The Genetic Basis of Sex Determination

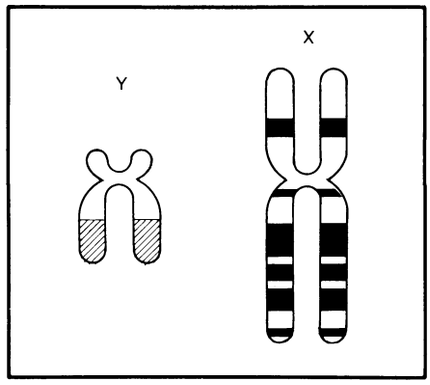
Human sex is known to be determined at the chromosomal level. If a fetus contains two X chromosomes in each cell, it will become a female. If it contains one X chromosome and one Y chromosome in each cell, it will become a male. However, it stands to reason that sex determination depends not just on the presence of a particular kind of chromosome, but on genes present on that chromosome. Research reported in the Nov. 20 NEW ENGLAND JOURNAL OF MEDICINE suggests that a major sex determinant gene may have been found.

Some years ago, investigators discovered that skin from a male mouse grafted onto a female mouse elicited an antibody response. Subsequently they found that the female mouse's antibodies were reacting to a particular antigen present on cells in the male mouse, but not in the female mouse. They named the antigen "H-Y" antigen, because it induced graft rejection. Last year, Stephen S. Wachtel of the Memorial Sloan-Kettering Cancer Center and his colleagues found that the H-Y antigen is present on the cells of the human male as well as on the cells of male mice, because male mouse antiserum to the H-Y antigen bound to male human cells. Consequently Wachtel and his colleagues decided to use a related serological technique to see whether the H-Y antigen might be coded by a gene on the human Y chromosome.

They took white cells from three men with abnormal chromosomal patterns—specifically two Y chromosomes instead of one in each cell. They put the cells in the presence of mouse antiserum to H-Y antigen. Then they put cells from men with the normal XY chromosomal pattern in the presence of the same kind of antiserum. The cells with the YY chromosomal pattern bound much more to the H-Y antibodies than did the cells with the XY chromosomal pattern, suggesting that the former contained more H-Y antigen.

The amount of antigen present on the cell surface is usually related directly to the number of determinant genes that are present. So in reporting their results, Wachtel and his team conclude: "The fact that human males possessing two Y chromosomes have excess H-Y antigen indicates therefore that a structural [gene] locus or positive regulatory locus for H-Y antigen is located on the Y chromosome in man. . . ."

The results of this particular study, in fact, are bolstered by several clinical observations Wachtel and his co-workers have made of women with a Y chromosome. These women had testes, and they had H-Y antigen on their cells.



Human Y and X chromosomes compared.

With one possible exception, this is the first gene to be assigned to the human Y chromosome. In an editorial in the same journal, Park S. Gerald, a physician at Children's Hospital Medical Center in Boston, hails the report as "a major event in human genetics." But even more intriguing and potentially important is the possibility that this gene may play a major role in sex determination.

Wachtel and his team explain why. During the past year or two, they have also found that the H-Y antigen is present in many different animal species, suggesting that the gene for this antigen has played a crucial role in evolution. What's more, they have found that the antigen is linked with sex within a species. For example, if the male in a species has the antigen, the female does not. If the female has the antigen, which is the case with birds and some amphibian species, the male does not. Now that they have found that the gene for the H-Y antigen is present on the human Y chromosome, they are all the more inclined to believe that it may be a major determinant of sex.

How might the gene determine sex? They speculate that the H-Y gene may be concerned with the development of the undifferentiated embryonic sex organs into either male or female sex organs, depending on the species. In humans, the H-Y gene would decide that the primitive sex organs become testes rather than ovaries.

Meanwhile, Wachtel and his co-workers want to learn more about the location of the H-Y gene on the human Y chromosome. They are studying the expression of the H-Y antigen in persons with structurally modified Y chromosomes to learn more about the precise location of the H-Y gene. For instance, they recently observed one woman with Turner's syndrome. She had both an X chromosome and a Y chromosome and the H-Y antigen. The Y chromosome, however, appeared not to be a total chromosome, but only its short arms. If this was really the case, then the H-Y gene probably lies on one of the two short arms of the Y chromosome. They are now looking at a male patient whose Y chromosome consists of only short arms. If he too expresses the H-Y antigen, then they can be more confident that the H-Y gene resides on one of the chromosome's short arms.

Wachtel and his colleagues are also continuing to explore the H-Y gene's apparent role in sex determination. As Wachtel told SCIENCE NEWS: "We want to study strange animals, like the lemmings that dive into the sea. For some reason—it's not clear—the females of that species have both an X and a Y chromosome. They are normal females in every respect. They just happen to have a Y chromosome which does not make any sense in the context of what we understand about sex determination. But according to our theory, they should have no H-Y antigen, even though they have the Y chromosome. So far, we have looked at three of these lemmings, and none of them has the antigen." □

Requiem for a star—or baptism of fire

Out in the constellation Perseus a star is dying—or perhaps being born. Astronomers are not quite sure which, but there seems to be more opinion on the side of dying. Both births and deaths continually occur in the life of the galaxy. But the exact process under observation, which may be either the beginning of the formation of a planetary nebula (death throes) or the last stages of the implosion of an interstellar cloud (birth pangs), is estimated to last no more than 25,000 years in the several billion that the average star survives. So the chance of catching one in either act is rather slim.

The object is an infrared source called CRL-618. (CRL is for the Air Force Cambridge Research Laboratory's catalogue of infrared sources.) It was identified by William E. Westbrook, a graduate student at the California Institute of Technology, who died before his paper could be published in the Dec. 1 ASTROPHYSICAL JOURNAL (not yet received at the time of this writing). Westbrook found CRL-618 during a search of infrared sources discovered in an Air Force rocket survey.

Apparently CRL-618 consists of an invisible, hot, condensed object with a surface temperature above 32,000 degrees. K. (the sun's surface temperature is about