a sodium-iodide-based instrument, although of a different geometry than that of the crystal ball. It was designed by a Columbia University/State University of New York at Stony Brook collaboration. According to Paulo Franzini of Columbia, the group reported at the Leipzig meeting that it also had radiative transition data for the energy range covering the zeta and had found no effect.

Statistical and estimated systematic uncertainties make the findings less incompatible than they first appear. The resolution will come with more data. A new 6-week run is under way at DESY and another search is under discussion at Cornell. Better statistics are only a few months off.

As far as theorists are concerned, there are two major stumbling blocks to understanding the zeta. One is the frequency with which it is produced in upsilon decays, which is much too high. The branching ratio for a particular decay path is the fraction of total decays that follow the path. "For most of the possible interpretations of the zeta as some kind of exotic particle, the branching ratio for its production from ordinary particles would have to be low," says Weinberg. The branching ratio for the production of a Higgs from an epsilon, according to the simplest version of the Standard Model, is about 100 times smaller than the 0.5 percent reported by the crystal ball group. Expanded versions with more than one Higgs do better, but there is another problem.

Why does the zeta come in $1S$ but not $2S$ upsilon decays? Since both consist of a bottom quark and antiquark, there should be no difference in the rates at which they decay into a Higgs. Many theorists have already started in on this problem. One early hope—that the interactions between between $2S$ and $2P$ (orbital angular momentum $=1$) states may somehow suppress the production of Higgs particles—now seems unlikely to be the full explanation.

The least revolutionary explanation for the zeta is that it is the singlet $1S$ (quark spins antiparallel) upsilon that should have a lower mass than the triplet $1S$ and has not yet been found. However, the theoretically predicted mass is so much greater than that of the zeta that no one gives this explanation much chance. "It is essentially impossible for the zeta to be the [singlet $1S$]," says Bloom.

The most revolutionary candidates come from the contenders for a more all-encompassing theory than the Standard Model provides. In supersymmetry, for example, all the elementary constituents of matter have twins. The zeta could be a bound state of two gluinos, the twins of the gluons that carry the color force between quarks, as these have been predicted to form during heavy meson decays. Here the theoretical branching ratio is only a factor of 10 lower than the experimental one.

A finding possibly related to the zeta is about to be published by a group working at Stanford called the Mark III collaboration comprising physicists from Caltech, the University of California at Santa Cruz, the University of Illinois, Stanford, and the University of Washington. According to David Hitlin of Caltech, who is spokesman for the group, there is a particle of mass 2.22 GeV, the xi, that is produced in radiative decays of the psi particle. It likewise is long-lived with a lower bound on the lifetime twice that of the zeta.

If the zeta and xi are related, what are the options? Henry Tye, a Cornell theorist, says that it is conceivable that these are particles comprising four quarks rather than two, so-called molecular hadron states. Burton Richter, the director-designate at Stanford, suggests the particles could be signals of internal structure within the quarks themselves.

All in all, theorists have complained of a lack of experimental evidence that can help them select which of many proposed paths they should follow in extending the Standard Model into a more complete account of the world of elementary particles. If they are lucky, the zeta particle may start them on their way.—**ARTHUR L. ROBINSON**

Steroid Hormone Systems Found in Yeast

Sex steroids and corticosteroids in yeasts may explain their pathogenicity and yield clues to the evolution and function of hormones

David Feldman, who is chief of endocrinology at Stanford University School of Medicine, has spent most of his career studying steroid hormones in humans. But a few years ago he sat in his backyard with his colleagues and discussed how far back in evolution mammalian-like steroid hormones and receptors might go. "People kept looking at simpler and simpler organisms [and finding hormones and receptors]," Feldman noted. "But they went in small jumps—to amphibia or sharks. We felt it was worthwhile to make a big leap back and look for mammalian-like steroid receptors and hormones in really simple organisms."

Since there was already evidence for yeast peptide hormones, Feldman and his colleagues decided to look for steroid hormones and receptors in *Candida*, a well-studied yeast that frequently infects people, especially when their immune systems are suppressed. Working with David Loose, a graduate student, Feldman and David Schurman, an orthopedist at Stanford who is interested in joint infections, looked first for the receptors. "To our amazement, we found a binding site for corticosteroids that looked somewhat like the receptors we see all the time in mammalian cells," Feldman recalls. "We got very excited and we asked, 'What is it there for? They must have something like a hormone as well.' "

Now Feldman and his associates have discovered what appear to be mammalian-like receptors and steroid hormones in at least three different species of yeast—a finding that has implications for the understanding of what hormones do and how hormone systems evolved as well as possibly for the treatment of fungal infections, since some of these yeasts are pathogenic. It also fits in well with recent, and independently developed, findings by Jesse Roth of the National Institutes of Health and others that peptide hormones, such as insulin, are widespread, occurring even in bacteria (*Science*, 12 March 1982, p. 1383).

The first thing that the Stanford researchers point out is that these are not hormones in the usual sense of the word. Ordinarily, endocrinologists define a hormone as a substance that is produced in one part of the body and acts on cells elsewhere—a chemical messenger within an animal. Since yeasts are single-celled

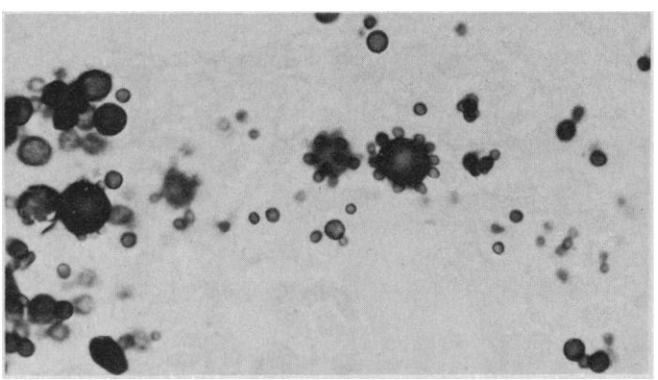
organisms and since these hormone-like substances are also found in the medium that surrounds them, the "hormones" are acting more like pheromones. It is well known that peptide hormones, unique to yeast, are critical for mating. But what is extraordinary is that these simple single-celled organisms and humans make chemical messengers that can bind to each other's receptors. For example, *Candida* not only has receptors that bind glucocorticoids, but it also makes a substance that both competes for the *Candida* receptors and binds to mammalian glucocorticoid receptors.

Feldman is particularly intrigued by their most recent finding. When he and his associates at Stanford and at Syntex Corporation looked at *Saccharomyces*, the common bakers' and brewers' yeast, they found that it has receptors that bind estrogens, although it does not have glucocorticoid receptors. Very recently, they found that it actually produces the human female sex hormone 17β-estradiol. "This is the one time that we believe we have finally identified the hormone in the yeast," Feldman remarks. "The startling thing is that it is identical to the human hormone." This discovery raises the possibility that people may be ingesting small quantities of estrogen when they drink alcoholic beverages, Feldman notes.

In further studies, Feldman, Loose, and E. Price Stover of Stanford joined forces with their Stanford colleagues David Stevens, who is chief of infectious diseases at Santa Clara Valley Medical Center, and Angela Restrepo of the Corporacion De Investigaciones Biologicas in Medellin, Colombia, to look for steroid hormone receptors in the pathogenic yeast *Paracoccidioides brasiliensis*. The organism, they find, has estrogen receptors.

The most immediate clinical implication of this work is a new understanding of the pathogenicity of *P. brasiliensis*. This yeast, which causes a devastating disease in South America, infects about 75 men for every woman. At first, researchers explained this unusual sex ratio by saying that the men worked in the fields where they inhale the organism. But Restrepo established that men and women have equal contact with the fungus. Because of their work with the other yeasts, the Stanford scientists suspected that the organism might prefer men because it has sex hormone receptors that bind these hormones and recognize sex steroids. The hormonal environment of the host might determine the ability of the fungus to cause the infection.

Stevens cultured the organism, which is a biohazard, and the researchers looked for male and female sex hormone receptors. They found no androgen receptors but did identify estrogen receptors. Then Restrepo discovered that estrogens inhibit the conversion of the mycelial form of the organism, the form that is inhaled, to the yeast form of the fungus that produces the infection. Although the investigators have not yet looked to see if *P. brasiliensis* makes its own estrogen-like hormones, they expect that it does and, says Feldman, "We presume that the organism's own hormone regulates its conversion from mycelia to yeast."



Yeast—Paracoccidioides brasiliensis

Estrogen inhibits transformation to this disease-causing form of yeast. [Source: Mary Ann Liebert, Inc., J. Exp. Pathol. **1** *(No. 3), 241 (1984)]*

At least one other fungus may also have its growth regulated by steroid hormones of its host. David Drutz and his colleagues at the University of Texas in San Antonio have found sex hormone receptors in the pathogenic yeast *Coccidioides immitis*, which infects people in the southwestern United States, causing as many as 25,000 to 100,000 new infections each year. The yeast infection seems to disseminate more frequently in pregnant women, which may be an indication that its growth is affected by its host's hormonal environment.

Another aspect of this story involves a drug used to treat fungal infections. Allan Pont, who is now at Children's Hospital in San Francisco, Stevens, Feldman, and others have found that the antifungal drug ketoconazole inhibits the production of steroid hormones, including both cortisol and testosterone. Testosterone inhibition may account for one rare side effect of the drug—the growth of breast tissue in men. Pont, Stevens, and others then decided that they may be able to exploit this effect of the drug by using it in higher doses to treat prostate cancer—a condition in which it is beneficial to suppress the production of testosterone.

Then Feldman, Stover, and Loose looked to see if ketoconazole also binds to and blocks human glucocorticoid receptors. They found that it does. Because ketoconazole both inhibits cortisol production and blocks its action at the receptor, the Stanford researchers speculate that the drug may be useful as a glucocorticoid antagonist. Work with ketoconazole helped Feldman, Lee Wagner, Paul White, and other Stanford colleagues to understand the side effects of etomidate—an anesthetic that is an analog of ketoconazole. Because of etomidate's structure, they suspected that it too might interfere with steroid hormone production. They found that it, like ketoconazole, blocks the production of corticosteroids, a discovery that is of practical importance.

Etomidate is frequently used in Europe as a sedative, particularly for patients on respirators in intensive care units. But the use of this drug has been associated with an unexpectedly high mortality rate in this critical care setting. Feldman and his associates suggest that the explanation is etomidate's suppression of cortisol production. "The one thing you don't want to do is remove cortisol from people under stress," he says.

But, for basic scientists, the most interesting question about these yeast hormone systems is the one that is still unanswered: What is the physiological function of steroid hormones in yeast? The three yeasts that Feldman and his colleagues have studied are very similar evolutionarily, yet only *Candida* makes a corticosteroid-like substance. *Paracoccidioides brasiliensis* responds to estrogen and *Saccharomyces* makes estrogen. The two most likely possibilities are that the yeast use these hormone systems to communicate about sex or about food. Still, as Feldman points out, "we haven't proved that these are really hormones and receptors until we show a function."—GINA KOLATA

Additional Reading

1. D. Feldman *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **81**, 4722 (1984).
2. D. Loose, D. Schurman, D. Feldman, *Nature (London)* **293**, 477 (1981).
3. D. Loose *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **80**, 7659 (1983).