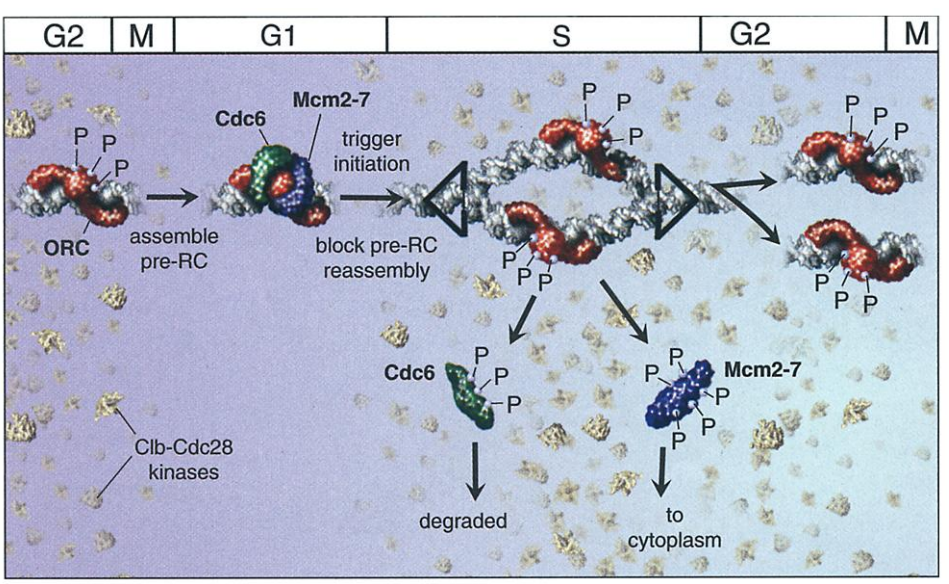
In the 28 June issue of *Nature*, a team led by Joachim Li of the University of California, San Francisco, reports that three separate pathways, all under the control of the master coordinator, a protein kinase known as Clb-Cdc28, must work together to prevent a second round of DNA synthesis from getting under way before the cell divides.

The current findings are an outgrowth of work done over the last 5 years indicating that Clb-Cdc28 does double duty in controlling DNA replication. When cell division begins, a group of proteins called the prereplicative complex (pre-RC) comes together on each of the many origins of replication where DNA synthesis begins. Once assembled, the pre-RCs stand poised to initiate replication but don't do so until the cell suddenly activates the Clb-Cdc28 kinase. That's when the enzyme shows its versatility.

It first triggers replication by the assembled pre-RCs, but once they fall off the origins of replication, it inhibits assembly of new pre-RCs that would reinitiate DNA synthesis. As a result, Clb-Cdc28 triggers one and only one round of replication. Then, once the cell divides, Clb-Cdc28 shuts off and new pre-RCs can assemble for the next round of cell division.

Although the details of how Clb-Cdc28 prevents reinitiation remain sketchy, researchers over the past few years have found several potential targets through which it might prevent reassembly. As a kinase, Clb-Cdc28 has the ability to add phosphate groups to other proteins, including three components of the pre-RC. Two of these are so-called initiator proteins: Cdc6, which is targeted for degradation when phosphorylated by Clb-Cdc28, and the protein complex Mcm2-7, which is kicked out of the nucleus when thus modified. The origin recognition complex (ORC), a group of proteins that is also part of the pre-RC, harbors sequences that look like Clb-Cdc28 phosphorylation sites, but researchers haven't proved that. They have also had trouble proving that the three targets help prevent reinitiation, because separately rendering each of them immune to Clb-Cdc28's influence doesn't remove the block. That led them to postulate that all the proteins, and perhaps others, have to work together to prevent reinitiation.

Now, Li's team has provided the experimental proof for the cooperation by making yeast cells in which all three potential targets




**Safeguard.** Activation of the Clb-Cdc28 protein kinase triggers DNA replication (S) and acts through three targets (ORC, Cdc6, and Mcm2-7) to prevent a second round of replication. Inactivation of the kinase after mitosis (M) allows a new round of replication.

can override regulation by Clb-Cdc28 simultaneously. The researchers did this by eliminating the potential phosphorylation sites in ORC and adding a sequence to one of the genes encoding a protein in the Mcm complex that prevents the complex from leaving the nucleus. They also put the gene for a degradation-resistant version of Cdc6 under control of an inducible promoter. That let them express Cdc6 even when Clb-Cdc28 activity is high and Cdc6 is normally degraded. The altered yeast cells could no longer block DNA rereplication. But the yeast cells didn't copy the DNA over and over again: For reasons that are currently unclear, they produced only about one genome's worth of extra DNA.

An important implication of the result is that control of the replication trigger is separate from that of the block for pre-RC reassembly, an outcome Li deems fortunate. When he began the work, he recalls, he was concerned that, like Clb-Cdc28 itself, the targets would be needed to initiate replication, as well as to inhibit formation of the pre-RCs. If that had been the case, he says, the cells wouldn't have replicated at all and "we would have been stuck." The fact that that wasn't the case, Li adds, indicates that there are other phosphorylation sites on those proteins or additional proteins that trigger initiation of replication.

The results "show that there are multiple levels of control of prevention of the rereplication," says molecular biologist Stephen Bell of the Massachusetts Institute of Technology, a finding that, he notes, emphasizes just how important that function is. Bell is also intrigued that inhibiting pre-RC assembly and triggering initiation are regulated separately. "The simplest model would have been that they were coupled, but once again the cell defies expectations."

–R. JOHN DAVENPORT

ARCHAEOLOGY

## Unwrapping a Modern Mummy Mystery

**BERN**—Last October, police in Pakistan's remote province of Balochistan seized an ornately carved mummy coffin on offer to art dealers for $11 million. A golden plaque on the coffin included an Old Persian cuneiform inscription suggesting that wrapped inside were the 2600-year-old remains of a daughter of King Xerxes. But like a pulp-fiction mummy unraveling in front of horrified onlookers, the exalted Persian princess's pedigree has fallen to pieces. Indeed, the intriguing circumstances read like the plot of a dime novel. The female mummy now appears to have been a relatively recent murder victim or else a body snatched from a grave shortly after death—two grisly scenarios that have scientists digging for clues to her true identity.

Recent analyses have shown that the artifact is a fake, but that the corpse is very real. Last week, a German team announced that it is conducting radiocarbon dating of muscle, skin, and bone snippets from the mummy to find out how long the toothless and tongueless bandage-wrapped body has been dead, which might help determine whether her broken back indicates foul play. "The mummy is clearly a fake, and this may have been a murder," says curator Asma Ibrahim of the National Museum of Pakistan in Karachi.

Although the discovery initially caused a sensation last fall, it wasn't long before archaeologists and others began to voice suspicions. Scientists were dubious about the cuneiform inscription, which bore a few textual mistakes. They also looked askance at the preparation of the mummy, which was not fully desiccated. "The mummy's bandages were so hard and thick, we had to use an electric drill to cut through them," says Ibrahim, who says that genuine mummies are more easily unwrapped. Further inspections and computed tomography scans of the body, now in a Karachi mortuary, showed that the woman's back was broken and that her mouth and stomach were "full of a powder," samples of which are now being analyzed, Ibrahim says.

**A royal hoax.** Scientists have debunked claims that this mummy was a Persian princess.

CREDIT: NATIONAL MUSEUM OF PAKISTAN

In a further plot twist, the Iranian Cultural Heritage Organization said last fall that it planned to take legal action to seize the mummy. The grounds: a suspicion that the mummy may have been an ancient member of the Persian royal family smuggled into Pakistan from Iran. In January, however, a delegation of Iranian experts—citing errors in the breastplate inscription and other flaws—declared it a fake. A month later, *Archaeology* magazine weighed in, reporting that a U.S. expert on Old Persian texts had concluded that the cuneiform on the mummy casket was likely a modern falsification lifted in part from a 520 B.C. inscription of King Darius at the Behistun site in western Iran.

In the meantime, Ibrahim had sent samples from the coffin, the matting under the mummy, and the bandages and resins to Pakistani experts and to the German Archaeological Institute in Berlin for analyses. The Pakistan Atomic Energy Commission's laboratory agreed to stray outside its bailiwick to radiocarbon date some of the materials. "We wanted to get Pakistani scientists involved," says Ibrahim, who in April issued a report finding that the materials were of recent origin and concluding that the mummy is a fake.

Ibrahim says that recent tomography scans and other analyses indicate that the body—whose bones show signs of osteoporosis—is that of a woman older than 50 who died probably within the past 5 or 6 years. However, to chase Ibrahim's hunch that the mummy is a murder victim or was dug up by grave robbers shortly after it was interred, Pakistani detectives would need a better idea of the time and place of death.

The detective assignment is being taken on by physicist Gerhard Morgenroth, who says his lab at the Friedrich Alexander University of Erlangen-Nuremberg, Germany, is working "to give as exact a time frame as possible" for the woman's death. Earlier this year, the German Archaeological Institute in Berlin sent Morgenroth samples of cloth and matting from the coffin. He has dated them using accelerator mass spectroscopy, which detects minuscule concentrations of elements. This spring, Morgenroth's tests determined that the fabric "could not be more than about 40 years old," as it contains traces of radioactive isotopes from nuclear-weapons tests carried out between either 1958 and 1960 or 1992 and 1994. The BBC, which is preparing a documentary, has commissioned Morgenroth to carry out such tests on the mummy's tissue samples. These tests, now nearing completion, should be able "to date the mummy's time of death to within 2 or 3 years," he says. But they can't place where the woman died. Meanwhile, Ibrahim fears that a ring of mummy-fakers may try to produce and sell similarly false artifacts.

If there's a lesson to be learned, Ibrahim says, it's that it pays to scratch below the surface of any archaeological claim. "The wooden coffin was beautiful and very convincing, so the flaws were not obvious at first," she says. Now Ibrahim would like to see the mystery solved—and those who perpetrated the hoax brought to justice.

–ROBERT KOENIG