ated as gas clouds collapsed to form the first galaxies, could have done the job, but the numbers have never quite added up. "Now we can breathe a sigh of relief," says JILA's Shull. The amount of carbon the Keck researchers found, he says, implies a large enough population of early stars to make the numbers come out right. By bathing the early universe in ultraviolet light during their lifetimes and jolting it with energy from supernova explosions at their demise, these stars could have heated and ionized the primordial gas, as well as laced it with carbon.

That heating could also help explain why the galaxies seen today are so large, according to computer simulations by Princeton's Ostriker and his colleagues. If the only source of heat in the very early universe was the afterglow of the big bang, as standard theories suggest, the thermal pressure of the primordial gas would have been low enough for it to collapse on relatively small scales, forming much smaller galaxies than those we see. Perhaps, says Ostriker, this first round of small-scale collapse did take place, forming the first generation of stars, which then "heated up the universe." Once those stars burned out or blew up, a new stage of galaxy formation began on much larger scales.

Still, it may be too soon to embrace a new, stars-first picture of the early universe, says Tytler. He cautions that young galaxies, too faint to see, might be responsible for the carbon in the contaminated clouds; the pristine ones could still be patches of primordial universe. To find out, Lick's Michael Keane plans to check whether the contamination becomes rarer in more distant—and hence earlier—clouds, existing at times when galaxies would be less likely to have formed. If the carbon does persist, astronomers may have to reckon with an unseen first generation of stars after all. And that means observers will have to press still deeper into the Lyman-α forests for their glimpse of unsullied nature.

–James Glanz

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PARASITOLOGY

Trypanosome Mystery Solved?

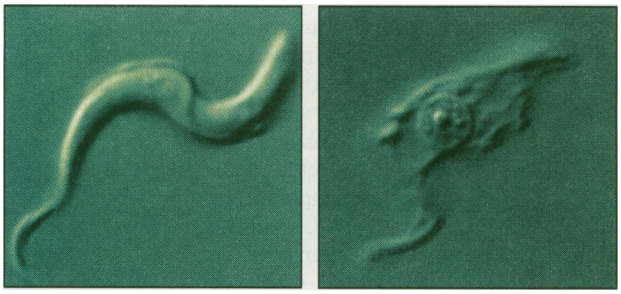
A parasite can be defined as "one frequenting the tables of the rich." But not all parasites find humans to be a rich feast. Take the tiny flagellated protozoan called *Trypanosoma brucei brucei*. In cattle, it causes a disease closely resembling African sleeping sickness in humans. Indeed, the prevalence of this veterinary disease makes it impossible to raise livestock in much of Africa. But even though the parasite can infect humans, it doesn't make them sick because it rapidly disintegrates in the blood.

Exactly what in human blood kills the protozoan is a mystery that traces back nearly a century. But now, molecular biologist Stephen Hajduk and his colleagues at the University of Alabama, Birmingham, may have provided the answer. On page 284, they report purifying a protein that destroys the parasite in lab culture. "What they appear to have done is solved one of the major puzzles in African trypanosomiasis," says George Cross, a molecular parasitologist at Rockefeller University in New York City. If subsequent work verifies that, it may be possible to use the gene encoding the protein to create productive, trypanosome-resistant strains of cattle for Africa.

In spite of its obvious significance, for decades, parasitologists had no idea what the human trypanosome killing factor could be. The first clue came only in 1978, when cell biologist Mary Rifkin, now at Mount Sinai Medical School in New York City, found that the killing component resides in the high density lipoprotein (HDL) fraction of blood serum, best known for its role in removing cholesterol from the blood. "This was a very strange finding," recalls Rifkin. "No one had a clue as to how this could be."

Rifkin moved on to other projects, and Hajduk's group decided to take on the tedious task of purifying the killing factor. The Alabama group narrowed the search to a small HDL subfraction, which they called trypanosome lytic factor, or TLF. It was from this material that the researchers eventually pulled out what they think is the killing factor—a protein closely related to the blood protein called haptoglobin, which binds hemoglobin released from dying red blood cells and helps prevent loss of iron from the body. One indication that they have the right protein is that an antibody to haptoglobin blocks trypanosome killing by TLF.

This result is surprising, says Linda Curtiss, a lipoprotein biochemist at Scripps Research Institute in La Jolla, California, because haptoglobins have not previously been known to associate with the HDLs, nor have these proteins been implicated in defenses against infectious diseases. The result suggests that HDLs may play "an important role" in the body's defenses, Curtiss notes.



PHOTOS BY STEPHEN HAJDUK

Blowout. The trypanosome on the right has been exposed to a lethal dose of human HDL and is dissolving.

After identifying the TLF, the Alabama group went on to sketch out a possible mechanism by which the protein kills the trypanosomes. Their previous work suggested that TLF is taken up by the parasite, where it gets into the lysosomes: small membranous sacs filled with digestive enzymes. The researchers now believe that before TLF is taken up, the haptoglobin-related protein binds hemoglobin, and once this complex is in the lysosomes, the low pH there stimulates an enzymatic activity that haptoglobin and hemoglobin have when together. This in turn generates free radicals that damage the lysosome's membrane, causing the potent lysosomal enzymes to spill out and digest the parasite from the inside. "Hajduk and his colleagues make a convincing case that the haptoglobin-related protein is the key element in the killing of *T. b. brucei*," says Rockefeller's Cross.

Cross adds, however, that some important questions remain to be answered before this medical mystery is put to rest. For one thing, two trypanosomes that are otherwise identical to *T. b. brucei*—*T. b. rhodesiense* and *T. b. gambiense*—do cause sleeping sickness in humans, and researchers wonder how those strains survive in human blood. Another issue is raised by the observation that the haptoglobin-related factor is not the only substance in human blood that may protect against *T. b. brucei*. Rifkin and Stephen Tomlinson of New York University report in the March issue of *Molecular Biochemical Parasitology* that serum from two patients who have a hereditary disease in which the HDLs are missing still shows some ability to lyse the trypanosome. "It certainly confuses the issue," says Rifkin.

The final proof of the importance of the haptoglobin-related protein will only come, Cross says, if researchers can introduce the human gene into mice and show that the animals gain protection against *T. b. brucei* as a result. That experiment is next on the Alabama group's list of things to do. And if that experiment works, it will not only solve the mystery of human resistance to the protozoan but could also open the door to trypanosome-resistant cattle.

–Karen Schmidt

Karen Schmidt is a free-lance writer in Chapel Hill, North Carolina.