PHOTOGRAPHS BY **JAY GULLIXSON**

Roots

When clumps of her hair started falling out, geneticist Angela Christiano began a scientific search for the causes of baldness. She found the first gene linked to baldness and is close to finding a scalp treatment that will prevent and cure hairlessness. So why haven't the drug companies beaten a path to her lab door?

TO UNDERSTAND ANGELA CHRISTIANO AND HER SEARCH FOR A baldness cure, you have to understand her hair. At 33, Christiano has really big hair. Too big for any hat, too big for many rooms, statement hair, whoa! hair. Then there's the rest of her, which is, well, bountiful, because it has to be if it's going to go with her coiffure. And the details are outsize, too. Check out that va-va-va-voom makeup; the large, flashy jewelry; those fingernails, which are a good two inches long, so long that she has to type with their tips, as if her fingers were on stilts. When Christiano makes an entrance, you half expect to hear a band start up.

Since she is a geneticist—a remarkably accomplished one for her age, with more than a hundred articles in leading scientific journals to her name—her appearance can throw people. Once, at a meeting in Japan, the lights were lowered before she stood up to give her presentation, and when the lights came back up, there was an audible gasp of astonishment that such a learned disquisition had come from someone who looked like…that. But that was Japan. At Harvard, when she taught a class at the medical school, the students responded with a standing O. Christiano did try to tone herself down all through graduate school. She wore horn-rim glasses, quit the eye shadow, the eyeliner and all the blush and let her fabulous hair go flat against the sides of her head. But you know what? "I was completely miserable," she says in her sex-kittenish voice, a voice so small and lovely you wonder where it comes from. "Everyone thought I was sick."

Christiano's hair would not be on our minds today if it hadn't started to fall

BY JOHN SEDGWICK

HEAD GAMES Despite her thick locks, Angela Christiano had a personal motivation for her research into the genetic causes of baldness. She found seven bald spots on her head, which she dubbed her "dwarfs."

out in big, terrifying clumps three years ago, shortly after her thirtieth birthday. Hair defines Christiano so absolutely that it's almost as if she *is* hair, all our hair, not only the gorgeous female hair that is backlit in commercials but also the less gorgeous hair that thins so alarmingly, usually on male scalps, dwindling down and down to those few, lonely strands that incipient baldies (like me) obsess over. Christiano could see where those clumps might lead, for her mother and her grandmother are both nearly bald and a second cousin is afflicted with a rare disorder called alopecia universalis, which has produced cue-ball hairlessness over her entire body. "The poor woman doesn't even have eyebrows," Christiano notes.

Christiano tried to be cool about her ailment, dubbing the seven gruesome bald spots that soon appeared "the seven dwarfs." But when a geneticist sees such a family clustering of a trait and discovers that she herself is, as geneticists say, one of the *affecteds*, "that is the time when great panic sets in." Christiano was determined to find the genes that caused her condition—preferably before they had a chance to exterminate every last hair follicle in her body—and, in so doing, strike a blow against the looming hairlessness that scares us all. That's the way she is. According to her friend Robert Burgeson, a professor of dermatology at Harvard Medical School, it is Christiano's empathy that sets her apart from other high-powered researchers. "Angela picks problems that are important not just to scientists but to regular people," he says.

Scientists rarely work on their own illnesses. The grand scientific endeavor is supposed to be above such petty self-interest. But Christiano went at the genetics of her hair problem all the same, largely because somebody had to. "The hair field is about fifty years behind the rest of genetics," she says with some annoyance. "All we've got is a freeze-frame view of what's involved." Christiano was determined to produce the movie that showed how those different elements interacted over time to produce the misery of baldness in all its forms, whether it be her own disease, alopecia areata (which she has been able to treat, at least temporarily, with the injection of steroids into her scalp), her cousin's alopecia universalis or the male-pattern baldness called androgenetic alopecia, which causes the half of the male population that eventually gets it (including me) to go crazy and the other half to swell with undeserved pride.

In the fall of 1997, Christiano made her first big discovery. She found the "hairless gene," which causes a rare, purely inherited version of alopecia. It was the first gene implicated in the development of baldness. In finding it, Christiano offered the first glimmer of understanding of the fundamental causes of baldness (which stands in contrast to the more superficial discoveries that resulted in the development of the hair-growth drugs Rogaine and Propecia) and the first solid indication that scientists might someday be able to stop the shedding and help baldies regrow lost plumage. To Christiano the genes are nothing less than switches that turn hair growth off and on. Even the people at Pharmacia & Upjohn, the maker of Rogaine, who could potentially be put out of work by the news, hailed Christiano's discovery. "It marks the beginning of a new era in hair research," says Ron Trancik, director of research for Pharmacia & Upjohn. University of Miami professor Marty Sawaya, M.D., widely recognized as the dean of hair researchers, says, "Angela's discovery is the first wave of something different and new."

Christiano was hoping for this kind of reaction. But in going down so deep, into the tiny squiggles of DNA inside cells and into the complex connection between hair and brain, where the mysterious "shed now" signals may originate, Christiano may be going deeper than the pharmaceutical industry is prepared to venture. Now, in persisting in her research into the genes that control male-pattern baldness, this lone researcher, this "baby," as she calls herself, is exposing the serious limitations of a pharmaceutical culture that, to be blunt, may not really want to cure baldness at all.

CHRISTIANO UNDERTAKES HER PIONEERING explorations at Columbia-Presbyterian Medical Center in the bustling, mostly Latino neighborhood of Washington Heights in upper Manhattan. Inside, the hospital seems like one big, jammed, crazy-making emergency room. As an assistant professor of dermatology and genetics at Columbia University's College of Physicians and Surgeons, Christiano has her laboratory here, on the fifteenth floor. And if her coworkers had been paying any attention, they would have known that something big had happened in October 1997, because they would have heard quite a commotion.

Understand, Christiano was seventeen months into the gene hunt by then. She had switched the focus of her research to baldness from epidermolysis bullosa, a hideous, blistering disease that can cause a newborn's skin to be stripped away during passage through the birth canal. As you can imagine, that took some intellectual retooling. Through the on-line medical service Med-Line, Christiano had come across a medical report about a family of hairless Pakistanis living on a remote hillside four hours by jeep from Islamabad. By sending a snapshot of her own widening bald spots, she persuaded the author and two colleagues to drive out and take the Pakistanis blood for genetic testing. She was horrified by the photographs of the family she got back. "They were haunting," she says. "Especially the children. All these little kids with no eyelashes, no hair anywhere." Later, through an Irish colleague, Christiano would arrange for blood samples from a troupe of hairless Irish Gypsies roving about the United Kingdom, and through a chance meeting with another colleague on a bus in Spain, she would locate some hairless Palestinians on the West Bank. And, in a brainstorm, Christiano would investigate some species of hairless mice, with emphasis on one particularly horrid-looking variety, the rhino mouse—so named because of its bald, wrinkled skin—that would be sent to her by a farmer who saw a program about her quest on NBC's *Dateline.*

Still, at this point, she had completed all the essential work, some of it lucky, much of it inspired and all of it exhausting, and she'd painstakingly sifted through the genes, trying to pinpoint different mutations in the hairless gene that caused this form of hair loss. Each blood sample helped her narrow

her search from the genetic equivalent of a continent to a country, then to a state, a city, a neighborhood, a house, a room.... And then, finally, there it was, on the fifteenth exon of the hairless gene on the short arm of chromosome 8. In effect, it was a single typo in the strand of letters 3 billion characters long—the now familiar A, T, G or C—that code for the proteins that make us who we are. But it showed up as a low, bluish hump on the genetic readout, indicating there was an A where a G should have been.

If you're good, you get a feeling for such things, and Christiano, sleepily running a long fingernail across the printout early one morning in her cramped office, knew at once that this was it. And people around her knew, because she jumped up and ran screaming down the hall. "Oh shit!" she yelled. "Oh shit!" over and over, at the top of her lungs, because for some reason no other words would do. "There was a lot of hopping and a lot of yelling," she recalls quietly. "It was kind of orgasmic."

She and her colleagues published their paper describing the discovery in *Science* in January 1998, beating a German competitor into print by two days, and the news generated an astounding round of publicity, partly for the discovery and partly for the unexpected nature of the discoverer. Christiano comes from Nutley, New Jersey, the only child of a manicurist and an Amtrak conductor. As a genetic dermatologist, she thinks of herself as little more than a beautician with a few extra degrees. A screenplay and a book detailing her life story as an American-style Madame Curie are in the works.

Two years ago, Christiano made her first big discovery. She found the "hairless gene," which causes a rare, purely inherited version of alopecia. "It was kind of orgasmic," she says.

Yet the one thing Christiano expected, indeed counted on, has not occurred. She has not been showered with drug-company money. A few years ago, when researchers at Rockefeller University discovered an obesity gene they termed "ob," Amgen bought it for $20 million. "And all those guys had was a mouse mutation, not the human one," Christiano says. Christiano has not received a single call from anyone in the pharmaceutical industry, whether it be to discuss ways to fund her research, to inquire about its possible significance, to ask about her future plans or just to say hello. This is a non-development that baffles pharmaceutical insiders as well. "Really?" replied Keith Kaufman, the director of clinical research at Merck Research Laboratories, the maker of Propecia, when I told him. "Even I'm surprised by that." Pharmacia & Upjohn's Ron Trancik couldn't get over it, either.

BY THE STANDARDS OF THE PHARMACEUTICAL INDUSTRY, Angela Christiano is a flyspeck, a creature virtually indistinguishable from air. She has only four researchers in her tiny Columbia-Presbyterian laboratory, which she shares with a breast-cancer researcher. Her limited equipment is far from state-of-the-art. She spent a grand total of $10,000—all of it provided by the National Alopecia Areata Foundation—on her search for the hairless gene. By contrast, Merck looks like a large, well-endowed university, spreading out over several square miles of Rahway, New Jersey. Also well financed are Johnson & Johnson, Pfizer, Bristol-Myers Squibb and the rest of the "big pharmas," as they're known.

In their search for new markets, the drug companies have widened their attention from the treatment of genuine illnesses to Viagra-type lifestyle enhancements, and they have come to rest their eyes on the balding pates of the American public. The numbers, after all, are promising. At least forty million Americans suffer from some form of inherited hair loss. And there is apparently no limit to how much they will spend on their hair. According to the American Hair Loss Council, 45 percent of balding men would trade five years of their lives for a full head of hair. Today Americans spend an estimated $7 billion per year on hair-loss remedies. Rogaine and Propecia, the only two FDA-approved baldness drugs, gross $165 million a year between them, and yet, according to Merck's own research, only 5 percent of Propecia users show "great improvement" after two years of pills. Christiano expected the drug companies to jump at the chance to reach down into the genes where, researchers agree, the cure lies. Start-up biotechnology companies have been built—and seen their stock prices skyrocket—on far less. So why have the drug companies treated her with such indifference?

PART OF THE ANSWER LIES IN THE STAGgering complexity of the body's hair-production system. Each of the 100,000 or so hairs atop the average person's head is a relatively simple structure, primarily a long shoot of keratin, a structural protein also found in fingernails. Under an electron microscope, a hair looks like the trunk of a palm tree. But the real action is down below, for a strand of hair is merely the visible product of a fantastically intricate root system. Each hair comes complete with its own tiny muscle (which is why your hair can stand up), nerve endings (for processing an infinite variety of sensations, from a seductive caress to a vigorous tug), nerve receptors (for receiving stress signals from the brain), oil (for skin lubrication) and blood supply (for nourishment and hormonal transmission). It's as if each hair had its own motor, sensors, power supply and Internet access.

The pace of production is remarkable. Hair grows faster than any other part of the body except bone marrow, about a half inch a month, and it grows in prodigious quantity: A woman with a shoulder-length cut is carrying thirteen miles of hair on her head. Each hair grows for only two to seven

years (which limits how long one's hair can be), then rests for about a month before another hair appears behind it and pushes it out. Each hair has its own shedding cycle, which is lucky—otherwise we'd all be bald periodically. About a hundred hairs a day take the long fall. Despite the lamentations about those hairs on the pillow, the comb or the shoulders, they aren't the problem. The problem comes when their hair follicles start to *miniaturize.* That is, with each subsequent cycle, they grow thinner, shorter and paler until, after four or five cycles, they become nearly invisible. "If you can block that cycling, you can block the hair loss," says Jerry Shapiro, M.D., director of the University of British Columbia Hair Clinic. Unfortunately, nobody knows how.

As for the technical causes of miniaturization, it has been apparent for some time that male-pattern baldness runs in families, suggesting a genetic link. (Contrary to folklore, mothers are not solely responsible; fathers can pass along the trait, too.) Until Christiano came along, however, no one had a clue as to which genes might be responsible. The male hormone testosterone was implicated in the '40s, when James Hamilton, a Yale anatomist, studied about a hundred men whose testes had been surgically removed before puberty. None of them, he noted, ever went bald, even though many of them had bald relatives. However, they would go bald when given testosterone (surely a case of adding insult to injury)—but only if there was a family history of the condition. (Unfortunately, there is no evidence that balding men, contrary to their reputations as Lotharios, are any more virile than the norm.) That's about where the basic science stands today. "Baldness is a product of genes, hormones and time," summarizes O'Tar Norwood, M.D., an Oklahoma City hair-transplant specialist best known as the creator of the widely used Norwood scale of male-pattern baldness.

Despite knowing these essential elements, the pharmaceutical industry made little progress in the search for baldness treatments until 1974, when a Cornell University researcher named Julianne Imperato-McGinley published in *Science* some curious information about two dozen pseudohermaphrodites in the Dominican Republic. Pseudohermaphrodites are so named because they possess the XY chromosomes of males but their external genitalia at birth resemble those of baby girls. Each one has a tiny penis, scrotum and testicles that are infolded to look like a vagina. In the Dominican Republic, these pseudohermaphrodites were raised as girls until puberty when—and this must have been quite a surprise—their "vaginas" blossomed into the standard male equipment. The pharmaceutical industry would not have paid much attention to the news if Imperato-McGinley hadn't also noted that none of the pseudohermaphrodites developed enlarged prostates and none went bald. She also detailed a possible explanation: The pseudohermaphrodites lacked a particular enzyme, 5-alpha-reductase, that converts testosterone to a hormonal by-product called dihydrotestosterone, or DHT.

One might think the pharmaceutical industry would have been scouring the world for this kind of discovery. But, in fact, drug-company researchers are much more inclined to sit back at company headquarters and monitor such reports from the field. Merck first seized on Imperato-McGinley's findings to develop a drug that would shrink enlarged prostates. The drug, Proscar, finally came out in 1992; it worked by mimicking the DHT-limiting effect of the 5-alpha-reductase deficiency. Merck then embarked on an effort to come up with a lower-dosage version to stimulate the hair growth that the pseudohermaphrodites experienced. That drug, which appeared six years later, was Propecia. Now, in a case of pharmaceutical me-too-ism, Glaxo Wellcome is in the middle phase of human trials of a drug, code-named GI198745, that will go Propecia one better, mimicking the effect of a second type of 5-alpha-reductase enzyme as well, and with a 99 percent efficiency in blocking the conversion to DHT, surpassing Merck's 65 percent.

Propecia followed the first FDA-approved treatment for baldness by ten years. That was Rogaine, and it was another of the lucky bounces the industry depends on. Just as Propecia was derived from Proscar, Rogaine was developed from a drug used to treat a separate condition, in this case Loniten, an antihypertension pill. When Upjohn was putting Loniten through clinical trials in the '70s, researchers noticed a curious fact: The men in the study were growing what Ron Trancik delicately terms "unwanted hair" on parts of their bodies. Which parts? "I've seen a very nice clinical photograph," says Trancik, "of a man standing with his arms folded across his chest with a massive amount of extraneous hair on his arms." In the business, this is the kind of medical event on which fortunes are made. Upjohn rushed to develop a topical version, which was marketed to men as Rogaine in 1988. Recently, the company, now called Pharmacia & Upjohn, has come out with a more concentrated form of the lotion. According to studies by George Cotsarelis, M.D., of the University of Pennsylvania Medical Center, only 10 percent of patients taking the original Rogaine grow any hair, and most of the hair they do grow is peach fuzz. Still, in 1998, Americans bought nearly $100 million worth of the stuff. Propecia appears to work a little better to stabilize hair loss. According to Merck's studies, two-thirds of patients were rated as "improved" after two years of the pills, although, having looked at the company's pictures of the individuals' scalps, I would say the improvements were subtle. Last year $68 million worth of Propecia was sold in the United States.

BUT THAT WAS THEN. BOTH THESE HAIR growth products are based on research that dates back two decades or more, and the more effective one, Propecia, works exclusively through hormonal intervention (Rogaine depends on what Trancik calls "a nonspecific biological response modifier," probably one that stimulates blood circulation to the hair follicles). In Norwood's genes-hormones-time triad, that leaves genes and time. Time is presumably unalterable, but what about the genetic component? Though the big pharmas have chosen not to deal with Christiano, they have not given up on the genetic angle. By most accounts, the leading edge of the pharmaceutical companies' push into the mysteries of genes is occurring at Johnson & Johnson's Skillman, New Jersey, unit, in the laboratory of Kurt Stenn, M.D., a biochemist. When I called Stenn to find

out what he was up to, he couldn't tell me without getting clearance from the higher-ups in corporate communications, which turned out not to be forthcoming. "We haven't counted enough eggs yet," he said somewhat mysteriously.

Christiano tracked down a family of hairless Pakistanis living on a remote hillside outside Islamabad.

Such secrecy has lent a Cold War–style melodrama to the occasional hair-research meetings where industry types and academics commingle. There are few hair-research specialists, no more than one hundred worldwide, but even if there were 1,000, Christiano would have no trouble telling which were from industry. They are the ones with their heads down, she says, silently scribbling into their notebooks or typing into their laptops while the academics give their presentations. "It's very creepy," Christiano says. "The drug-company people only ask what you're doing. They never say what they're doing."

It may well be that the drug companies are acting disdainfully of Christiano for the simple reason that they are far less interested in finding a one-shot baldness cure than in developing a continuing treatment, like Rogaine or Propecia, that generates lucrative repeat business. The University of Miami's Marty Sawaya suspects as much: "I've been told by industry people, 'We don't want to cure a disease, we just want to treat it, so we will continue to have people to buy our stuff.' " Then she adds, "But if you ask them about it directly, they'll definitely deny it." Spencer David Kobren, author of *The Bald Truth,* a detailed look at hair-loss treatments, is even more pointed: "If Christiano ever finds the genes that lead to a baldness cure, all the pharmaceutical companies are screwed. They don't want her to succeed. They want a lifetime customer. That's the sad fact."

But even if the big pharmas are interested in a genetic cure, they might decide it makes smart business sense not to strike a deal with someone like Christiano. Merck declined to give its reasons, but a spokesman for Pharmacia & Upjohn said Christiano's research "wasn't as far along as we would need to see for business purposes." And they would know, because, following academic tradition, Christiano has published her results in full. As for any future work, the pharmas can wait and see. If she comes up with something big, they can strike a deal if they have to. If she fizzles, they've saved themselves some money. And even if she finds all the baldness genes she is looking for, who is to say she or anyone else will be able to put them to use in an effective therapy? Thus the big pharmas keep their distance from Angela Christiano.

But there may be a flaw in such thinking, one that might be slowing the pace of progress on the genetic front. In this hermetically sealed atmosphere, where drug-company insiders have frank and full discussions only with themselves, misconceptions can fester, and that might be happening currently with the drug industry's genetic efforts. It is difficult to ascertain what the drug companies are up to, but what little they have let slip is puzzling both to Christiano and to several other independent researchers I contacted. Kurt Stenn's lab at Johnson & Johnson has produced only one paper, a brief abstract that was published in January 1998 in the *Journal of Investigative Dermatology.* It suggests that Stenn's laboratory has concentrated on trying to go one step back up the trail from the 5-alpha-reductase deficiency that underlies Merck's Propecia, to see if either of the genes on chromosomes 2 and 5 that code for the enzymes are implicated in male-pattern baldness. Christiano finds that astonishing. "We already know what that mutation causes, and it sure isn't male-pattern baldness," she exclaims. "You get a pseudohermaphrodite." Stenn told me he was forbidden by company rules from talking to reporters.

Even beyond that little problem, Christiano finds Stenn's whole approach simplistic. It is clear from his paper that Stenn is hoping to find a single gene that is responsible for male-pattern baldness. Yet single genes have effects according to what is known as the Mendelian model, meaning they exhibit either one manifestation or another, in the way that Gregor Mendel's famous peas were either wrinkly or smooth. The Mendelian view applied to Christiano's Pakistanis, who were either completely hairless or *(continued on page 238)*

Star Warrior

(continued from page 203) impressed with myself when I'm doing it. I've always loved motorbikes. Maybe it comes from Elvis Presley movies. They're quite cool, aren't they?"

McGregor craves speed. He is a tad manic. He "wasted no time" getting married and getting his bride "up the stick." He makes movies back-to-back. He drives fast and eats fast and exists in a palpable cloud of buzzing energy. Change does not frighten McGregor.

When asked about why he chose to get married so young, at 24, McGregor says, "I got married because I wanted to get married."

When asked if he found such a heavy commitment off-putting, McGregor says, "I never look back and say, 'Oh, my life used to be like this and now it's like this.' I don't understand what the transition is. I don't know what changes other than that you're married. Having a child is a much bigger thing. Such an emotional, life-changing thing. Seeing my daughter asleep. Waking up half the night. You wear a hole in your carpet circling your flat with this screaming wee bundle. It looks like they're going to explode, but they smell so great. The smell of your baby's breath when she's screaming is so beautiful."

McGregor believes in family. He changes nappies and walks the rounds and tells his wife she's beautiful when she needs to hear it. Aside from family and himself, he is not a big believer in much. And he doesn't trust those who adhere to the Word, be it the Lord's, Buddha's or Darth Vader's.

"I don't necessarily get on with religious people. It's too comfortable in a way to believe that somebody else is in charge and destiny is all planned out and we're all redundant. I can't accept that. I think we're in charge. I don't like people coming up to me in the tube and asking me what God thinks of my life today. Fuck off. How dare you ask me anything? I don't know—morality and rules, I don't really go in for that sort of thing."

So it's true, his reputation for being a bit feral, the family man with a wild hair? He grins. "It annoys me when people say things that aren't true. But being reckless is fine. I quite like being reckless."

HERE IS WHAT ELSE EWAN MCGREGOR likes: Sushi. Duck. Cameron Diaz (his costar in *A Life Less Ordinary*). Beer. Singing. Golf. Martin Donovan. Steve McQueen. Chet Baker. Oasis. Cameron Diaz. Eddie Izzard. American cars from the '60s. That guy who did *sex, lies and videotape*, that guy with the camera. Yeah, James Spader. Motorcycling. Jimmy Stewart. And De Niro. Of course De Niro. Oh yeah, and Cameron Diaz.

There are others. That guy who directed *The Getaway*. That singer with the warbly voice. His knowledge has yet to catch up to his enthusiasm. "I was once talking about Robert Shaw, who plays the shark catcher in *Jaws*, and I was saying how he's so underused these days, and then somebody told me he'd been dead for fifteen years or something. Guess he's not doing much lately. Ha, ha!"

As for heroes, there is only one. Billy Connolly.

"I never laugh so much as when I watch his stuff. He's hysterical. He's angry, and he swears a lot. Nobody can swear like Billy Connolly. He swears so well. So properly. He packs opera halls on his own. He stands there for three hours on his own. I couldn't do it. It's easy to be witty and dry on radio or television interviews. But not for an hour and a half when there are thousands of people waiting for you to be witty and dry."

When it's suggested that anchoring a play is about the same, McGregor shrugs. "I guess. But I don't have that kind of talent. I have confidence in my work. I don't want to say I'm talented, because that'll be above my head in quotes: 'I'm very talented and have a huge penis.' " He chuckles, then goes for the obvious gag. "Better than having a small penis. *[Beat]* And no talent."

George Lucas isn't worried. "Ewan's talent will win out over everything. He's got a great future. He will survive *Star Wars*."

McGregor agrees. He knows that he is, like his grandmother, happier in motion. Reflection is ponderous, dull. Which is why when he's asked, "Is this what you expected your life to be like?" he doesn't hesitate, not even a breath, before saying, "Yeah. I never even for a moment considered it not working out." ●

Allison Glock is a GQ *writer-at-large.*

The Baldness Gene

(continued from page 219) not, but it would not seem to apply to male-pattern baldness, which produces widow's peaks and chrome domes and everything in between. "It's not like this man has it," Christiano says in exasperation, "but this one doesn't." Also, single-gene disorders tend to be rare, odd afflictions, such as Lou Gehrig's disease, not ones that affect a quarter of the adult male population. Indeed, it may be for all these reasons that Stenn's abstract closes on a bleak note: "The results indicate no significant linkage of [male-pattern baldness] with any of the selected markers on chromosome 2 and 5." In other words, they didn't find anything. Christiano notes that, as far as she knows, none of the people in Stenn's lab have a background in complex human genetic traits. "I don't think they're getting good advice," she says. "They must not be using any consultants."

To Christiano and most other researchers in the field, male-pattern baldness has all the earmarks of a complex trait, one that is the product of a number of genes, probably six to eight, operating together in an intricate sequence that will take some time to decipher. By this multigenic model, each gene would contribute a degree of baldness: The more genetic mutations you inherit, the balder you become.

While Stenn's lab has come up empty, Christiano has made remarkable progress in collecting the relevant genes. She believes the hairless gene is almost certainly one of them. Last summer, with little fanfare, Christiano located what she believes to be another. This one is called the "nude gene" because it is responsible for the hairlessness of a laboratory species called the nude mouse. She lucked into the finding: She was tipped off by a colleague to a young Sicilian dubbed the "nude human" because she bore many of the mouse's same hairless characteristics. When her DNA was matched against the mouse's, the mutation jumped right out. "That one was much too easy," Christiano says. She has two more possible genes "in the pipeline" for delivery in the coming months. She figures the rest will have to be located by the more conventional method of assembling sibling pairs of genetically related baldies and then cross-referencing for common genes. She expects it will take one more year to find all the genes, and then comes the fun part: trying to set those genes in motion so she can see exactly how they interact to produce baldness—and thus discover what interventions are available to prevent, or even reverse, hair loss.

It may be that Stenn's more simplistic approach is the only one that conforms to the pharmaceutical industry's overriding imperative to produce immediate, marketable results. Let the ivory-tower types ponder the big picture; the drug business has to get an effective drug out the door today. Says Jonathan King, a biologist at the Massachusetts Institute of Technology who does consulting work with the pharmaceutical industry, "The drug companies have an astute understanding of their business plan. They know they are in the drug business, and it is a business." Remarkably, drug-industry types don't care how their drugs work, so long as they do. "At a molecular level, we don't know what it's doing," Ron Trancik admitted about Rogaine in an unguarded moment. According to one academic colleague in whom Stenn has confided, Stenn has "had his head banged against the wall a few times" by the corporate types. Says this colleague, "They tell him, 'This is all nice and

The Baldness Gene

theoretical, but where's the product?' " If Stenn can find a single gene that produces male-pattern baldness, then he greatly simplifies the task of producing a treatment. The more genes involved, the harder that job becomes. On the other hand, if there isn't a single gene, he's wasting his time.

To Christiano's way of thinking, such reductionism is not only misguided; it also denies the fundamental nature of hair. Hair isn't simple, and that's the point. In Christiano's estimation, the drug companies respond to the obvious complexity of hair growth—with all its cycles, hormones, unexpected communication pathways and abundance of genes—by denying it, by picking away at the tiny, manageable pieces, even though this yields only partial, unsatisfying solutions. Christiano prefers to see hair in all its fullness, almost to luxuriate in it. She believes much of the complexity will soon be tamed by rapid developments in the field, chiefly the continuing progress of the human genome project, which is scheduled to complete the mapping of all the genes in the human body by 2003. And despite the skepticism of the drug industry, Christiano is convinced gene therapy is coming closer by the hour. Christiano envisions a baldness treatment that would work as a kind of genetic salve, stimulating dormant hair follicles. She's planning to produce it herself. She even has the name of her company picked out, but slyly won't say what it is. In the meantime, she continues to watch anxiously in her handheld mirror for any signs of another outbreak of her own disease. But perhaps she should look on the bright side. Whatever hair she might lose, others could gain. •

John Sedgwick is a GQ *writer-at-large.*

The Sicilian Mob

(continued from page 211) They are desperate for dollars down there right now. They are listening to all ideas." I cannot get past how much Carlo Zambrini, the general manager of Spadaro's Maho Beach hotel, resembles the handsome actor who played Connie Corleone's turncoat husband, Carlo Rizzi, in the original *Godfather* movie. Trim, bronzed and athletic, Zambrini is dressed in a pressed Hawaiian shirt and white linen pants. A tousle of thick sandy hair frames his alkaline blue eyes and cut cheekbones. His English is flawless as he "regrettably" informs me—for the fourth day in a row—that his boss, Rosario Spadaro, is still too ill to meet with a reporter. Through the plate-glass window of the lobby bar, soft sunlight filters through the stands of coconut palms and almond trees shading the shorefront of the Maho Beach Hotel and Casino. Spadaro, Carlo Zambrini reiterates, is bedridden with a severe case of laryngitis, brought on by the flu. "I am sorry. It will be impossible to talk to him."

Meanwhile, he cheerfully informs me that, of course, many Europeans—"yes, certainly, including Italian firms"—are exploring ways to expand into Cuba. The city of Havana, he says by way of example, has plans to double its current 12,500 hotel rooms by the year 2002. "So there is a need on the island for people with tourism expertise." Even American companies, he says, are bracing for the post-Castro binge. McDonald's is mapping Havana street corners; US Air is planning regular flights.

His remarks also call to mind a conversation I had in Miami's Little Havana with Alfredo Duran, an influential Cuban American attorney and a Bay of Pigs veteran who once served time in one of Castro's prisons. Duran, who belongs to a committee pressing the United States to open up a dialogue with Castro, envisions the post-Fidel Cuba as the Western Hemisphere's version of the frenzied, hypercapitalist Hong Kong. "Remember," he told me with a knowing smile, "globalization is not so much into democracy as it is into the *appearance* of democracy." That would suit La Cosa Nostra just fine, although the concept would be beyond your average Colombian cartel.

As if reading my mind, Zambrini says, "Right now the Cubans are being a little greedy. You want to open a hotel in Havana or Varadero Beach? 'OK, fine,' they say, 'but you also have to open one on a deserted end of the island.' "

A muscle, as if caught on a fishhook, twitches deep in his jaw. "There will indeed be a tourist explosion," he says. "But organized crime? Please! It is a myth."

HAVANA

It is New Year's Day, the fortieth anniversary of the success of his revolution. Fidel Castro, 72 years old, has returned to the roots of his movement's struggle, the eastern seaside city of Santiago de Cuba. There, from the balcony of the town's Spanish-colonial city hall, he delivers a florid speech denouncing capitalist imperialism. He predicts that the world's "new economic order must fall." Castro's beard is gray, his green jungle fatigues somehow not quite so imposing as in times past. There is an echo of King Canute vainly attempting to stop the tides as the Cuban dictator completes his harangue with his standard rebel yell: "Socialism or death!"

Five hundred miles away, at a café in the plaza of La Catedral de San Cristóbal in La Habana Vieja, a thirtysomething Havana Univer-