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CELL SEER:
THE MAN WHO CAN READ THE FUTURE IN YOUR CELLS

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Lurking deep within our chromosomes are markers of our destiny. And only Jorge Yunis can spot them

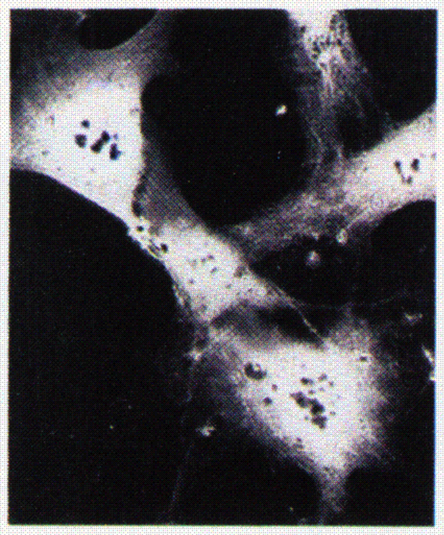
THE CELL SEER

BY KATHLEEN McAULIFFE

Geneticist Jorge Yunis has turned his lab coat into the mantle of a soothsayer. Donate a tablespoon of blood for his genetic physical and the University of Minnesota medical researcher will be able to tell you a great deal about your past and future—perhaps more than you want to know. He'll tell you, for example, how bits and pieces of the chromosomes of your apelike ancestors were reshuffled over evolution to produce you. From the beaded pattern of dark and light on individual chromosomes, he can also spot subtle genetic defects that can lead to mental retardation, infertility, and even social disorders. He is presently refining a cancer test that healthy people might someday be able to take to get a better idea of their susceptibility to different types of the disease.

Yunis has been reluctant to look at his own chromosomes, and the test isn't yet available to the general public. "I've got good genes," he says cavalierly. But those who are nearest and dearest to him rarely escape examination.

"When Jorge and I



were first married," recalls his wife, Mary, over dinner one night, "he requested a blood sample. But I never did find out the results."

"Well?" Everyone at the table looks anxiously to her husband.

"I took out more life insurance for her," he says.

"Weren't you afraid of what you might find out?" I ask them.

"No," Mary answers. "There's cancer in my family, so I already have a good idea of what my genetic Achilles' heel might be."

Colleague Bill Hoffman, another friend who had been invited to dinner, adds, "I donated blood for one study."

"That was my monkey paper," Yunis interjects.

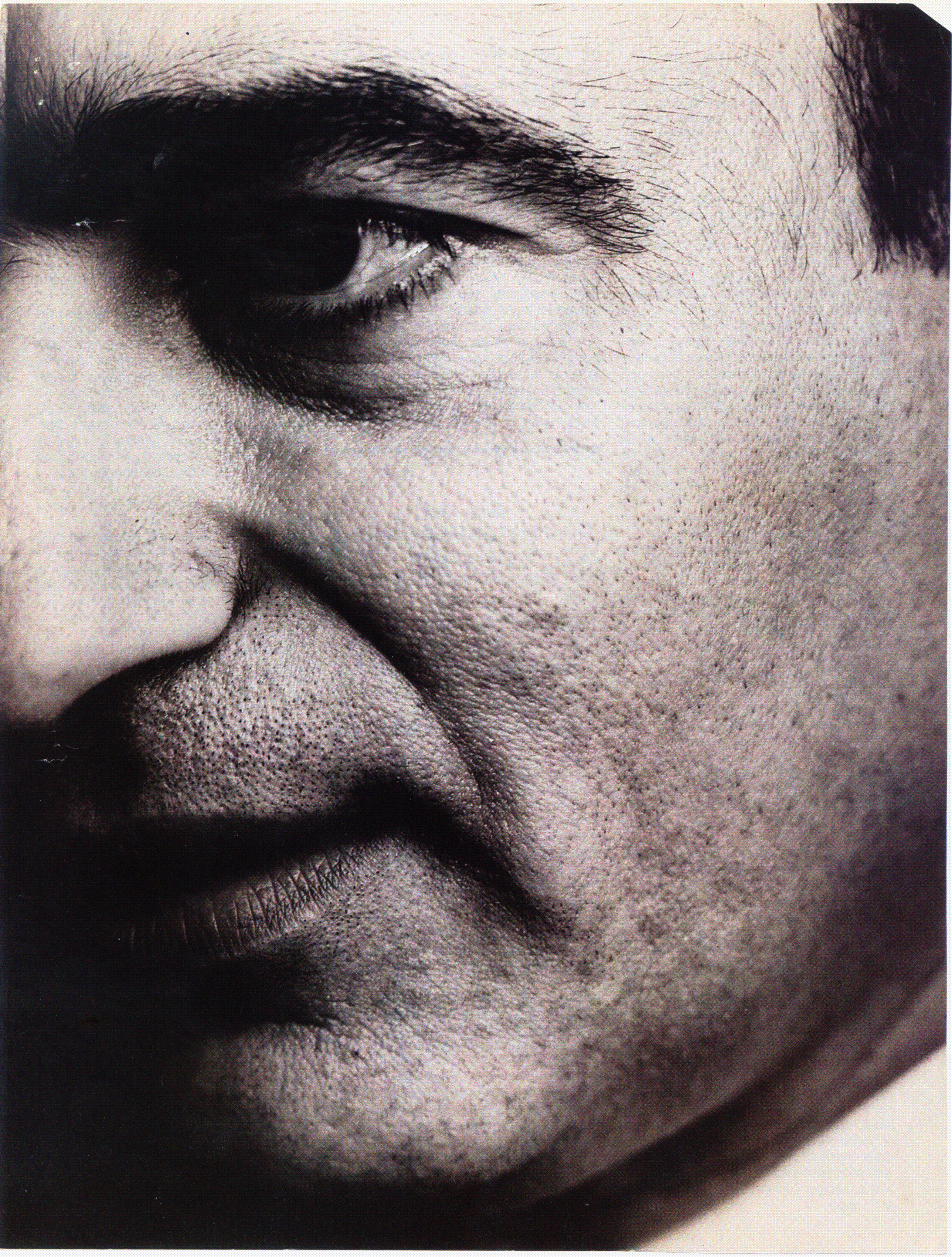
"What did he find out?" the group asks.

"I have no Y chromosome," Hoffman says. "It was quite a blow to my manhood."

"I didn't say you had no Y chromosome," Yunis insists. "I just said that it was small and was likely to float away."

Yunis's genetic forecasts are not always guaranteed to please, but for the bold of heart, they suggest a scientific rationale for preventive measures that could extend life spans and improve the odds of producing healthy offspring. Already his research has spawned numerous applications. For scholars of natural history, it has opened up a pathway for retracing the footprints of evolution. For the forward-looking clinician, his work has paved the way for a new test to determine how long cancer patients are likely to live—and therefore the best therapy to offer them. Yunis has identified a dietary substance—folic acid—that might help to prevent cancer by protecting our chromosomes from damaging agents. And the Colombian-born physician has pushed the frontiers of prenatal diagnosis so far that he has become in-

PHOTOGRAPH BY DAVID MICHAEL KENNEDY



timidated by his own prophetic powers.

"With my technique, it is now possible to screen the developing fetus for incredibly tiny imperfections—missing kneecaps, mild mental retardation, even a tendency toward premature graying of the hair when the child grows up," Yunis says. "There is just no telling how parents might react to that kind of information."

Fearful of ushering in a brave new world of eugenics, Yunis refuses to publish his paper on this particular technique. The document has languished in an office drawer for the last three years.

At age fifty-one, Yunis is a youthful-looking man with dark, heavyset features and an engaging smile. His conversation roams freely from El Greco paintings and Latin classics to fine wines and gourmet cuisine (his specialty is Arabic cookery). His scientific interests are equally eclectic. In an age of specialization, Yunis boasts expert knowledge of cancer, birth defects, reproductive disorders, primate evolution, and anything else that chromosomes can reveal about man's fate. Seven books and more than 150 publications are testimony to his productivity. In the past year alone, he has published papers in *Science, Nature,* and *The New England Journal of Medicine,* as well as in other prestigious scientific showcases.

Although Yunis is well respected by his peers, his work is somewhat controversial. "Some laboratories—our own included—have had difficulty replicating certain findings he has observed in cancer cells," says Dr. Robert S. Sparkes, of the University of California in Los Angeles. "But that may be because Yunis is a very careful researcher and spends a lot of time and effort to get the results he does."

Actually, it's easier to find those who applaud Yunis's work than those who question it. "Yunis is a very fine investigator," says Dr. Susumu Ohno, head of the department of biology at the City of Hope Research Institute, in Duarte, California. "If his findings hold up, they could turn out to be of major significance—especially in the area of cancer prevention."

A self-taught geneticist, Yunis attributes much of his success to his father, a Lebanese emigrant who settled in Colombia. He was a man with big ambitions for his five sons. "He sent us to school before we were three," Yunis says in English that lapses into the clipped syllables of his native Spanish tongue. "My father ran a hotel, but for some reason he had this idea that we would all be doctors. And when we grew up, the five brothers were supposed to start a clinic—the Yunis clinic."

To this aim, Yunis senior talked a Swedish ichthyologist (fish expert) staying at his hotel into tutoring his sons in science in return for free room and board. Yunis thinks back on his first teacher with great affection. "He would often accompany us into the forests of northern Colombia to study the wildlife and draw charts of the rivers that were teeming with different types of fish," Yunis says. "It was a highly unusual education for our very hot village, where siestas were considered more important than science."

In the end, his father's vision was realized—at least in part. The five brothers all completed their medical training by age twenty-one. But the Yunis clinic never materialized. "My father wanted us to be doctors, but our Swedish tutor wanted us to be scientists," Yunis explains. "I guess you could say that we struck a compromise. All five of us went into pathology so that we could continue basic research."

Yunis arrived at the University of Minnesota's Mayo Memorial Building in 1959, having confused it with the prestigious Mayo Clinic, a separate medical institution headquartered in the nearby city of Rochester. But the erroneous choice of campus suited him. With a small staff, a microscope, and a good measure of ingenuity, he pioneered innovative techniques for studying chromosomes, eventually earning himself an international reputation. "In only the last five years," says Dr. Joe Hin Tjio, a preeminent geneticist at the National Institutes of Health, in Bethesda, Maryland, "Yunis has risen very quickly to prominence."

"It's now possible to screen the fetus for imperfections—missing kneecaps, even a tendency toward a premature graying of the hair when the child grows up."

Yunis's work builds upon a landmark discovery by Tjio, who in 1955 found that a human cell typically contains 46 chromosomes. Each chromosome is a long, stringy body that carries hereditary information in the form of threadlike molecules of DNA (the substance of genes). Under a microscope, chromosomes look like floppy X's, except for the male's sex chromosomes—the twenty-third pair—that consist of an X and a smaller chromosome, designated Y. When a cell divides, each chromosome in that cell produces a duplicate of itself, so that each daughter cell will end up with the normal complement of chromosomes.

The information encoded in each chromosome's DNA determines vital bodily functions. This "master molecule of life" instructs pancreas cells to produce insulin, brain cells to make neurotransmitters, and eye cells to synthesize light-sensitive pigments. And, in turn, the impact of all these different genetic instructions determines such gross physical characteristics as height, shape of face, and body strength.

Like many other medical researchers, Yunis has tried pinpointing the precise chromosome location of the genes involved in different types of birth defects and diseases—information essential for devising better methods of prevention and treatment. A major step toward this goal was accomplished in 1970, when Sweden's Porjborn Caspersson discovered that if cells were stained while in the process of dividing, each chromosome would display a pattern of dark and light bands. Moreover, if a person had specific bands missing, or a band had broken and attached itself to another chromosome, the defect was often associated with a physical abnormality.

As important as this breakthrough was, the early staining techniques had many drawbacks. At most, only 640 bands could be detected on each chromosome, and they were often too fuzzy for doctors to discern genetic abnormalities with any certainty. To make such subtle distinctions, researchers would have to stretch out the rubbery chromosomes. This would reveal a finer gradation of banding. Researchers tried boiling chromosomes, subjecting them to digestive enzymes and a variety of other tortures—all to no avail. That is, until Jorge Yunis entered the picture.

Through perseverance, imagination, and sheer brute force, Yunis succeeded where others had failed. First he devised chemical methods of arresting large quantities of cells at exactly the same stage of cell division. Then—in the words of colleague Hoffman—"he delivered the crowning blow."

"Originally," Yunis explains, "I would suck up the cell suspension with a syringe, and as I squeezed out the contents, I would whip the cells onto a glass slide taped to the wall. Splat! Splat!" His eyes light up like an executioner enthralled with the sight of blood. "Unfortunately," he continues, "this proved too aggressive. The chromosomes were splattered beyond recognition."

Yunis decided to try a gentler method. "I thought photoflow—a photographic chemical that reduces surface tension—might help to stretch them out," he says. "And in fact it did. The problem is that it worked too well. The chromosomes became so stringy that the second you slithered them onto the slide they would wriggle right off again."

When coaxing failed, Yunis reverted to coercion again: "I got this idea to blow on the chromosomes to flatten them out. So I built a machine with a little mouth. Then I'd place the chromosomes on a glass slide in front of the mouth, and a burst of air would shoot out at them."

The "mouth" worked well enough until Yunis came up with the supreme method of chromosome torture—a refined version of the "splat" technique. Standing six feet above a glass slide placed at a 25° angle to the floor, Yunis flicked the cell suspension down onto the target. The tilted slide turned out to be the key to success. Rather than splattering on impact, the chromosomes ran down the slide, spreading out in beautiful banded formation. "I can usually score a bull's eye

from six feet away," Yunis says.

The big drop yielded a bonanza of bands. Where the old technique showed only one band, as many as five subbands were now visible. With gravity on his side, Yunis could detect a remarkable 4,000 bands per 46 chromosomes in each human cell—or more than four times the number previously discernible. And today, by switching to an electron microscope and making further refinements, he is almost up to the 10,000-band mark. "It is estimated that there are about sixty thousand genes carried on the human chromosomes," Yunis says. "That means that there is an average of approximately six genes per band."

Almost overnight Yunis's forceful tactics had cancer cells divulging their darkest, innermost secrets. "In 1980," he says, "only fifty percent of cancers were thought to involve chromosome defects. But with our high-resolution chromosomal analysis, it soon became apparent that virtually all cancers—that is to say, some ninety-seven percent—involved one chromosomal aberration or another."

Yunis risked his professional reputation by proclaiming that chromosomal defects were not a side effect of the cancerous process but a cause. "In hindsight, our assertion may not seem so daring," Yunis says. "But at the time, we were really out on a limb."

Yunis observed that cancers of the blood and lymph glands often involved translocations: One chromosome swaps pieces with another. In contrast, solid tumors—cancers of the lung, colon, and eye—usually involved deletions, in which bands or even large parts of a chromosome are lost. Even more important, Yunis found that certain chromosomal alterations could be powerful clues to how long the patient would live.

Yunis cites acute nonlymphocytic leukemia—a common blood cancer—as an example. Pathologists can distinguish only among six different types of leukemia based on the outward appearance of the cancer cells. Cancers that look alike, however, do not always behave alike—one may prove relatively slow growing and another very aggressive. As Yunis learned, chromosomal rearrangements are a much more reliable measure of how serious the disease will be.

For example, if a patient's cancerous cells have an upside-down segment on the sixteenth-largest chromosome, chances of survival are excellent: The patient is likely to go into complete remission. Patients with an extra copy of the eighth-largest chromosome have a fair prognosis: Average survival is ten months. Multiple chromosomal defects foretell the bleakest outlook. The patient is likely to die within ten weeks.

An accurate prognosis is crucial to doctors faced with difficult therapeutic choices. Leukemia victims with a short time to live, Yunis points out, stand the most to gain from experimental treatments. On the other hand, patients with more moderate conditions are better candidates for bone-marrow transplants because they are likely to live long enough to benefit from the procedure. Finally, patients with excellent prognoses can continue with standard chemotherapy.

By matching the therapy to the disease, chromosome analysis promises to be an indispensable asset in prolonging survival, as well as sparing patients unnecessarily aggressive treatments. "Within two years," Yunis predicts, "the test will be used routinely in the diagnosis and treatment of leukemias and lymphomas—and probably many more cancers after that."

In the meantime, Yunis is turning his forecasting talent to the task of identifying healthy individuals *prone* to cancer. He has recently discovered some 51 "fragile sites" on human chromosomes—specific areas vulnerable to attack by chemical carcinogens, radiation, certain viruses, and other as-yet-unidentified cancer-causing agents. Chromosomes tend to break and rearrange themselves at these weak points, setting the stage for the malignant transformation.

"More studies have to be done to verify the link," Yunis says, "but twenty-six fragile sites are already known to lie at or very close to the break points identified in leukemias, lymphomas, and solid tumors."

Yunis first made the connection between cancer and fragile sites when he analyzed healthy cells taken from leukemia victims. In

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four out of five patients, healthy cells showed the greatest genetic weakness at the precise points where chromosomes in the cancerous cells had actually broken apart. Yunis has since uncovered a similar relationship in victims of other cancers.

Yunis's technique for identifying fragile sites is to subject the chromosomes in cells to chemical stress. He then looks at the percentage of cells whose chromosomes develop little nicks or clean breaks. On the average, only 6 percent of cells show a defect at any specific chromosome site. But sometimes one type of gap or breakage will appear in as many as 30 percent of a donor's cells. In these cases, Yunis believes, the person may run a high risk of getting cancer.

A lot more clinical data are needed to bear out his hunch. So Yunis is embarking on a three-year clinical study of healthy people and cancer patients. If the correlation between cancer and fragile sites holds up, a simple blood test that reveals a predisposition to the disease could become available.

As in his other discoveries, good luck played a part in the unveiling of fragile sites. Yunis's initial technique for detecting chromosomal weaknesses was to culture blood cells in a medium deficient in folic acid—an essential ingredient needed in the manufacture of thymidine (one of the chemical building blocks of DNA). In this challenging environment, chromosomes broke down at their weakest points. But this method revealed only about 16 fragile sites, usually of the severest type, which earlier researchers had found to be inherited in certain families.

Then fate intervened in the form of a fortunate mishap. "A postdoctoral student in our lab had donated blood for our study, and the chromosomes came back like this," Yunis says, shoving a photograph under my eyes. It looks as if someone had dropped a hand grenade in the middle of a snake pit.

"I had never seen anything like this," Yunis says. "I thought, *Oh my God, this poor woman is going to die of cancer!* But then I calmed down. As a scientist you can't get overexcited by these things. Your attitude is to sit back and analyze what happened—to see, for instance, if you did something different than usual."

An investigation revealed that there had been a slipup in normal laboratory procedures. After depriving the blood cells of folic acid, a technician had added caffeine to the culture, mistaking it for a second batch of cells in another experiment.

Today Yunis has made caffeine part of his standard test for fragile sites—adding it to a batch of cells reveals more subtle chromosomal weaknesses in cells than depriving them of folic acid alone does. Coffee and tea drinkers, however, will be relieved to learn that caffeine by itself does not appear to damage chromosomes. Instead, it inhibits DNA repair mechanisms, thereby exaggerating whatever harm the folic-acid deficiency has induced.

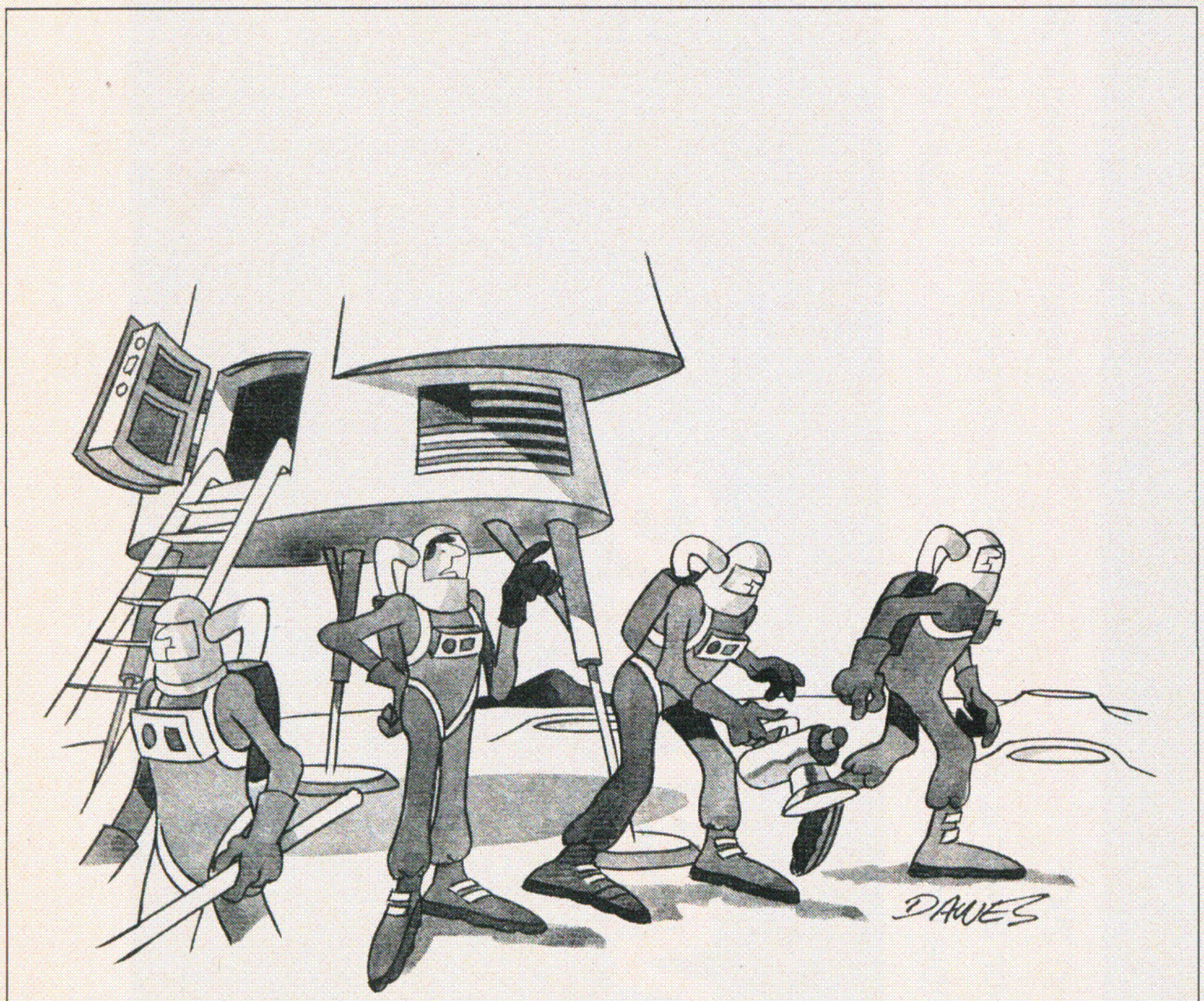
If the test lives up to Yunis's expectations, it could have a revolutionary impact on preventive medicine. In the industrial sector, for example, it could help to identify workers who are most susceptible to toxic chemicals in the workplace. Already, Yunis and other investigators have observed that petroleum-based products—notably insecticides and pesticides—tend to act at specific sites on chromosomes five and seven. If farmers with fragile sites at these locations are shown to be at increased risk of developing cancer, they may wish to avoid undue chemical exposure. Likewise, cigarette smoke frequently damages certain parts of chromosome three. By screening smokers with a marked weakness in that area, it might be possible to warn these people of their increased risk of lung cancer.

Prevention might also take the form of more frequent medical checkups to detect cancer at the earliest possible stage, when the disease is most responsive to treatment. Yunis suggests that high-risk individuals might want to avoid consuming large amounts of caffeine—provided its harmful action on genetic-repair mechanisms is borne out by in-depth clinical investigations. Finally, preliminary findings from his lab suggest that people predisposed to cancer might be able to protect their chromosomes against breakages by increasing their intake of folic acid. A B-complex vitamin, folic acid is prevalent in leafy vegetables, asparagus, fruits, liver, whole-grain breads, and cereals.

So far, however, only three people—including Yunis and his wife—have had their blood cells analyzed before and after taking a daily supplement of folic acid. Although the sample is far too small to draw any firm conclusions, Yunis was encouraged to discover that the chromosome breakage rate at fragile sites was reduced by about 95 percent. "And I drink lots of really strong Turkish coffee," Yunis adds.

Despite Yunis's findings some members of the medical profession remain skeptical of just how useful the discovery of the connection between cancer and fragile sites will prove to be. "Laboratory techniques for eliciting fragile sites may subject chromosomes to stresses not ordinarily encountered inside the body," says Mariano Barbacid, of Maryland's Frederick Cancer Research Facility. "To determine the prognostic significance of these sites, they must be characterized at a [more basic] molecular level."

Already there has been considerable progress toward this goal. In recent years much fanfare has surrounded the discovery of some 20 oncogenes—or cancer-causing genes—on human chromosomes. Because all human cells carry these seeds of destruction, molecular biologists have been trying to figure out what makes oncogenes attack certain cells and spare others. Yunis believes he knows what the initiating event might be. He has tracked at least six oncogenes to fragile sites.



"Hodges, check for radiation. Williams, set up the cameras. Dailey, look for women."

"It may be that when chromosomes break or rearrange themselves in the vicinity of an oncogene," Yunis says, "genetic control mechanisms break down, causing an otherwise harmless gene to express itself inappropriately. The cell begins to divide out of control, and cancer is the result."

By scrutinizing human fragile sites, Yunis has succeeded in identifying two new oncogenes. Progress in tracking down the genetic culprits behind cancer makes him hopeful that better treatments will evolve quickly. "In a few years," he says, "perhaps it will be possible to deactivate specific oncogenes, eliminating cancer without the dangerous side effects of surgery, radiation, or toxic drugs."

Like many creative people, Yunis always has a multitude of projects under way. Cancer is only his latest preoccupation. From 1976 to 1979 much of his time was spent at the University of Minnesota's Chromosome Clinic, where he regularly met with patients suffering from congenital defects, mental retardation, and infertility. His work from that period, though less publicized than his recent studies of fragile sites, led to the identification of more than a dozen well-defined new chromosomal disorders.

For years, the cause of many abnormalities—from reproductive problems to behavioral disturbances—has puzzled the medical profession. With Yunis's enhanced diagnostic powers, however, at least some of the mystery has vanished. Though far from a cure, the identification of a genetic problem early on can spare patients from undergoing unnecessary—and grueling—tests. And in some instances early diagnosis gives them a head start on remedial training.

"This little girl had difficulties in school," says Yunis, holding up a photograph of a five-year-old with slightly odd facial features and short stature. "Her parents wondered if there was something wrong with her, so they brought her to the clinic." Yunis found a tiny part of a band missing at the end of her second chromosome.

Yunis often sees patients with fertility problems. For example, a thirty-two-year-old man sought consultation because his childless wife had suffered five consecutive miscarriages. Yunis discovered that bands on one of the man's chromosomes were upside down. Instead of trying again, the couple began to consider adoption. "In as many as one third of all couples who are plagued by infertility or multiple miscarriages," says Yunis, "one of the partners will suffer from a small inversion."

Not all chromosomal defects cause a problem. As far back as the late Sixties, Yunis made what he considers to be the most important—if not surprising—discovery of his career. By studying gross chromosomal alterations and the physical effects they produced, he deduced that very little of our DNA actually contains genetic instructions. He estimated that as much as 90 percent of our hereditary material consists of repetitive nonsense that can be lost or reshuffled with little or no harm to the individual.

Consider Down's syndrome (also referred to as mongolism), in which a person inherits part of a third copy of chromosome 21. If the extra segment is mostly dark banded, the individual might suffer from mild retardation but will not display mongoloid features. Should the extra segment be largely white banded, however, the individual will show the classical syndrome of slanted eyes, broad forehead, and pronounced retardation. From this and similar observations, Yunis determined that most of man's genes reside in the white bands of our chromosomes. In contrast, the darker bands seemed to be littered with so-called junk DNA.

"The only reason I had the nerve to propose this radical theory was because I knew so little about genetics at the time," Yunis says, smiling broadly. "I was just a physician and quite naive, so I had no idea that I would be clashing head-on with the whole dogma of biology. In fact, one scientist thought my ideas were so preposterous that he told me I had no business being in a research laboratory. 'Go back to the wards,' he told me."

"If the correlation between cancer and fragile sites holds up, a simple blood test that reveals a predisposition to the disease could become available."

(In an ironic footnote to the history of science, his debunker was recently awarded a prize for the discovery of nongenic DNA in chromosome dark bands.)

Despite the less than enthusiastic response of his peers, Yunis forged ahead. Over and over again he noted that the dark bands on chromosomes could be jumbled or lost without jeopardizing the health of the individual. Damage to the light-banded regions, however, almost invariably had a devastating impact. Soon Yunis began applying this fundamental insight to prenatal diagnosis. But it was not until recently, when he perfected techniques for seeing as many as 10,000 bands on the chromosomes of each fetal cell, that prenatal diagnosis took on startling new predictive power.

For over a decade many women in their third month of pregnancy have undergone a procedure known as amniocentesis, in which fetal cells are removed from the womb's amniotic fluid and subjected to chromosomal analysis. Today amniocentesis is routinely used to diagnose Down's syndrome and a handful of other genetic defects. With Yunis's improved banding techniques, however, it is now possible to detect many more of these disorders in early pregnancy.

The boost in resolution power is as dramatic as jumping from low to high magnification on a microscope. "It's no longer a question of whether the child will be born severely handicapped," Yunis says. "When you can see incredibly minute genetic imperfections in the developing fetus, the line between what is defined as normal and abnormal starts to blur."

A fetus missing a tiny subband on chromosome five, for example, will later in life have premature graying of the hair. "People with this defect usually go gray in their late teens and twenties," Yunis says. Should the entire chromosome five be missing, a tendency toward premature graying will be compounded by other abnormalities. The child will be born with a soft larynx that causes what is known as cat-cry syndrome: The infant's wail sounds like a mewing cat.

Yunis has helped to pinpoint tiny genetic flaws that underlie such developmental abnormalities as extra fingers or toes, an anus that fails to open properly, missing kneecaps, cancer of the eye, short stature, and I.Q.'s that are low but still within the normal range. Paradoxically, however, with his increased predictive power has come increased uncertainty.

"Not all chromosome defects are related to specific abnormalities," Yunis cautions. "If you see an extra white band where it shouldn't be, you can be reasonably sure that the child will be adversely affected. But you can't always say what the problem will be. It might be a clubfoot, a cleft palate—such afflictions can be produced by many chromosomal aberrations. So a lot of the time you can make only rough guesses about the overall severity of the condition."

In addition, a chromosomal defect can sometimes be canceled by the mitigating effect of other genes. "Men with an extra Y chromosome may tend to be tall and mean," says Yunis, "but that correlation may prove true in only, say, thirty percent of the cases. Because of the unpredictable impact of genes on other chromosomes, an extra Y cannot be viewed as a card to criminality."

All these limitations to science's prognostic powers make Yunis leery of how the public might apply this knowledge. "Will parents want to abort every fetus that shows even the tiniest defect?" he asks. "And if not, where will they draw the line? At mental retardation or blue eyes?"

Already, his worst fears have been confirmed. "A delegation from China recently came to visit me," he says with a sigh. "They wanted to know how to apply the ten-thousand-band technique to prenatal diagnosis because the Chinese government, in an effort to curb its population explosion, is offering economic incentives to couples that will have only one child. So they want that one child to be as perfect as possible."

Yunis refuses to take part. His paper describing the technique was kept locked up in a file drawer during the Chinese delegation's visit. Like the legendary Dutch boy who

held back floodwaters by plugging his thumb in a hole in a dike, Yunis is single-handedly trying to block yet another overwhelming force—the unregulated use of such technology. "I have no intention of publishing that paper," he says point-blank.

Yunis's interest in chromosomes extends beyond genetic defects—as a sideline to his other studies, he has begun to investigate their role in evolution. He has examined different members of the primate family to determine how microscopic chromosomal changes eventually were translated into species changes.

Evolution, his investigation shows, is a far more conservative process than ever imagined. A mere sprinkle of genes is apparently all that distinguishes us *Homo sapiens*—with our aptitude for language, music, and mathematics—from our cousins, the great apes. Although man and chimpanzee branched off at least 5 million years ago, Yunis has found that 99 percent of our genes match theirs.

"Small variations in genes can account for great biological differences," he says. "For instance, tiny mutations in a key regulatory gene may have had a dramatic impact on primate evolution by increasing gestation time in the womb. In almost every species studied, a long gestation correlates with larger brain capacity and greater life span."

His research also suggests that nonsense DNA may have played a key role in evolution by creating breeding barriers between two closely related species. Because this excess hereditary baggage is of little survival value, it is not vulnerable to natural selection's rigorous pressures and can therefore evolve much more quickly than the gene-coding portions of our chromosomes.

"If members of the same species become geographically separated for a long enough time," Yunis points out, "their nonsense DNA will change rapidly—at least on a geological time scale. So when the isolated animals are later reunited, their chromosomes will no longer be able to pair properly when they try to mate. The result is that you have two new species where before you had only one."

By comparing the chromosomes of man, chimpanzee, gorilla, and orangutan, Yunis has attempted to reconstruct the course of evolution. "You work backwards," he explains. "You look to see what chromosomal changes occurred, how, and in what order. As it turns out, there is only one solution to the puzzle."

According to his calculations, orangutans were the first to diverge from the hereditary tree, leaving a hominid that gave rise to the gorilla and a human–chimpanzee forefather. Branching off on its own unique path, the chimp line appears to have undergone many transitions before the modern species emerged. By comparison, the human line seems to have changed very little after this branching point. "This would imply," Yunis says, "that the human–chimp progenitor more closely resembled us."

Fascinated by this human–chimp ancestor, Yunis has drawn up a map of its likely chromosome configuration. The map might help solve a problem: There is a scarcity of skeletal remains from geological beds dating between 4 million and 10 million years of age—the epoch during which this relative is believed to have roamed the earth. The study of molecular evolution, though still considered suspect in some quarters of paleontology, could prove science's best hope of filling this gaping hole in the fossil record.

With interests that run the gamut from cancer to evolution, Yunis has little time to reflect on all the ramifications of all of his discoveries. "Some creationists call me up from time to time," Yunis says, "and ask, 'How can you say we're the descendants of some kind of chimp–man when God made us all?' 'Don't ask me,' I say. 'I'm a scientist—not a philosopher. I report only the facts.' "

But when it comes to his genetic forecasting, Yunis clearly is concerned about how society will interpret his findings; witness his attempt to hold back the tide of knowledge in the field of prenatal diagnosis. Yet sooner or later the dam is going to burst—and then what? Yunis can scarcely grapple with all the complex legal, ethical, and philosophical issues his research raises. The questions posed by his genetic prophecies alone would take an institution of men the better part of a lifetime to sort through.

How, for example, do parents deal with the information that their child's learning disability or aggressive tendencies may be related to a genetic abnormality, which they can do nothing to correct?

Tests for cancer predispositions pose particularly sticky questions. "Right now, our diagnostic ability is outpacing our capacity to treat a whole range of conditions," says Dr. Francis Ruddle, of Yale University. "So what good does it do to tell someone that he's susceptible to a serious disease that can neither be prevented nor cured? One might even argue that you were doing that individual more harm than good. Of course, [genetic] research should eventually lead to improved therapy, but until such time, there's apt to be an uncomfortable hiatus."

In the end, the toughest questions will probably have to be resolved by individuals, each weighing all the factors that make up his own predicament. For those with the courage and discipline to undertake preventive steps, Yunis's work clearly offers enormous progress. For others, the benefits of early warning may be offset by the terror of knowing too much too soon.

My own chance to peer into the void of the future came at the end of my visit to the lab, when Yunis requested the customary blood donation.

"My father died of colon cancer. Will you be able to see if I'm likely to get it?" I ask.

"Perhaps," Yunis says. "There's a fragile site often involved when that type of cancer is hereditary."

"But colon cancer can't be easily diagnosed or cured, can it?" I ask.

Yunis shakes his head.

"Thanks," I tell him, "but no thanks."