

# CAN'T BEAT THIS IRON MAN

## Breaking Records in Science

By Peta Owens-Liston

**J**erry Kaplan is caught between two worlds, one of which most of us can't even see. Captivated by the boundaries between the internal world of a cell and the world outside it, Kaplan has become a liaison-of-sorts for those of us who know little about the vital microbe world that circulates within us, let alone how to pronounce the “landmarks” of such obscure geography: *transporters*, *ferroportin*, *hepcidin*, *endocytic vesicles*.

Much of this language evolves from the iron metabolism research Kaplan has immersed himself in for the past 27 years as a professor of pathology at the University, attracting more than \$10 million in grant funding. “Iron is exciting—especially on a biochemical basis,” explains Kaplan, whose passion for his research is tempered by an exacting mind and a wry sense of humor. Iron, fundamental to all living beings, strikes a fine balance in the body—too little of it and you're anemic; too much of it and you suffer from iron overload, known as hemochromatosis.

Yet, how do our bodies regulate iron so we maintain just the right amount? “Ah ha!” exclaims Kaplan, bolting from his chair with boyish enthusiasm. “That is the big question. And I happen to have found a piece of the answer.” Darting around his office while spouting directives at himself, his computer, his laptop, he arrives back at the table with some visuals—several circular diagrams and the glowing image of what appears to be a green honeycomb.



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Three years ago, Kaplan discovered that the hormone hepcidin regulates iron entry into the blood by controlling an iron transporter known as ferroportin. Hepcidin signals ferroportin to not release iron into the blood stream. If your body does not have enough hepcidin in it to regulate ferroportin, you end up with iron overload.

Such a discovery is music to the ears of those suffering from iron-related diseases. This includes about a million people in the United States susceptible to iron overload and worldwide some 3 billion people afflicted with iron deficiency.

## The Science Never Stops

At 62, Kaplan never stops thinking about “his” science. After taking a bath—a creative incubator of sorts for him—he'll call lab colleagues with 10 new experiments to start the next day. While casting a fly fishing line, a favorite pastime, his thoughts flow over the results and variables and possibilities of his ongoing research.

At times, so absorbed in his work, Kaplan takes little notice of the “non-cellular” details. Like the time he caught his sleeve on fire in his lab while hunched over the meticulous inner workings of his research. “Jerry, you're on fire!” a colleague yelled. Another time he showed up to work in a pair of shoes that almost matched. Kaplan, a slight man with glacial blue eyes, shrugs his shoulders at such things.

“Jerry's grasp of science is so comprehensive, that even if it is not his area of expertise, he can still ask the most pointed questions and suggest experiments,” says longtime colleague and pathology faculty Diane Ward, who works in Kaplan's lab. “Although rigorous and frank, Jerry is great to work for as long as you can get over the fact that he is thinking more about your projects than you are.” His direct style and laser-like focus appeal to some and intimidate others. “Jerry is very opinionated and rarely wrong,” says colleague John Phillips, who has worked with Kaplan for some 15 years.

“He's what you call a ‘macher,’” adds Jim Kushner, program director for the Huntsman General Clinical Research Center. “That's Yiddish for an important person, someone of substance who gets things done.” Kaplan is one of 11 at the University to have received the Benning Presidential Endowed Chair, which recognizes outstanding researchers.

As assistant vice president for health sciences for research since 1993, Kaplan now spends more time at his desk “reading, writing, and thinking” than he does in the lab. Yet like metal to magnet, he gravitates toward it whenever he can. “Not a day goes by, weekends included, that Jerry isn't in here,” says Ward.

On this particular day, Kaplan tells his lab technicians to put down whatever is in their hands. There are a few long moments relished beneath a subtle grin, then he announces: “We got it—the grant.” Cheers, tears, and even a little jig take place. Someone calls for ice cream, someone else for champagne. Clearly enjoying the reaction, Kaplan quietly watches with that understated grin.

A prolific grantsman, Kaplan currently has seven active National Institutes of Health (NIH) projects and has received support from the NIH for more than two decades, which recognizes him as a leader in his research field. “A level of trust has been formed based on performance between Kaplan and the NIH,” says Daniel Wright, director of the hematology program. He points out that Kaplan has been the recipient of two NIH Merit Award grants, known as “tenure” grants, which will support a project for 10 or more years. “These are peer-reviewed and given only to those doing projects that are seen as meritorious and cutting edge,” explains Wright.

Some of this grant money goes into employing students in Kaplan's labs. Students covet this experience, using it as a stepping stone toward successful careers. Michael Babcock, who now works for a pharmaceutical company, recalls publishing his first paper while he was an undergraduate in Kaplan's lab. “Jerry taught me how to *do* science—I don't think most people going into graduate school really know how to do this yet. He was interested in helping you

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think about what you were seeing in the data and focusing on how the experiment was done. The data had to be right and true,” says Babcock, recalling a Kaplan who weaved in and out of his labs, while reciting poetry and Steely Dan songs.

“The projects in his lab tended to be difficult and detailed,” remembers Marie Tuttle, who says Kaplan was like a father to her since she worked with him from high school through her second year in medical school. “I learned that things are not as simple as they first appear and that there are lots of layers and steps you have to go through to get answers.”

## The Plot Thickens; Characters Come To Life

To avoid the sweltering heat of Brooklyn, as well as the polio epidemic, Kaplan’s father, a haberdasher, sent his family off to the Catskill Mountains for the summers. In a boy’s paradise, Kaplan and his brother spent their days rummaging through the woods, searching under rocks for what slithers or crawls, and fishing the lakes. Some of these critters—salamanders, frogs, snakes—took up residence in Brooklyn with Kaplan. A boy’s mind had embarked on a journey to study “life in all its many forms.”

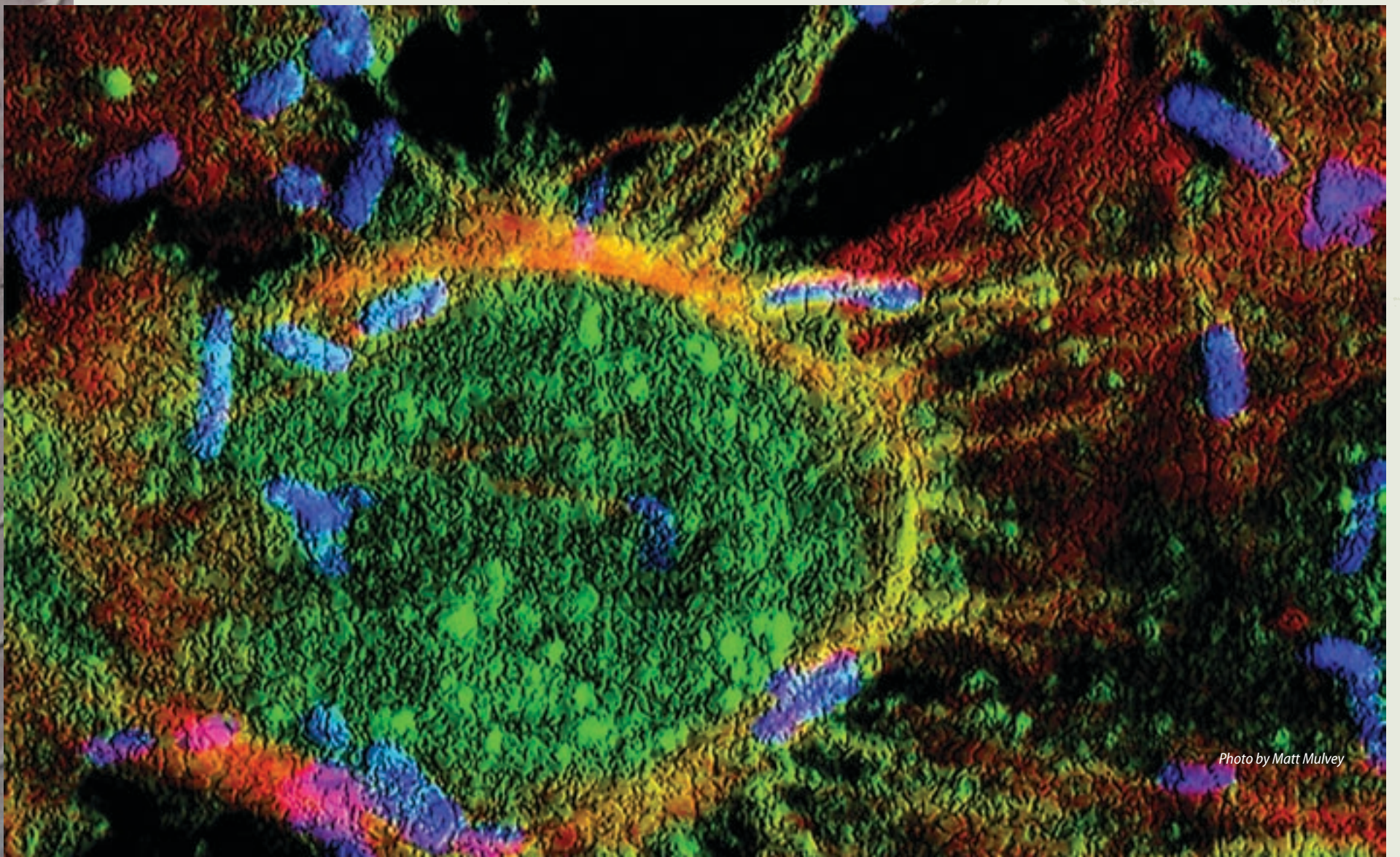


Photo by Matt Mulvey

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Eventually, literary characters rather than creatures spurred on Kaplan’s interest in biology. As a teen, he met the pioneering scientists in the *Microbe Hunters* and the progressive physician in Sinclair Lewis’ *Arrowsmith*. The final temptation came while studying Biology at the State University of New York, at Stony Brook where he read a research paper on how bacteria regulate genes, written by Nobel laureates Francois Jacob and Jacques Monod. “This was like poetry to me. I thought, if I can do anything like what these guys have done, then it will have been a life well spent,” recalls Kaplan, calling it a moment of epiphany. He followed this path to Purdue University, where he earned his Ph.D. in biological sciences and then to Harvard Medical School, where he did a fellowship in microbiology and molecular genetics.

In 1980, Kaplan accepted a job offer from the University of Utah School of Medicine after his wife, Sandy, pointed out the obvious: “Every time you come back from Utah, you’re happy. So, yes, let’s move there.” It was one of the best decisions he ever made, says Kaplan. He recalls the collegiality among faculty and the exciting science taking place at that time—methods to map and identify disease genes and the manipulation of mouse genes were taking off. It was clearly an environment where faculty collaborated and shared their research.

“When I came to the U, I was a card-carrying member of the American Society of Cell Biology. Now, I would call myself a geneticist because my colleagues have taught me genetics,” states Kaplan. He recognized that yeast would be an ideal model system for studying iron transport, so to take advantage of this he had to learn genetics and collaborate with U geneticists already working with yeast.

The yeast genome was one of the first to be understood and its cells are similar to human cells, allowing scientist to manipulate the sequences to study how certain variations, or mutated DNA, might play out in the human body. With yeast, scientists can grow millions of the mutated cells and divide them among various experiments (subject them to various environmental stresses, etc.)

in order to see how the cells function or malfunction. The findings then can be applied to humans, resulting in new discoveries and possible cures for diseases.

In Kaplan’s office is a framed picture he refers to several times. It rests against the wall for lack of a nail, yet this piece of “art” is important. What looks like a still life of scrambled eggs is really a magnified image of a mutated gene; one that causes Chediak-Higashi Syndrome, an inherited disease that is often fatal. The world within this cloned gene is Kaplan’s latest exploration.

Kaplan’s energy is restless and his mind never still as he navigates this evolving world of science. He balks at the prospect of creativity playing a part in his work—he’s a scientist, not an artist. It is Louis Pasteur who sums up Kaplan’s idea of ingenuity in science the best: “Chance favors the prepared mind.”

