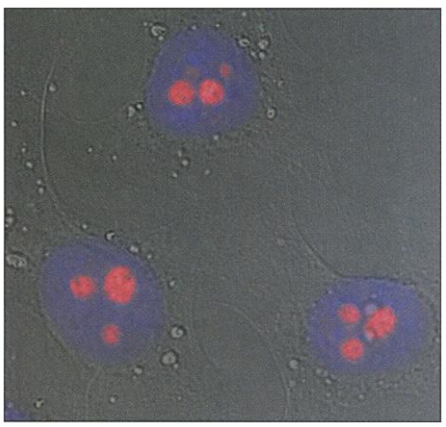
CELL BIOLOGY

Stripping the Nucleolus Down to Its Proteins

The human genome may be the mother of biological blueprints, but it's spawning plenty of offshoots: more modest lists of molecules powering often crucial bits of cells. The latest such roster—271 proteins identified in a compartment of the cell nucleus called the nucleolus—is a first step toward fully deciphering this organelle, a critical element in the construction of ribosomes, which go on to make proteins. With scientists now debating the nucleolus's role in additional functions, including cell cycle regulation and gene silencing, this starter list of proteins—30% of which are uncharacterized—offers plenty to chew on.

To assemble the protein map, the largest ever reported for a single organelle, cell biologists Angus Lamond of Scotland's University of Dundee, Matthias Mann of the University of Southern Denmark in Odense, and their colleagues at both institutions melded a decades-old method with cutting-edge technology and the latest human genome data. Applying an updated version of a 1960s technique, they treated human nuclei with sugar and sound waves and, using a centrifuge, separated the relatively dense nucleolus from its gelatinous home in the nucleus. Mass spectrometry combined with searches of human gene databases enabled the biologists to identify and characterize what they found.



Revealed. The nucleolus (red) has 271 proteins and counting.

"It's like being in a candy store: They've got all these wonderful proteins," says Joseph Gall, a cell biologist and staff member of the Carnegie Institution of Washington's branch in Baltimore, Maryland. Still, he and others caution that painstaking research lies ahead. "It is a framework for future work," says Tom Misteli, a cell biologist at the National Cancer Institute in Bethesda, Maryland. "But it doesn't really answer any single question."

As Lamond and his colleagues report in the 8 January issue of *Current Biology*, 191 of the proteins have been characterized, and over half of them share links to the nucleolus, adding a layer of certainty to past research. This set includes various ribosome builders, as well as other proteins that process and transcribe ribosomal RNA, a necessary step before the ribosomes can be assembled and pushed out of the nucleolus.

The remaining 90 or so characterized proteins participate in a hodgepodge of functions. They include molecular chaperones, which prevent other proteins from sticking together; translation machinery, which coaxes messenger RNAs and ribosomes to form proteins; and so-called DEAD-box proteins, which control the structure of RNA. "The actual overall complexity of the nucleolus was somewhat surprising," says Lamond, who suspects that it's far more than a ribosome factory.

That's likely to be the case, cell biologists agree. But the British and Danish team's list may also include non-nucleolar, contaminant proteins, say Gall, Misteli, and the researchers themselves. Without a membrane, the nucleolus is notoriously difficult to separate from the nucleus, and even the purest sample could contain molecules that accidentally stuck to it during the split. In addition to those that may have erroneously made the cut, several dozen known ribosomal proteins are absent from the roster; Lamond agrees that more nucleolus proteins remain to be found.

Nevertheless, biologists believe that only by paring down the nucleolus to its biochemistry can they read its part of the script. Surprises are expected. –JENNIFER COUZIN

MILITARY RESEARCH

Army Ordered to Hunt Down New Technology

Congress has ordered the U.S. Army to be all that it can be to promising high-tech start-up companies. Lawmakers have given the Army $25 million to establish an independent venture capital fund that will take an ownership stake in companies with promising military technologies. The unusual approach is drawing good reviews from some analysts. But some of the Army's own science advisers doubt that it can succeed, much less ever turn a profit.

The new venture fund is included in a $317 billion defense spending bill signed last week by President George W. Bush. It's aimed at shaking up a $1.2 billion Army R&D program that critics say has been too slow to deliver battlefield advances, from lighter weapons to better communications systems. The Army is also accused of relying on a few well-established defense contractors and overlooking smaller companies with better ideas but less political clout. "There is a bit of the hardening of the arteries over there," says Greg Dahlberg, acting Secretary of the Army under President Bill Clinton and now a top Democratic staffer on the House Appropriations subcommittee that oversees the Pentagon.

New venture. Congress hopes a new R&D investment fund will bolster the Army's arsenal.

To help unclog the Army's technology pipeline, Dahlberg and other fund supporters have borrowed an idea from the Central Intelligence Agency (CIA). In 1998, the CIA set up In-Q-Tel, an independent venture capital fund that has since funneled nearly $50 million into several dozen youthful information technology companies. The fund looks for firms that can both produce promising new intelligence tools and turn a healthy profit selling products to other consumers, and it sometimes takes a stake in the company. Eventually, the federal investment is supposed to generate enough income to make the fund self-sustaining.

Although In-Q-Tel is still far from breaking even, last year an outside review panel praised its contribution to modernizing the CIA and told Congress to continue funding it. The $25 million in start-up cash for the new fund will come from an across-the-board tax on the Army's basic and applied research budgets, although legislators fenced off several dozen projects deemed essential.

Army officials have already begun to assemble a wish list of technologies to guide fund managers—to be recruited from government and the private sector—in their search for "those nimble young companies that don't usually deal with the Army but have a lot to offer," says Army chief scientist A. Michael Andrews II. One potential pool of candidates, he notes, will be the several hundred researchers who have won recent grants from the Army's small business development program.

CREDITS: (TOP TO BOTTOM) RONEN ZILBERMAN/AP; A. LAMOND/UNIVERSITY OF DUNDEE

This month Andrews and others will begin to wrestle with a slew of organizational issues, including whether to establish the fund as a new entity led by a seasoned executive (like In-Q-Tel) or to ask an existing outfit to manage the $25 million pot. Officials appear to favor the In-Q-Tel model but not its estimated 15% administrative costs. "I'm looking to hold down the overhead," Andrews says.

Whatever model is chosen, some analysts question whether the Army's venture into high-tech investing can pay off. Last year, for instance, an Army Science Board panel concluded that existing research funding mechanisms could meet the Army's needs. It also warned that creating a venture fund could embroil the Army in "tumultuous" debates over how to spend any potential income. But it questioned whether products made for the military will also be attractive to other consumers; the Army now earns less than $500,000 a year in royalties from products it helped develop, the panel noted.

Such concerns, however, don't worry the fund's backers. Although Dahlberg says he doesn't expect the fund "to change the world, it will help get [the Army] closer to the creative smaller organizations." House appropriators, he adds, are ready to boost its annual budget, to up to $50 million, if things go well over the next few years. Success could also mean spreading the concept to the other armed services. **–DAVID MALAKOFF**

ASTRONOMY

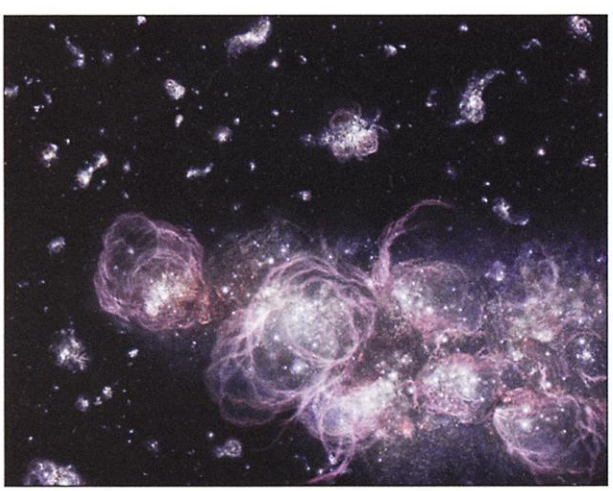
Star-Spangled Universe Dawned in Early Light

Hollywood directors would have filmed it differently, but Mother Nature started her performance with the grand finale. A few hundred million years after the big bang, long before anyone was around to appreciate the spectacle, the universe blazed with the most violent burst of star formation it has ever experienced. Since then, the rate of star formation has decreased, and the current activity is just a fizzle compared with the natal fireworks.

That new screenplay contradicts earlier scripts, which suggested that star formation gradually increased until a "baby boom" took place some 4 billion years after the big bang before dropping off again. "All analyses so far have missed a substantial part of the starlight in the very early universe," says Ken Lanzetta of the State University of New York, Stony Brook, who presented his results at a press meeting at NASA headquarters on 8 January 2002. A paper describing the new theory will soon be published in *The Astrophysical Journal*.

To learn about the early universe, astronomers examine very distant galaxies, whose light took billions of years to reach Earth. Three tiny patches of sky, known as the Hubble Deep Fields, have been studied in exquisite detail, both by the Hubble Space Telescope and by other instruments in space and on the ground. But according to Lanzetta, "even the deepest images made by Hubble are not sensitive enough to detect most of the light in the very distant universe." As a result, astronomers can glimpse only a small fraction of the amount of star formation in distant galaxies. "At these large distances, our telescopes see only the brightest parts of the galaxies," Lanzetta says. "The faint and intermediate-bright parts are below the observational threshold. But it's the intermediate-bright parts of galaxies where most of the starlight is being produced."

To calculate how much of that light had dropped below the range of visibility, Lanzetta and his collaborators analyzed all available observations of the Hubble Deep Fields. For some 5000 faint galaxies, they first determined their distances by studying their colors. More-distant galaxies appear redder because their light has been stretched more by the expansion of the universe. Then the astronomers calculated how much energy was produced in each pixel of the images. By comparing these results with data from nearby galaxies, the team was able to estimate how much starlight earlier analyses of the Hubble Deep Fields had missed—like a listener reconstructing the repertoire of a distant marching band by comparing recorded music with the booming of the bass drum. Lanzetta's technique "is really very



Brilliant debut. An artist's conception shows the spectacle of star formation that illuminated the early cosmos.

CREDITS: (TOP TO BOTTOM) DON FIGER/STSCI/NASA; ADOLF SCHALLER FOR STSCI

ScienceScope

FAME Flames NASA last week abruptly canceled a mission to obtain precise measurements of 50 million stars. The Full-sky Astrometric Mapping Explorer (FAME) was slated for a 2004 launch, but burgeoning costs prompted the space agency to abandon the project.

FAME's price tag had grown from $160 million to $220 million, primarily because of design and delivery problems with two dozen digital imaging cameras. And the final cost was likely to go higher, according to NASA officials and Kenneth Johnston, principal investigator and an astronomer at the U.S. Naval Observatory in Washington, D.C. "It's a great disappointment," says Johnston, who had hoped to convince the Department of Defense to cover the additional costs. The mission, selected in a tough 1999 competition, would have helped astronomers understand stellar evolution and the distance scale of the universe.

Accidental Death Tennessee authorities say that Harvard biochemist Don Wiley died in an accident. Wiley mysteriously disappeared on 15 November 2001 from a Memphis bridge over the Mississippi River; his body was found on 20 December 2001 some 480 kilometers downstream (*Science*, 4 January, p. 31). This week, Shelby County Medical Examiner O. C. Smith ruled out both foul play and suicide. Instead, Smith believes Wiley fell from the 35-meter-high bridge after leaving his rental car to check it for minor damage. Alcohol consumption, a seizure disorder, and a gust of wind caused by a passing truck all may have caused Wiley to lose his balance and fall over a thigh-high guardrail. He died from the impact on the water.

High Eye on the Sky Champagne flowed atop a remote mountaintop this week as astronomers dedicated the new 8.1-meter Gemini South telescope at Cerro Páchon in the Chilean Andes. The new $184 million telescope joins its identical twin, Gemini North, at Mauna Kea, Hawaii. Together, they give astronomers from the seven nations footing the bill—the United States, United Kingdom, Canada, Chile, Australia, Argentina, and Brazil—access to the entire sky.

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