

# DR. J CRAIG VENTER

## ORAL HISTORY

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### COMPUTERWORLD HONORS PROGRAM INTERNATIONAL ARCHIVES

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Edited Transcript of a Video History Interview with  
Dr. J Craig Venter  
President and Chairman of the Institute for Genomic  
Research

Recipient of the 2003 EMC Information Leadership Award

Location: Center for the Advancement of Genomics  
1901 Research Boulevard in Rockville, Maryland.

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Interviewer: Daniel S. Morrow (DSM)  
Executive Director, Computerworld Honors Program

## TABLE OF CONTENTS

- “Least Likely to Succeed”
- The Classic Second Child
- Learning To Succeed
- Early Rebellions
- Self-Discovery in the Navy
- A Link to the Future
- Epiphany in Da Nang
- A New Resolve
- Learning in Real Time
- Working on Adrenalin
- NIH Years
- The Human Genome Project
- The Politics of Science
- Breaking Away
- The Whole Genome Shotgun Method
- Always Look Forward
- Making History at Celera
- The Importance of *Drosophila*

- The Media as a Tool
- Changing the “Whole Face of Medicine”
- Leading a New Revolution
- Human Databases
- “Whence Cometh” Innovation
- Honor and Integrity
- At Jefferson’s Table
- The Patenting Process
- Remembering J Craig Venter

DSM: Today is Monday, April 21st, 2003. We're interviewing J. Craig Venter. The interview is taking place at the Center for the Advancement of Genomics, 1901 Research Boulevard in Rockville, Maryland. It's made possible by a generous grant from EMC and the Chairman's Committee at the Computerworld Honors Program.

The Interviewer is Dan Morrow, Executive Director of the Computerworld Honors Program. The program was established in 1988/89, to seek out, honor and preserve the history of the global information technology revolution by Roger Kennedy and the Smithsonian Institution's National Museum of American History, Patrick McGovern of International Data Group, and the chairmen of 42 of the world's leading information technology companies.

This oral history is being recorded for distribution to more than 140 national archives, museums, libraries and universities in more than 50 countries around the world. Without objection, the complete video/audio transcripts of this interview will become part of those international scholarly research collections and made available complete or in edited form to the general public on the worldwide web. This discussion however is private, and should any participant wish to withhold from the public record all or part of the recordings of these sessions, that request would be honored for a period not to exceed 25 years. All present here are honor bound to respect such a request by remaining here in the room and accept professional, personal, and I might add, legal responsibility to abide by those agreements.

### **“Least Likely to Succeed”**

First of all, thank you very, very much for spending this morning. Let's begin at the beginning. Tell us when and where you were born and something about your parents.

CV: I was born in Salt Lake City, Utah, while my father was attending the University of Utah, in his and my mother's post World War II recovery from both being in the Marine Corps. They met in the Marine Corps in San Diego. They were actually married while in the Marine Corps, and I have an older brother who was born while they were in the Marine Corps. So I have a brother who was a military brat briefly, and I was actually born in the University. My father was going to school on the G.I. Bill, 1946.

DSM: Did you know either of your grandparents?

CV: I knew my mother's parents for quite a while. They lived into the 1980s. I knew my father's parents, but they both died when I was at a relatively young age. My grandfather died when he was 63 from complications of alcoholism. My grandmother died about six years later; I think it was the mid to late 1950s. They lived on a farm in Idaho and I remember visiting there one or more times as a child.

My grandfather was a chiropractor. He actually wanted to go to medical school, but growing up on a farm, had neither the time nor the money to do it. He revisited things by trying to become a chiropractor and going to chiropractor school.

I remember it well because I got a cold or the flu one time visiting them and was subjected to what I thought was physical torture, a twisting of my spine in all kinds of directions that was going to cure me of my cold.

DSM: How was the family drawn to Salt Lake City? Was this a result of military transfers because of the war?

CV: No, I think it was because my father's parents were very strong Mormons and lived in the area. I guess people are quite often drawn back to their hometowns after the military; it was the closest thing to the vicinity.

DSM: You moved at a very early age to San Francisco.

CV: Yes, at age two or younger. I don't remember the move particularly.

DSM: Was San Francisco was the first place you remember as a child?

CV: Yes, I spent my entire youth there.

DSM: What are your earliest memories of San Francisco after the war? It must have been a wonderful place to grow up as a boy.

CV: It was actually very lightly populated. I was in a town called Millbrae that was surrounded by woods on all sides. The San Francisco Bay at the bottom, and then hills going up and the reservoirs on the top. I remember quite clearly in the 1960s when they mowed down all the woods, filled in all the lakes, and built tract housing. It was actually a very tragic time as the Bay area expanded.

DSM: Just south of San Francisco near the airport?

CV: That's right, right above the airport. In fact the airport expanded to be the largest city there, I think.

DSM: That's true. A question I've asked over the past 15 years is about early stories. Are there stories that your parents used to tell about you that gave any hint of what you were going to do throughout your life?

CV: Not at all. In fact, I was probably chosen as the least likely to succeed. I was always in trouble as a kid. It's probably hard for kids today to imagine; they have very structured lives, going to soccer practice and all the after school activities. Basically, my life was completely unstructured. Even so, it still seemed way too structured for me. Kids were just told to go play and we could wander all over the city as long as we were back in time for dinner. Your mode of play was basically subject to your imagination. It wasn't based on having expensive toys or anything other than bicycles for getting around.

DSM: So you were free to roam the woods and hills above the town.

CV: That's right. Maybe they didn't know how far I was roaming, and that's why I was free to do it.

DSM: How far did you go?

CV: We'd see how far we could go on bicycles and get back in time for dinner and things like that, so we'd get several cities away.

## **The Classic Second Child**

DSM: What about grammar school? When did you first start school?

CV: I think I started too early, so I was always the youngest in the class. I was not emotionally prepared for it. I think I peaked in kindergarten and went downhill from there.

DSM: You made up for it later.

CV: Much later, and it took a long time. The first class I clearly remember is the third grade because I had a very attractive young lady as an instructor who used to take me out and buy me milkshakes. We had a nice student/teacher bonding relationship. But I changed schools every year. I didn't think I did badly enough that they wanted to hold me back, but they didn't want me back. They pawned me off on the next school in the neighborhood each year.

DSM: Did you learn to read early? Is that why you started school early?

CV: It wasn't like what I've done with my own son or what you see today. It's very aggressive early education for kids. I don't remember it as being particularly something that was pushed, but it was not at all discouraged. I think my brothers and sister and I all were fairly early readers, but I was very little interested in academics. There's lots of reason perhaps why. I think I was a classical second child. My older brother is roughly 18 months older and was a super achiever when it came to school. So probably my way of getting attention was to be a super "un-achiever". I did everything but pay attention to academics. I was always stirring up trouble, getting in fights during recesses and doing interesting, fun things.

DSM: We're about the same age and grammar school is about the time, at least for me, that I began to run into my early first heavy-duty technology. Our family got a television set about 1952. I was wondering about your own early technology experiences. Did you use to sit around and watch the radio and listen to it?

CV: Yes, radio was a big thing. I remember building crystal sets as a kid and listening intently as I scratched the crystal around mostly from kluged-together parts. The radio was a big thing.

I remember very clearly when we got the first television. I think it was something like a 7-inch screen that was very hard to see in a huge box. There really wasn't much to watch. I think there was a family ritual of watching some shows in the evening. Color TV wasn't around for a long time before we switched away from our little box to a color TV. I think we were at the, not the bottom end of the economic ladder, but what the standards were of what middleclass or lower middleclass was economically then was very different than today.

I remember my parents getting their first car, which was a 1940 Studebaker that basically was my grandfather's car. When he was unable to drive, instead of selling the car they gave it to my parents. Before then, I remember going shopping with my older brother and my mother where shopping was done by taking a wagon and walking a ways to the store and bringing the groceries back in a wagon.

DSM: A Radio Flyer.

CV: Yes, a Radio Flyer. Exactly.

DSM: Did you know that you were poor when you were growing up?

CV: No, I didn't have a clue really until I got into high school. It was a high school in a mixed economic area in Millbrae/Burlingame where some of my friends in high school had brand new Thunderbirds and Corvettes. My brother and I kluged together \$100 and bought an old Ford. There was a huge class and social differenced based on money that I was not aware of until that time. It really didn't matter. You did things based on your imagination.

I used to build a lot of wood constructs—forts and other things. Basically every day was consumed with creative play that probably is something kids today are really missing out on. I think being creative is a key part of my success in science. I've argued that because I was avoiding school and was out constructing things from scratch that I was constantly building on my creativity. I think most people that spent their time in school had it beat out of them or taught out of them one way or another.

DSM: You were in high school at a really interesting time, 1959.

CV: I started in 1960.

DSM: You were a junior or a senior when John Kennedy was killed.

CV: Yes.

DSM: Do you remember where you were?

CV: Oh, yes. Absolutely. I was at the high school and it was a big thing because around the Bay area the health marches—the 50-mile walks—became a very big part of social life—their physical fitness program.

CV: That's right. I think he had more social impact; people paid attention much more to anything I've seen since to a large extent.

## Learning To Succeed

DSM: Did your brother teach you to swim?

CV: No, I actually learned to swim at the YMCA taking classes. I guess the reason for it was I had a near drowning incident when I was a very young age; I think I was two or three. I went off a diving board or something, so my parents were determined that I would learn to swim. I actually got into swimming as a competitive sport.

DSM: At the Y?

CV: Not until I got into high school.

DSM: I'd like to talk about high school teachers that made a difference. Was there a coach at the high school or was it like the YMCA or a club?

CV: It was both. I had I think a very good coach at the high school, a guy named Dick Lewis who was actually wounded in the Korean War. I also took part in what was called AAU at the time—the Amateur Athletic Union, a private swim club with an ex-Olympian as a coach. His name was Ray Taft. Actually, taking part in athletics was probably the key event in my youth where I learned that by applying myself I could succeed.

DSM: How good were you?

CV: The first year I really stunk because I wasn't really interested in working out. I thought that was a painful ritual. But after doing things for the first year, I got very motivated to win. I went from being at the bottom of the league the first year to being the champion the second year and went on for the next three years to win everything.

DSM: What strokes did you swim?

CV: Primarily backstroke, 100 and 200 back. I held an American record for about a week. That's more than a lot of people can do. I think people like Ray Taft, my coaches, thought I had serious Olympic potential. The problem is I didn't really know how to swim, and they said that I was winning by sheer determination, not by having any style. That's something I think that's followed me throughout my career. Ray Taft was sure that if he could teach me how to swim I could easily win the Olympics. Swimming carried me into my next career, but only briefly.

DSM: You graduated in –

CV: 1964. I barely graduated.

DSM: I heard that there was a critical D-minus. Do you remember the teacher, your government teacher?

CV: Yes, I got a D-minus instead of an F. If I'd gotten an F, I wouldn't have graduated.

DSM: Do you remember the name of the teacher?

CV: I don't. It was because I wrote a paper about Goldwater. Remember, this was the time of Goldwater running for president.

DSM: 1964.

CV: I wrote this very pro-Goldwater paper and it obviously appealed to the teacher, so he passed me.

## **Early Rebellions**

DSM: You immediately left high school and went to work at Sears.

CV: I left the San Francisco Bay area. I was 17 when I graduated and headed to Southern California, just to get away from all the things associated with school and get away from my home life and set out on my own.

DSM: Were your parents and siblings horrified at this?

CV: Yes, but my father left home when he was 17 to join the Marines, so they had trouble really quarreling with it. I decided I was going to take up a surfing career, even though they didn't have careers in it. It was just going to become an occupation. Obviously to support it I had to get a job, and the main job that I could get was a night clerk at Sears putting price tags on things in the warehouse. It worked out fine because it left the days free for surfing and it gave me enough money to live on. I had a house in Tuston, California initially with five or six other guys. I could only stand that for a while. It was the grossest living that I'd ever been in, and so eventually I moved on to 15th Street in Newport Beach and had a roommate. It was a small apartment right on the beach, right by the Wedge, which is one of the world famous body surfing spots.

DSM: We were discussing a disproportionate tendency about folks in this industry to blow things up.

CV: Even going back earlier, there was a big annual trip up to Chinatown in San Francisco where one could buy all kinds of explosive devices, from firecrackers to cherry bombs to even larger things. The main use that my friends and I put those to is we'd build these elaborate, miniature forts with these little army men—little plastic army men. I would save up my 25-cent allowance to go buy plastic models that cost about a dollar.

We'd build the models and we'd build these elaborate scenes and then we'd learn that not only could you blow them up quite dramatically with all these fireworks, but the plastic models and all the plastic army men would burn wonderfully and melt and drip plastic all over and create wonderful scenes. A lot of time was spent procuring illegal fireworks.

DSM: Would you a cherry bomber or M40?

CV: Cherry bombs were sort of where I peaked. Occasionally an M40, but they got a little big. Things would disappear when you used those, so that kind of ruined the drama. Kids are missing out today because they can't do that, right? Fireworks are illegal everywhere. You can't even get sparklers now. I think they should make kids play with firecrackers.

DSM: Absolutely. Crash scenes with the airplanes.

CV: Absolutely.

DSM: Lighter fluid.

CV: That's right. Lighter fluid was the favorite chemical.

DSM: Right. We were going to talk about some of your school experiences.

CV: These were part of school too. Although I was blamed all the time, I never flushed a cherry bomb down the toilet. I want to make that clear to all the high school principals who thought that I was doing that.

DSM: Actually there were some experiences in school you said that we should probably talk about.

CV: I guess I had a very natural rebelling tendency. It probably had to do with the type of memory that I have as well, but I thought the stupidest thing I'd ever seen in school was spelling tests. You were given a list of words to memorize and the next day you had to regurgitate them in a spelling test. I wasn't particularly good at that type of memory, so I just refused to take the test, which the school didn't know what to do with me. They were calling my parents, who got even more upset about it and thought by strapping me to a chair and making me learn how to spell words it would help. It made me want to rebel even more. I think one of the greatest ironies is the person that worked out the largest spelling in history of 3-billion letters has trouble spelling fundamental words.

DSM: But only four letters.

CV: That's right. I had the wrong alphabet when I was a kid.

DSM: We were talking about Newport Beach, and I thought it would be a shame for graduate students 100 or 200 years down the road not to have a firsthand description of what Newport Beach was like in the 1960s. Just tell us what it was like. Who was there and what were you doing?

CV: It's very, very different than today. The houses were old wooden structures that were all faded with the sun. There was a small boardwalk. It was like a scene right out of one of the early *Gidget* or surfing movies. Basically we just lived at the beach. Two-man volleyball was the main sport for out of the water, and then drinking and more entertaining things. It was right there with the Wedge, which is one of the toughest bodysurfing beaches in the world because it's a direct shore break. Every year, two or three people get broken necks there. It was always a challenge to start out every morning bodysurfing there and then trying to surf around there. It was a very open environment—a lot of kids living there. Now kids can't possibly afford to live within probably 50 miles of there. It was just a wonderful party place that I continued to go up to every weekend, even when I was in the military.

DSM: What music do you remember?

CV: There was always music. I guess the one that comes to mind the most around that time was the Loving Spoonful, because I was dating a girl that had a younger sister that was more attractive.

## Self-Discovery in the Navy

DSM: Two years working at Sears at night and surfing.

CV: No, I didn't last two years. Basically, I was incredibly naïve. I didn't realize that there was a war going on, so I actually got drafted in 1965. I didn't even last a year and I was drafted into the army. I called my parents to let them know that I'd been drafted into the army and I think they were very glad that I was going into the military, because they thought that was the best thing for me. They were constantly threatening me with military school. The best thing was they couldn't afford it, so I never went to military school. The only thing is they were very upset about me going into the army because they were both Marines. The Marine Corps really looks down on all the other services, particularly the army.

It was probably the one useful piece of advice I really got from my father. He suggested that I should go and talk to the navy recruiter. I drove my little hotrod from Newport Beach up to the Bay area in order to see the navy recruiter, who was actually aware of my swimming abilities. I was recruited to be on the navy swim team and was told all I had to do was train for the Pan Am games. If I were good enough for the Olympics, I wouldn't have to wear a uniform, just a Speedo. But there was one caveat, and the caveat was I had to go through boot camp because everybody had to go through boot camp. But once I was through boot camp all I would do was train with the swimming team.

DSM: This is about 1966.

CV: 1965. In fact I was in boot camp starting in the fall of 1965 and it was in December 1965 when Johnson basically faked the Gulf of Tonkin incident, as we now know from history.

DSM: And sent the Marines.

CV: He sent the Marines and scaled up the war in Vietnam and had his big TV and radio address and at the same time cancelled all military sports teams. Here I was with my one caveat in the middle of boot camp, which if you've been to boot camp you know is probably the closest thing one could imagine to being in prison. Maybe prison's not so tough. I don't know.

DSM: Were did you do your basic training?

CV: In San Diego.

DSM: Do you possibly remember the name of that navy recruiter?

CV: No, I don't.

DSM: What about your drill sergeant?

CV: I have a picture of him in my office.

DSM: Do you really?

CV: Yes, and in fact, he was really an interesting character. I have a picture of my graduating class. You can try to pick me out with my little pork pie hat out of the lineup. He was an interesting guy because, with my approach and view of discipline, I was not impressed at all with the military. After having, along with everybody else, my head shaved and all your clothes removed and replaced with a uniform, the goal is to dehumanize you in every way possible.

DSM: This is not Newport Beach.

CV: No, this was definitely not Newport Beach. I went from being a long-haired surfer to being in what felt like a POW camp. I was sitting outside these barracks talking to a friend saying that I had worked out a plan and I was going to break out. Actually I was going to swim out because the Navy boot camp is right on this little river that flows out in the San Diego Bay. I worked out with a two-mile swim, which I could easily have done—that I'd be out of there and maybe swim up the coast to Newport Beach. I had no plan after getting out. But the company commander was sitting on the other side of the wall listening to this whole thing. Actually he was a very decent guy.

When everybody got together he said he overheard this conversation. He said he wasn't totally sure who it was, but wanted to remind everybody what the consequences would be of doing that—like a ten-year prison term at hard labor. I don't think they do it any more, but it was very clear there what hard labor was because anybody that screwed up on anything in boot camp, there was this yoke that you had to wear across your shoulders. It was a wooden yoke that had two big sand buckets, and basically you had to run all day. If you stopped there were two Marine guards that would beat you with batons if you slowed down or stopped. It was serious and it was visible. I decided to revise my plan and that was not such a good idea. But I found a new way to excel, because after Johnson's announcement, I had to come up with a new career. Part of boot camp training is that the military used to give what amounts to an I.Q. test to every recruit or draftee.

I think it's actually bad that we've lost the draft, because I think it was very healthy to have half the military being people who absolutely hated the military. I think it was good for us as a nation, versus now where we have nothing but professional soldiers. But out of 35,000 some-odd recruits/draftees, I got the highest score on the intelligence test and they gave me my choice of any schools that I wanted to go to. I was immediately elevated to be the education petty officer. My responsibility for the three-and-a-half months I was in boot camp was to supervise some of the true village idiots that I was in boot camp with. Some of them had never finished grade school. They were right off farms. People were there as an escape from prison where they'd shot people. I had to make sure they learned all the basic things to pass. But it was a good, because I found there was an office for all the education petty officers where we could escape a lot of the brutality of standing out in the sun for ten hours at a time and things at attention.

DSM: This was stripes and an increase in pay.

CV: Oh, I don't think there was any pay in boot camp. If you were good they fed you, right? But I had to find a new vocation because I was not now going to be training for the Olympics. I was determined to make the most out of being in the military. I thought of what it was like to try and get a job with no education and being a night clerk at Sears. I briefly drove a fuel truck at San Francisco airport when I was in high school and worked various menial labor jobs. I was a baggage handler, where I learned never to check my bags on an airplane because we had goals—you got points based on how much you broke. The points you got the most for is if you got liquid dripping out of a suitcase. That was the highest score.

I saw that without specific training the future was not very bright. I was determined to get something out of one of the military schools. I looked at nuclear engineering and an electronics school because I really had my choice of any of the programs. I looked at things where I thought I could get a good job when I got out and afford to go surfing or something. But all these schools all had a catch: you had to extend your enlistment for twice the length of the school. Some of these schools were like two-year programs. I got the last three year enlistment out of California, so instead of being in the military for three years, I would have been in for seven or eight years. That had no appeal to me whatsoever. I wanted to get out as quickly as I could.

There was one school they offered me that you didn't have to extend your enlistment for. They didn't tell you why you didn't have to extend it. It was hospital corps school and the reason why is most people didn't live long enough.

DSM: Yes, the casualty rate is like 100 percent.

CV: It was pretty high, so they didn't make people promise to stay in longer. They wanted to encourage people to go in that direction.

DSM: Both your dad and mom had been Marines. They didn't tell you that navy corpsman got...

CV: After I was in the military, there wasn't a lot of outside communication anyway, so I was very much on my own. But I had always had an interest in medicine. In fact looking back, in my seventh grade yearbook you had to list what your future was going to be. I listed a doctor, which was pretty stunning, seeing that I was not doing well in school at all. I didn't know quite how that was going to happen. I always had that fundamental interest, so I decided that was a good route to follow. They didn't tell you about the war in Vietnam or that the chances of being sent there were virtually 100 percent.

DSM: I was going to ask how aware were you of the war? As I remember with the first Marines being sent to the Gulf of Tonkin, there was an evolving awareness.

CV: In contrast to what people think of San Francisco today as being a hyper-politically aware environment, I found that growing up there, it was a very, very naïve environment. You were very sheltered from the outside world, maybe because there wasn't television 24 hours a day. These were suburbs that were pretty lily white, where the biggest thing people worried about was if they could get into the country club or not. There wasn't a lot of awareness. There wasn't a lot of political action in that regard in my high school. There was very little on that front. Concentrating on surfing and some of my other activities, I wasn't particularly politically aware at the time. Even at the time of knowing that I was not going to be on a swim team because of the war, it didn't really dawn on me that going into the medical corps would likely involve me in the middle of it.

## **A Link to the Future**

DSM: Talk about your training. This is your first formal educational experience. Let's talk about how you were trained to be a medic.

CV: After boot camp I was sent to this hospital corps school, which was also in San Diego, but with a little bit more freedom. Basically it was class on the order of ten hours a day with a lot of simple fundamentals. Everybody had to practice doing injections on each other and drawing blood, principles of trauma, anatomy, things like that. It was actually very interesting, kind of intriguing stuff.

DSM: Somewhat like rescue squad training plus?

CV: Yes. In fact a lot of people that were in there were people that had been in ambulance crews and things, and they said it was about ten times the level of what they got. Most of the training was practical after the course work, but it gave a pretty solid foundation where you could go out and do things in a functional way.

DSM: Were there friends or mentors that you remember from training?

CV: Not until I finished the training and was actually on the ward. Most of the time was spent going up on weekends—weekend leave back to Newport Beach to party.

DSM: Would you wear your uniform?

CV: No, I wouldn't. Out the gate and up there. In fact, it got me in trouble more than once because getting back to base by Monday morning for the start of class occasionally was difficult.

DM: When were you sent to Vietnam?

CV: I was sent there in 1967, but I think the year I had before that was one of the most instructive periods of my life. After I finished corps training I was stationed in San Diego at Balboa Hospital, which was the largest military hospital in the world. I ended up on the infectious disease ward, which was a huge complex of several buildings. In fact one whole building was devoted just to tuberculosis. But it's a link to my future career, because basically every pathogen whose genome we've decoded, the interest in it started back at that stage. After corps school something sort of clicked and I just started enjoying learning. I found out I had a real aptitude, not only for the dexterity associated with medicine, but I could learn things faster than almost anybody. The intellectual part was really fascinating and a physician there who was head of the infectious ward took me under his wing and would train me on anything I wanted to learn.

DSM: Who was the physician?

CV: I'm terrible with names. It would be wonderful to eventually know who he was, because I learned to diagnose malaria under the microscope. I actually got so good at a lot of procedures, such as spinal taps and liver biopsies, that as a 19-year-old I was training interns and residents how to do these procedures. In a short while I became the head corpsman where I was responsible for about 100 corpsman on this fairly large ward. I just loved to do the mechanical things. I could draw blood better than anybody. At some of these, the hepatitis ward for example, you had to do about twenty tubes of blood. And there was an odd collection of people, because you had to deal with all the military dependents as well. These drug users were on the hepatitis ward, and you'd have to wake up some of these guys at 5 o'clock in the morning to draw twenty tubes of blood from them. They weren't exactly cooperative, so they appreciated my skill set, and in fact pretty soon wouldn't let anybody else draw blood on them.

You build a sense of accomplishment and you build a sense of skill sets—fundamental things like starting IVs that nobody else could do. You start to build a confidence in an area.

DSM: Did you have any idea that you were really bright until they gave you the test in the Navy?

CV: Probably not. I was amazed. Anybody else doing what I was doing would not have graduated from high school, so I was bright enough to get by doing nothing.

DSM: Thank goodness for the draft.

CV: Yes. That's what my father said, too. Looking back, I think it was a life-changing event, and I'm pleased it happened.

DSM: At the time.

CV: At the time it was not the best news to get from your surfboard.

DSM: Tell us about going to Vietnam.

CV: It was quite traumatic in many respects because by then I was very socially aware, and it became clear that sooner or later I was going to go to Vietnam. In fact there was a second draft, so every month there was a draft of corpsmen from the Navy into the Marines. Because of this relationship of running this ward and everybody very much appreciating my work—in fact I did work for most of the physicians—they were delighted to keep me there as long as possible. I got out of the draft for over a year, and then finally they said that I was running out of time and that I had to finally go. At the last minute my orders got changed and instead of going into the field with the Marines I got sent to Long Beach Naval Station to run the emergency room. That was a three to five months reprieve. I can't remember how long it was.

DSM: Was it an ER at Long Beach?

CV: The emergency room at the naval station at Long Beach.

DSM: So what was that like?

CV: It was actually wonderful. I had a girlfriend who lived in Pasadena with a TR-4 sports car, and it was just great. I was able to go to the beach every day. I loved running the emergency room. The fun thing was when drunks would come in with their heads split open because I was really good at suturing and I liked putting them back together again. It was quite enjoyable. In fact, I got a major commendation from the Navy from some guy at Bethlehem Steel who had his fingers chopped off in a machine. You have to remember, this was back around 1966. I picked up his fingers and packed them in ice, thinking naively they could be sewn back on. It was one of the first opportunities where that happened because the fingers were packed on ice soon enough. It was very enjoyable; just intellectually I was at the peak of things.

DSM: And you obviously took pleasure in doing the work.

CV: Oh, yes. Every fourth night I had a drier and we just prowled the streets of L.A. and Pasadena with this giant Cadillac Navy ambulance.

## **Epiphany in Da Nang**

DSM: I'm going to get you to Vietnam one way or another.

CV: It's important how I went to Vietnam. Long Beach was where a lot of transients came after they were sent back from Vietnam. One of the transients that came through there was a physician who was an epidemiologist researcher who had just come from the hospital in Da Nang.

DSM: This is about late 1966?

CV: Late 1966, even early 1967. Probably early 1967 by now. He told me my one chance for survival was to get sent to this hospital.

DSM: In Da Nang.

CV: In Da Nang, which seemed like trying to wish for a miracle at the time, because out of tens of thousands of corpsmen maybe a dozen would be sent there that year. He suggested I write a letter the Navy Surgeon General outlining all my skills in infectious disease and emergency rooms and actually volunteer to go to Vietnam if I got sent to this hospital, because I felt that I could actually do something of use. It became very clear if I hadn't done that I was going to Vietnam out in the field with the Marines. Basically they said, "You've got two months left and that's it." I wrote this letter and actually ended up getting orders to the hospital in Da Nang.

DSM: Describe Da Nang. It was a major airbase, a huge facility.

CV: It was traumatic from day one. We flew in these chartered, I guess, 707s. The first thing you learned was that flying in, the plane would totally black out. They would start from the very high altitude and dive in. You could see people shooting at you as you approached the runway.

DSM: So you landed in Vietnam with honor.

CV: Yes.

DSM: Do you remember who your C.O. was?

CV: No. Da Nang Hospital was a series of Quonset hut hospitals, a series of Quonset huts on the outskirts of Da Nang. In fact, just to tell you how brilliant our military was, it was set up under the Geneva Convention with all these red crosses on the roof.

It was set up as a buffer between the Marine airbase and Vietcong—the idea being that the Vietcong would read the Geneva Convention and not attack the hospital ever.

DSM: So there was a thin line of Marines between the defense line and the main...

CV: That's right. We had basically machine gun placements on the base that were active every night.

DSM: Was it anything like you imagined it was going to be?

CV: It was like M.A.S.H without pretty women. I mean it was...

DM: Constant.

CV: Just constant. For the first six months I was put in charge of the intensive care ward. Basically you worked from 7 in the morning until 7 at night, or 7 at night until 7 in the morning, except in times of major casualties when you just worked around the clock. We were fairly close to the beach. In fact, the beach was on the other side of the Marine airbase and the Special Forces camp. I used to go over there everyday and run six miles on the beach and swim in the ocean.

DSM: Is this China Beach?

CV: China Beach is on the other side of Da Nang and it was a much safer area. This is between Marble Mountain and Monkey Mountain if you ever locate the two, and it's now a famous surf spot resort area. I guess there are resorts on the beach and things. But back then there was just concertina wire, military bases, and gun emplacements. That's how I kept my sanity by running and swimming. I got a surfboard there and I used to surf all the time. I actually won a surfing championship in Da Nang. It was just unbelievably intense. The level of casualties is just hard to imagine.

DSM: Were you there in 1968 during the Tet offensive?

CV: I was there for the Tet offensive.

DSM: What was that like in Da Nang? Do you remember that?

CV: Oh yes. We were almost overrun. It's when I switched from being a pacifist to an activist. I decided I didn't want to be a random statistic.

DSM: There are two stories that I came across in my research about your time in Vietnam. One is about learning the difference between leaders who walk the talk and those who don't. And the other is the story about the two soldiers: one who survived and the other one who didn't. Could you tell us those stories?

CV: One is easier to tell than the other. The military patrols—I went out on a few. I tried to avoid them whenever possible. I was there during the Westmoreland years when our brilliant policy was in body counts, both our own casualties and Vietcong casualties. I think it's very similar to what just happened in Iraq where our casualties were just as important. In fact they wanted to have them because part of the justifications for each of these wars is trying to prove we're willing to take casualties to do something. If we went in and had no casualties in Iraq, the government would have considered it a failure. And it was very true. This was a formalized policy in Vietnam where Westmoreland got body counts every day. It's still amazing that after 30 years it's still hard to talk about it.

DSM: What I was trying to get to with my earlier question is: you said you came back from Vietnam having made a decision to resolve the injustices of human biology. There was a story about two soldiers that's associated with that. I was wondering if you could tell us.

CV: They were part of it in the sense that I clearly learned that there was far more to it than just biology. There was clearly a strong mental component, which certainly is applied to our interpretation of the human genetic code. We're more than just the sum total of our genes. I think it's part of our physiology. The story is about two different men that had pretty severe abdominal wounds. One was a young black man. His wounds were so severe that basically they didn't expect him to live through the night.

That's when I was running the intensive care ward which was a Quonset hut with twenty-one striker frame beds. Striker frames are the circular beds. There were just so many people either with spinal injuries or head injuries or double amputees, that it was easier to turn patients by flipping the entire bed. In the monsoon season we had to put big planks on the floor because it was always flooded out. But this was the intensive care ward where anybody came after surgery if their wounds were so severe that either they weren't going to survive or needed intensive care to survive.

This young black man was brought in and I was told that he wouldn't last the night. It turns out not only did he last the night, he lasted for quite a while. He was very lucid the next morning and just talked about all he wanted to do was really live and go back and play basketball. I think he was from Philadelphia. I'm not sure exactly where he was from. Every day that he lived, the physicians couldn't make any sense out of it because rightly he should have been dead. He was just alive out of sheer will. He eventually died. We got him so he was strong enough to try and survive a medivac to the Philippines and I was told that he died a week or two after he arrived in the Philippines. But he probably survived a month longer than anybody thought he had a chance to out of sheer will.

Another was a slightly older man. He seemed old at the time. He was probably in his 30s. Again, much less severe abdominal wounds. In fact, he was totally expected to recover, but basically gave up. Out of just simply giving up, he died within a day or two of making the decision that it was too tough for him to fight through it. It showed that human will and determination—something I'd been aware of in my own life—certainly had a major role in life outcomes, beyond just the biology.

But the biology constantly failed us. The tools, which were supposed to be the most sophisticated at the time in medicine, were incredibly crude. We had a huge malaria ward where all we could do was put people in and try and keep their temperature down. Basically there were no really effective drugs. Antibiotics we were so limited in what could be done then. One of the major casualties of the war, aside from drug use, was sexual disease, particularly syphilis and gonorrhea. They were epidemic because of the limited use of what was there. There was penicillin, streptomycin and sulfur drugs primarily. We look at the whole array of antibiotics today and that was it. Very quickly both syphilis and gonorrhea became resistant to the antibiotics, so there was nothing you could do. The ones that had it—it was called black syphilis or black gonorrhea—they basically were shipped to the Philippines where they had to remain until they were either cured or a new treatment came along. I've always been curious to know what the outcome of that was and how long some of them remained there, but obviously they didn't want them back out on the streets spreading these drug-resistant diseases.

Medicine was frustrating. During the Tet offensive, particularly where we worked for days around the clock, there was little you could do with major advanced surgery with the medicines that were there. Just the tools were severely limiting and not really designed for people that had their legs blown off. Amputees and double amputees were one of the more common things because of all the landmines. It was a failure of our political system. It was a failure of our knowledge of medicine and it was a failure even in some of these cases of psychological support for some of these guys. The whole thing was wrong and I became determined to change my life. I couldn't go back to just being a surfer—that I really loved what I was doing. I loved being able to change people's lives where I could.

That's been the mantra in medicine—you try and take solace out of the ones you can help. I also was a physician for a small village orphanage and I would go there once a week with a Jeep and an interpreter. It was just really enjoyable, where you found a bar of soap could go farther and just changing public health, personal hygiene habits with all the skin infections and diseases that started from those. A little bit of knowledge in that situation could go an incredibly long way.

DSM: You were 12 hours on, 12 hours off, how many days?

CV: Seven days a week.

DSM: And how many months in Vietnam?

CV: I was there 365 days. I had two one-week breaks. I had an R&R in Australia and another one in Hong Kong.

DSM: You came back to the United States in 1968, not exactly the happiest time to come home from Vietnam.

CV: Yes.

DSM: You were in Vietnam when Martin Luther King was killed.

CV: And Robert Kennedy. I got back in August 1968.

DSM: You came back before the Democratic Convention. What was it like for you, a golden California boy, after spending that time in Vietnam? What was it like coming home?

CV: Not very nice. I lasted twenty-four hours. I hopped on a plane to London just to get out of there.

DSM: You were twenty-two years old?

CV: I turned twenty-one in Vietnam, so I just turned twenty-two after I got out in October. So I was still twenty-one.

DSM: From Vietnam you went back to San Diego and from San Diego to London.

CV: It was actually San Francisco. I was up in the Bay area and went to a country club dinner.

DSM: In uniform?

CV: No, but just the sharp contrast of a year in a different culture to coming back to the ignorance and the complacency that helped drive the politics was hard to take.

DSM: I've been doing this for almost fifteen years, and I've interviewed lots of people. Only one was a combat veteran, World War II, and you're the only man that I've ever interviewed who served in Vietnam.

CV: It's rare in the circles that I'm in to find anybody else that was there. At NIH, the late Marty Rodbell—who won the Nobel Prize a few years ago and was a dear friend—served in World War II as a radioman, and he and I were comparing notes. He actually was sent to the brig one more time than I was. He had three to my two, but we were the only two actual military veterans doing science at the National Institutes of Health. In fact, the Public Health Corps was called the Yellow Berets. People went into the Public Health Corps to avoid Vietnam, but you could only do that if you already had a sufficiently advanced level of education. I was obviously not there.

DSM: How long were you in London before you came back?

CV: I spent several months traveling around Europe and then rented a chalet up in the Swiss Alps to just chill out for about six weeks. Then I came back to start school.

## **Learning in Real Time**

DSM: Did you start school thinking you were going to be a doctor?

CV: Yes. That was actually my intent and my motivation, but given my stellar academic record, I had to start at a junior college.

DSM: This was at San Mateo?

CV: I started at the college of San Mateo. I had to start my entire education over from scratch because there was nothing to show for it from the previous 12 years.

DSM: Quite a different Craig Venter starting at San Manteo from the one who was in high school.

CV: Yes.

DSM: How did it feel? You were an “old man” in college—twenty-two. But you knew you could do it.

CV: I didn't know that I could do it. Actually I had to learn in real time that I could do it. It was actually very terrifying for me because I knew what I wanted to accomplish. I was very focused, but it wasn't trivial. At the time the goal was to get a medical degree and maybe a practice developing world medicine, which is what I enjoyed so much in Vietnam. But to do that was a minimum of eight years of school and maybe another three or four years of training. I had almost twelve years in front of me to get back to doing the same level work I had just been doing with pretty traumatic experiences earlier. In my experience with school—just because it was never a happy experience—I had never learned to study. I didn't have any of the fundamental skill sets for doing it.

DSM: Math and chemistry alone should be terrifying. Were there people who made a difference when you were at San Mateo?

CV: Yes, there were two people who made an extreme difference. I do know these names. I was there for three semesters and an English teacher I had the first semester was named Bruce Cameron, who in fact was a late-in-life convert. He had a totally different career, decided he wanted to get an education, went to City College of New York, and ended up getting a master's degree. He had only been teaching English for a couple of years and was immediately supportive of somebody who wanted to learn but yet didn't want to follow any of the rules.

Another was a chemistry teacher, a young lady Ph.D. named Kate Murashige, who actually became one of the country's best-known patent attorneys later in life. I encountered her again at NIH. In fact, she worked for us as a patent attorney for a while. Both of them were just great teachers and supportive and in contrast to my prior experience made learning fun and meaningful. I think had I not encountered such people the first semester back, I probably would have gone in a different direction.

I was able to use my medical training and I got a job immediately as a respiratory therapist at Peninsula Hospital in Burlingame and ran all the respiratory treatments and the emergency cardiac arrest team treatments there. This was before you had to have certification as a respiratory therapist. I had a well-paying job and I was working my way through school.

DSM: You were working full-time?

CV: Full-time and going to school full-time. I had serious doubts whether I was going to make it, but I was determined to try.

DSM: What was the hardest part? You'd been away for so long.

CV: I'd never been there, so I couldn't really be away. It was easy to learn though. Maybe it's like those two guys with the abdominal wounds—it's a matter of wanting to do it. I was married at the time. I got married while I was in Switzerland and I was going through school with my wife who was from New Zealand. She had a perfect photographic memory and for tests could turn through the pages in her mind, read down the page, and look up the answer.

DSM: That's annoying.

CV: I had difficulty even imagining that. I had to work a lot harder in school to achieve the same level. I think what happened to me can apply to most people that want to do something. It's really a matter of how hard you're willing to work to do it. I wanted to do it badly enough and I overcame all the previous academic experiences I had and turned it into a positive one. But great teachers really made a difference.

DSM: You transferred out of San Mateo I guess in your third semester to...

CV: UC San Diego.

DM: ...and got your biochemistry degree in 1972.

CV: Yes. It was basically three years from start to finish, and then I decided to go into graduate school instead of medical school. I think for the first two years of college—top level community college or junior colleges—I actually got a better, more personal education than a lot of the students who were at UCSD for their whole time. But there's no substitute for a top university for exposure to the front lines of science.

I had some very influential professors that took a great interest in my ability and introduced me to science, and I actually published my first scientific paper in the proceedings of National Academy of Sciences as an undergraduate.

## **Working on Adrenalin**

DSM: What was the paper on?

CV: It was on proving that adrenaline worked on the outside of cells rather than on the inside, which was a big controversy at the time. My first study as an undergraduate was one that brought major international attention. It became the basis of my Ph.D. thesis, but also I'd never been exposed to that level of science before. What I was exposed to obviously in Vietnam was medicine. I was exposed to frontline science and found that I could use my intellect to make a fundamental breakthrough just by asking very simple questions. I just came up with the experiment—I just asked the question, how does adrenaline increase the heart rate? It turns out it wasn't known.

DSM: You obviously had a very personal interest.

CV: That's right. People supposedly study things that they have a connection to. I've been called an adrenaline junkie before, but I've always been fascinated by it. To get into this, the actual upper realms of science on something that fundamental, and that I could use my intellect to come up with some experiments to solve fundamental questions, it was the most rewarding thing I'd ever done. It immediately changed my goal from wanting to go into medicine to wanting to stay in basic science research.

DSM: Who suggested that you publish it?

CV: The mentor that I had, whose lab I started working in as an undergraduate, was the late Nate Kaplan. He is one of the world's most famous old-time biochemists who worked with Fritz Lipman, discovered coenzymes and made just some of the fundamental breakthroughs in biology. He had just gotten into the National Academy of Sciences and wanted this to be the first paper that he sponsored.

DSM: During all this time from being the second male in your family, through grammar school, through high school, starting at San Mateo, there was all this doubt. Did publishing this paper convince you that maybe you could do this work?

CV: Each step was really key. There was surviving that first semester and getting all "A's" and learning not only I could do it, but excel, propelled me to the next stages. But doing that first paper—the science itself and the reward for doing that—it's a theme that's there over and over again. There's been no substitute for it; my first scientific paper and at the level that it was, was an absolute thrill. But that was a postscript to the excitement and the reward that I felt for making the discovery in the first place.

DSM: You skipped the part about all “A’s” your first semester. I know your dad died really young. Was he still alive?

CV: He was still alive, yes.

DSM: What did your father have to say about that first semester?

CV: They didn't say much about the first semester. They were really diehard show-me people, right? And it was junior college; they waited until I got into a real university to see if I could survive.

DSM: Who was your dissertation advisor?

CV: It was Nate Kaplan. I stayed on and took my Ph.D. in San Diego. I joke now when I go back to give lectures there that I had both my combat training and my academic training in San Diego and for the genome program, it's not clear which was more important.

DSM: 1975, a newly minted Ph.D. What led you to Buffalo?

CV: It's an odd story in the sense that I have, as far as I know, the record for the shortest Ph.D. in history for the University of California, at least in biology. It was three years, and instead of doing it post doc before I even wrote my dissertation, I had offers for faculty positions. The main one was from Emory University in Atlanta, but I'd also gotten one from Buffalo. I wasn't really interested in either one. There was a new program with Abraham Goldstein rumored to be going to Stanford and I wanted to wait and apply for that program. But this was the time period of the mid-1970s. Academic employment was very difficult to find, and Kaplan had a huge lab, dozens and dozens of post docs that would send in hundreds of applications for faculty positions after four years of postdoctoral studies and not get a single interview.

DSM: Plus there were many people who stayed in school.

CV: That's right, to avoid the war. Kaplan got very annoyed that I was looking like I was being fickle. I had two bona fide job offers and I wanted to get a better one. The way I ended up in Buffalo is that the movie *Deliverance* had just come out and I watched it the night before going to the interview at Emory. Then I got to Emory and I talked to people there, and they talked about how those weren't actors in *Deliverance*. Those were actually people they were doing genetic studies on. You grew up in the south. I grew up in California. We looked at the south as a scary place, and the movie and these guys confirmed it. I couldn't get out of there fast enough, and all of a sudden Buffalo looked like the only alternative. So I moved from La Jolla to Buffalo.

DSM: That must have been a shock in and of itself.

CV: It was. Another time point was I went to see the play *A Chorus Line* in San Francisco the night before driving to Buffalo. There's this famous line in *Chorus Line* that "committing suicide in Buffalo is redundant." It was a real shock and quite a transition from La Jolla.

DSM: In 1975 you went from Southern California to the wonderful weather of Buffalo, New York, as a newly minted Ph.D., assistant professor.

CV: That's right.

DSM: Talk about what it was like then. This was just at the end of—1972 was Watergate—so it was the end of the Nixon administration. The Vietnam War was beginning to reduce the number of troops. What was it like to be teaching then?

CV: I made my mark the first day I arrived in Buffalo. It was clear to me the academic standards weren't quite the same as the University of California of San Diego. The day I arrived they asked me to take part in a thesis defense for a young woman who was just going to be getting her Ph.D., even though I was new a faculty member. It was something I had done a month before. I was vicious. I just thought she didn't know any of the fundamentals, and in my new view of academic rigor, I pointed them out and instantly embedded myself in the hearts and minds of some of the senior faculty there.

I taught in the medical school and the graduate school and the dental school, and they were all pretty much oblivious to it because, as you say, a lot of them were in school to avoid the draft. Many of them were there as placeholders, but certainly not all of them. A lot of them were very dedicated students that really wanted to get good training. In fact, one of my medical students was David Lipman, who's now head of NCBI. I didn't know this at the time, but he says he skipped all my classes, and maybe that's why I didn't know him. He thought it was so easy he could just study at home and do better.

DSM: What were you teaching? The requirement was half-time teaching and half-time you researching?

CV: Mine was more like one-eighth teaching and the rest was research. One of the values there for starting out was I had more money than almost any other faculty member. My work was attracting excellent funding. I had bigger labs and the most senior people. All the bright students wanted to work with me, which made the faculty there love me even more. I looked very different then. I had long hair and a very long bushy beard. This was a fairly conservative area and I confirmed everything they ever thought about California, I guess, the same way *Deliverance* confirmed everything I ever thought about the south.

DSM: Besides working on adrenaline, you met someone special in Buffalo. Can you tell me a little bit about that?

CV: Claire was one of my graduate students and was clearly the brightest student that I'd seen and clearly excelled at things. It developed into another type of relationship. It was legal I guess, back in the 1970s and early 1980s, for professors to have some type of relationship with their students. In fact, it was maybe required then. I don't know. It's not now. We got married after she finished her Ph.D., not before. A lot of the work that has happened up until the start of genomics was work that we had done together. She stayed in the lab, so all the work on receptors that went on for over a decade was a lot of things that were done together in parallel. In fact, we moved to NIH in order for her to get advancement. She had to be seen as heading her own lab and not being part of what was already viewed as a chauvinistic world working with a spouse. But up until that time all the work was together, and several years later it came back together in genomics again.

DSM: You were married in 1981. Obviously she wasn't repelled by a long-haired Californian.

CV: Although she made it mostly disappear.

## NIH Years

DSM: In 1984 you moved to the National Institutes of Health, section chief, still working on adrenaline.

CV: Initially working on receptors. I think that was the most significant move of my career for many reasons. It was actually a difficult move because I had a tremendous amount of independent funding, large amounts of grants, big programs. I was giving that up in exchange for fundamentally what was a negotiation. There was no separate appeal. It totally depended on the person over you how much you got for your research funding and that was weighed against having the freedom once you got the money to do what you wanted to do.

DSM: So what was the balance?

CV: The balance was I obviously wanted to be in a far richer intellectual environment than I was in. I mentioned Marty Rodbell before. He'd been at NIH basically his entire career and was actively trying to recruit me there. I think the work that I was doing in receptors was attracting a lot of international attention. That was the hot field at the time. Our work was leading much of what was going on, so there were a lot of intellectual reasons for going there. People like Marty also played a major role in getting me to move there. It was a balance, but I was very ready to get out of Buffalo.

DSM: And it's only about half the distance between Buffalo and Atlanta, so It's not really the south.

CV: That's right. Now if you go into Virginia, now that's the south, right?

DSM: Finishing the adrenaline receptor project, I gather, was perhaps bitter sweet

CV: It was actually a very important step where I had to retrain myself in a new field. I had tried while I was in Buffalo to get grants to do molecular biology, because it was clear that for the field to advance, I had to go into molecular biology. It was going to be dependent on those techniques and tools, because the protein was in too small of abundance to actually get enough to sequence the protein directly. Basically all the grant reviews would come back. If you didn't train with somebody in molecular biology, you couldn't obviously do it. It's typical of the NIH attitude and the approach for science funding in this country.

The first thing I did when I went to NIH is I set up a large lab there with tremendous resources, but shut down everything we were doing and spent the first year just retraining myself and everybody in my lab how to do molecular biology. Basically we read the literature. I hired a post doc that had been doing molecular biology for one year. It turns out he didn't know much more than anybody else did. Literally we just trained ourselves from scratch. Now I can say I was trained by a very famous molecular biologist, but at the time, until we publish the first paper sequencing the neurotransmitter receptor from the human brain, I couldn't have gotten a grant to do that research.

That's one of the fundamental problems with science in this country - people are really pigeonholed, and it's because there's the same people that control the input and output in science. They control whether your papers get published in scientific journals, and they control whether you get funding to do the research in the first place. So there's this group that becomes the elite in each field. As in any field organization, they do everything they can to remain the elite and nobody else comes in. That's a theme that comes up over and over again, and what happened in genomics—what's happened in every field.

DSM: From all we've talked about, I should have a pretty good clue where the sheer grit to buck the system came from. But wasn't it—even for an established professor and researcher with nine year's experience and huge grants and all that confirmation of your skills—didn't it make you the least bit nervous to be at the National Institutes of Health?

CV: Yes. It's a question of risk tolerance. Vietnam is something I carry with me everyday. The fundamental thing that I learned and almost anybody else learned that was there is that the worst thing you had to lose was your life. So I viewed basically every day since I got back as a gift, and I was determined not to waste it or have it ruined by other people's small thinking. I figured what's the worst that can happen if I take a risk and fail? Whereas the rest of our structure is built on keeping people in place, because they're afraid to take risks. Every place I've succeeded it was from taking what weren't extraordinary risks.

DSM: Or put into perspective, not at all.

CV: But they were risks that almost, or very few, would take.

## The Human Genome Project

DSM: I think your point about the draft becomes even more well-taken the longer this conversation goes on. Tell me when you first heard the rumors of this human genome project. It officially started in 1990, but had you heard talk of it before?

CV: Yes, the discussions started in the mid 1980s. In fact, it's something that I paid peripheral attention to. I liked the notion of it. You have to realize, I just spent a decade trying to get one gene, and so the notion of maybe having all human genes in a twenty-year period in a dedicated effort seemed intellectually like a good thing to me.

DSM: About then, again, you hadn't trained with a molecular...

CV: That's right. And the more I got to know them, I was glad I hadn't, but that's a different story. It's something that I was very much aware of and paid attention to, but I was more thinking parochially in terms of my own research. If there were literally hundreds and hundreds of proteins with the same structure as the adrenaline receptor, it would be better to get the structure of all those if I'm going to study the evolution of them by having the whole human genome and just picking those out, than having to spend even another decade getting one or a few. I wasn't thinking in terms of the field of genomics—which didn't exist yet—or what it would mean to have the whole human genetic code. I just spent a decade getting one. If that project goes on, it would help me with what I was doing because we'd have them all.

The next big step was 1986. The big step there was a paper that was published in *Nature* by Lee Hood and colleagues on their new approach for automating DNA sequencing. They attached four different fluorescent dyes to the bases of DNA, ran those down a single part of a gel, activated the dyes with a laser, which led them to be read out into a photo multiplier tube and therefore into a computer. I was just at the end of sequencing the first neurotransmitter receptor—the first gene neurotransmitter receptor, the first gene that I'd ever sequenced, this gene from the human brain. It took a year to get roughly 1,100 letters of this genetic code. It was one of the most ridiculous techniques that I'd ever seen. There were a few artisans in the world that really had it down to an art form, but the standard lab and our first sequencing gels were not pieces of art by any stretch of the imagination.

You literally had to guess quite often what the genetic code was as you read these x-ray films holding them up to the light. There were four lanes, one for each letter of the genetic code. They only showed up on the x-ray film because they were labeled with P-32. It was a messy technique that used a lot of radioactivity. It was difficult to interpret the data. It was very subjective. The reason I was drawn into molecular biology was to get away from the subjective parts of science where I'd seen case after case of even very famous scientists who built their careers out of telling a story versus having solid data. Eventually those stories would collapse quite often. They wouldn't collapse until that person died.

I liked the objectivity of molecular biology where I thought you either have the answer or you don't. You either have the sequence or you don't. But the technique was very messy, and I thought about whether I'm going to take part in sequencing more of these genes. I got very excited about this paper and I immediately contacted this fledgling level startup company, Applied Biosystems, and made arrangements for my lab to have the first automated DNA sequencer. It turns out I'm the last lab in the world they would have wanted to test it, as we had sequenced only one gene. It would hardly have been a roaring endorsement for them.

DSM: How did you make the sale?

CV: Because I was at NIH. They wanted a machine at NIH. Nobody at NIH was willing to approve the purchase of this machine because it was too new and very unlikely to work, but I had a secret fund that I had gotten from the Department of Defense for designing a detection device for them and doing some work for them. When I was told "no", I couldn't get money for this new machine, I used my own secret fund to buy it. I was very criticized when I brought this money into NIH. They said I had way too much of an entrepreneurial spirit and I shouldn't be bringing money into the government.

DSM: Describe your radical insight about messenger DNA and sequencing.

CV: Like most ideas when I get them, they don't seem all that radical to me. They seem just simply logical. In February 1987, I got the first automated sequencer, and then by the fall of that year I published the first paper in the literature actually sequencing two neurotransmitter receptor genes. They were the first two-gene sequences in history with the automated sequencer. It was now really going down this track and this is where I really got into genomics, because the discussion about the genome project was increasing. I was the only one on the planet with a functional automated DNA sequencer.

In fact, my then scientific director of my institute, the late Ernst Frieze, had been a post doc with Watson. Watson was just coming down to NIH to test the waters and maybe heading up the genome program. Frieze was very impressed with my data, particularly after he was the one who said, "No way in hell," was he going to give me money to buy a machine. He was very impressed that I'd gotten it to work and was trying to make amends for his blocking. He took me over to see Watson and had me bring my data. I showed Watson. Watson was really stunned. He said he had just come from Lee Hood's lab and Lee was still doing manual radiation-based sequencing. He wasn't even using the machine that he helped develop. Watson figured the field was really doomed and got very excited with the quality of the data that I had.

DSM: Was this the very first find you'd ever made?

CV: Yes. And he testified before Congress the next day that I had the best lab in the world and that I was going to sequence the human genome. I don't think he realized how right he was. I started doing two test projects in my lab. The irony was each institute of NIH was usually funded on a disease basis. I was in the neurology institute.

I was told that I could not work on the human genome, and they were very nervous about me making discoveries not relevant to neurology. In other words, if I made a major discovery in cardiology I had to keep it a secret or something. It wasn't quite clear how this worked.

I picked two regions with neurological diseases; Huntington's disease and myotonic dystrophy. I set out projects sequencing those parts of the genetic code to try and find those genes. These were the first two regions of the human genome that were sequenced in a deliberate attempt to sequence the genome. As part of doing this, we found that once we had about 100,000 letters of genetic code from Chromosome 4 and Chromosome 19, it was impossible to interpret the data.

I was at a meeting with all the leaders of the human genome project, and they said, "All we need is personal computers. Once we get the sequence we'll just run it through and find the open reading frames and find all the genes." So computing and computational approaches weren't even a part of any of the thinking on the genome project.

DSM: I was going to ask about that, because obviously this program is related to the impact of information technology.

CV: I set up the first bio informatics group because we had the first sequence that had to be naively interpreted. We tried to get the best algorithms that were around, set up a large computing team. We had a pretty good bank of Sun Computers, which were the hot things at the time, and found it was almost impossible to find the genes with any of the algorithms and approaches that were there. This is what led to the CDNA approach. We took the regions that were predicted by these programs as being the human axon. But because they were wrong as often as they were right, they had to be experimentally validated—something most myarthemathicians don't think about today. I would make PCR primers around these regions and then go to CDNA libraries, particularly human brain and human placenta because of their diversity, to see if we could amplify anything. If we could, I would then re-sequence and then compare it back to the genetic code. If there was a match, we knew that we had verified that it was actually a gene.

It was just simply logic to me, that we need CDNAs to interpret the genetic code. To sequence 30,000 base pairs of the human genome, which was the size clones—they were called cosmic clones—you had to randomly sequence around 1,000 pieces of DNA and then reassemble them in the computer. That was the limit of the calculations of the algorithms and the computers. So I reasoned, if we put all those together on average, we would get half of a gene at most. Knowing that CDNAs were important. I just put the two things together and said, "What if we just randomly pick 1,000 CDNA clones and sequence them?" And that's what we did. Out of the first 1,000 that we picked, we discovered close to 400 new genes in the human brain in about a week.

It was clear that it was a stunning breakthrough. We had to name the techniques, so we called them “express sequence tags”, because they were, just one sequence read of about 500 base pairs. Not the entire gene, but it was enough using the computational methods to identify quite often what the gene structure would be. Then you could just turn around and get the whole gene if you were interested. But imagine the change for me of ten years to get one gene to having hundreds of them in a very short period of time.

## The Politics of Science

DSM: Describe if you will the reaction at NIH to this. Good news/bad news, I guess.

CV: I've described Watson as not only being Machiavellian, but all you have to do is read his original book to know that his personal philosophy is “the end justifies the means.” It didn't match my philosophy, but he took this scorched earth policy to anybody that attacked the genome project or anybody that had anything that he thought would be viewed as a threat to it. He would attack it viciously. He saw my technique of rapidly discovering genes as being a huge threat to the genome project. Not because it was, but because in his shortsighted selling of the genome project to Congress, he said the whole goal of it was just to define the genes, and that would have a huge pharmaceutical and biomedical impact.

DSM: He was not keen on the mechanical approach to...

CV: Of course he was keen on the mechanical approach. That's what he wanted to do for sequencing the genome. He was very hypocritical about that. He viewed it as a threat, but instead of attacking the science, he did it in a very indirect way. He played what I called the patent card. NIH had filed a patent on the genes that I discovered.

DSM: This is like 1991, 1992?

CV: That's right, 1991. I didn't file the patent. The U.S. government filed the patent. It was actually run by Watson first and he refused to comment until it came out. Then instead of attacking the government of NIH for filing the patent, he used it as a means to attack me and what I was doing.

That was a pretty rude awakening for me. Here's somebody that I thought was one of the biggest names in the field of science that I saw acting not only in an abysmal fashion, but playing absolutely politics with something that I knew, and knew from a lot of other people, was considered a major breakthrough. But it was so attacked. Basically every day in the press I read some new attack on me. Some scientists didn't like it because in the paper that we published, we discovered genes that they'd been spending ten years trying to find. They said it wasn't fair.

To me the goal of science is to try and move knowledge and medicine ahead, not trying to move people's careers ahead. That's something that really showed up in genomics, but also shows up at every level of science. To many of these people it's more important that they make the discovery than that it gets made. It generated a lot of hostility from a lot of quarters until it became just so overwhelming as a technique that it was quietly adapted.

DSM: When I was making the remark about mechanics, there is a very famous...

CV: "The monkey could."

DSM: Stupid machines can be run by monkeys.

CV: It was more: what Craig's doing could be done by monkeys. Yes.

DSM: Tell me about your reaction to that.

CV: Let me set the scene. This was at a Senate Hearing. This was my first exposure as a young scientist being called down to the Senate. It was with Pete Domenici who was a real strong genome supporter, and a young Al Gore was on the committee. If you read the book *Gene Wars* by Watson's assistant at the time, Bob Cook-Deegan—Cook-Deegan indicates that Watson practiced this line for a week or two ahead of time, as part of his Machiavellian behavior. He tried to make it appear that it was spontaneous, but he practiced it over and over again to try and use there, which is difficult for me to understand. I try and put my energy into doing science, not finding clever ways to attack and ridicule people.

I brought up what we were doing. We had now published the paper on ESTs. I can't remember if it was Domenici or Al Gore who asked the question— what the government was with intellectual property on these—because it was a major issue with companies like Genentech that were insisting that government protect these with patents. They had brought this to many Congressmen's and Senators' attention and indicated that the NIH had filed a patent on the genes that I had discovered. That's where Watson had his well-rehearsed line that he burst out with as a means of trying to undercut this new field that I started (of express sequence tags) from being taken seriously by these two key supporters of the Genome project so that they would dismiss it, which they largely did. It was really played down of any significance until a few years later, after I left NIH and started TIGR. We discovered three new genes that Burt Vogelstein linked to colon cancer.

DSM: The event—with all the controversy about patents and about how un-American, unscientific, totally self-serving, blatantly evil—the patents were denied.

CV: The patents were basically withdrawn. It was such a political thing. It was one of the first things that Harold Varmace did when he became NIH director. It showed a fundamental lack of understanding of the system. These were patents owned by the U.S. government. The most that would happen is that myself and the other inventors would have gotten a very small royalty on top of our lovely federal salary. Yet it was portrayed that these were done out of personal greed, based on Watson's personalized attacks on these things. Everybody assumed there must be something to it, versus just a Machiavellian approach trying to defend his own budget.

Varmace had totally accepted this notion that it was done to make a personal fortune. I was now at TIGR. When he came into office he requested a meeting with me to get my view on what he should do with the patent applications. I urged him to proceed with them, to get them either thrown out quickly or accepted, so there would not be any ambiguity out there in the field. I didn't care which way it went. In fact, I was hoping they would be proven unpatentable. They would end up being patentable, but it did not matter. He then accused me of wanting to do this just for personal gain.

## **Breaking Away**

DSM: Let's talk about you and your wife founding TIGR. Tell us about the founding of it and the decision to do that with human genome services.

CV: It was based on the scale-up of EST sequencing. It was obviously going very well, and the Neurology Institute was increasingly concerned that I was doing things of broader relevance than just neurology. They were very cautious about that. The internal politics at NIH were very strange, in the sense that all the funding that was going to go into the genome project was all extramural funding and would not fund things at NIH itself. In fact, I upset a lot of the old guard at NIH by sending in a proposal for review to fund work at NIH. That made people very nervous because they didn't want their work ever subject to that kind of review, even though everybody at a university and research institute like ours is subject to that all the time.

It was very controversial at the time. It started out with Watson wanting to fund my lab as the center of things, to being incapable of doing it because he was trying to please all the mappers like Collins and others that didn't want sequencing to happen. It just got to be a very political environment.

I never thought I would leave NIH, and Claire never thought she would leave NIH. In fact, we talked about the only thing that would ever get us to leave is if we had our own research institute. It started after all the news about ESTs. It just shows you some people can read through the nonsense, because I started getting some incredible offers to head up biotech companies. One offer was for me to write my own check - get a signing bonus of up to \$5 million—if I would accept the job of being CEO. I said, "Is this a low level I.Q. test? What am I going to do, write it for two?" I didn't quite understand the offer, but it's the sort of thing that made me have to realize what I wanted in life—whether I'd rather just keep doing basic research or whether I'd rather have more than \$2,000 in the bank and a bigger sailboat.

I opted for the basic research, but the offers kept coming. Finally I said, "I don't want to head up a biotech company, but if I can get start-up funds to start a new basic science research institute that's a not-for-profit institute, I'll do it." That scared away a lot of investors. They don't like the word "not-for-profit," and so that gets them running pretty quickly. But Amgen offered to give me \$70 million to start a research institute around genomics and the EST method.

Then a venture capitalist, Wally Steinberg—in what's now a famous meeting—offered me \$15 million. I just got up and thanked him for his time and started to go. He was stunned, and he said, "Where are you going?" I said, "I'm going to California where I have a \$70 million offer." He turned around and said, "Well I'll give you \$70 million." His associates almost fainted because it turns out they didn't have \$70 million.

Nevertheless, he actually pulled it off, because they raised it publicly without me knowing they didn't have it. That was to form human genome sciences as a for-profit company. We would look for somebody to head that up, and I would run a new not-for-profit institute that I named TIGR. After the key people in my group decided to leave NIH to go with me, Claire, whose lab was an independent lab in a different institute—she was in the drug abuse and alcohol institute doing research where receptors were pertinent to that—decided that she wanted to move her lab. They didn't want to be stuck in the government if I wasn't there.

The two labs sort of left simultaneously. I think there were twelve of us that started TIGR. Our first year budget was \$4 million and it was supposed to scale up. Today, eleven years later, it's more like \$60 million and growing rapidly. By the end of this calendar year it's likely the combined budgets of our three research institutes will be over \$100 million. We'll have on the order of four- to five hundred scientists. It's grown a lot in ten years and has more funding from NIH and other government agencies per capita for the scientists than any other institute.

DSM: Would you describe the three other, the tri-part type structure?

CV: About a year and a half ago, when I left Celera with a boot in a certain part of my anatomy, I formed two other research institutes. One is the Center for the Advancement of Genomics, which was to follow up on the public impact—discrimination issues associated with our sequencing the genome—and to use data to deal with key social issues. We're trying to deal with race-based medicine, genetic discrimination. But we're using it by generating additional data, not just jaw boning on these issues.

The other institute is the Institute for Biological Energy Alternatives, where we're trying to make a synthetic chromosome, perhaps the first synthetic species. We're trying to use genomics from microbial systems to see if we can actually generate clean energy such as hydrogen, and at the same time sequester CO<sub>2</sub>, using again biological systems to try and reverse some of the damage that's been done.

DSM: Yes, I really want to talk about that later on. The twelve of you break away from NIH. What's the reaction at NIH?

CV: Bernadine Healy, the NIH director, was really stunned and upset about it. In fact, she wanted me to delay any public announcement because my friend and colleague, French Anderson, had just recently announced that he was going to leave to go work in his gene therapy company and transfer to USC. She was very worried that she would get attacked from Congress—two of biggest names there leaving at the same time. She wanted me to disappear for a week, so I entered a sailing race and went away for a week and came back.

But I'm sure some people were pleased because it took the complicated issues away from them. One of my favorite quotes is from Harold Varmus, who replaced Bernadine Healy, who lamented that they wished that they had somebody at NIH who was willing to do EST work and put the sequences in the public domain. Well, that's where I started when his colleagues basically chased me out.

I'm sure there were mixed feelings all the way around. At the time, everybody considered what it was. It was an extremely high risk. Both of us had guaranteed lifetime salaries. I had tenure from the second I moved to NIH, and Claire had just gotten tenure, even though it was promised years earlier. We had multimillion-dollar lab budgets, good teams. The federal salaries weren't great back then. They were between \$80,000 and \$90,000 a year. That's less than half of what they are now, a decade later. But, it was a great environment with some of the scientists we could work with and do things on a daily basis. Other than the federal bureaucracy and the insane rules, it was actually very hard to leave that for something that could blow up at a moments notice and have no employment.

DSM: Was that your biggest fear? What kept you awake at night regarding this whole adventure?

CV: Initially, just the excitement of doing it. I could look around me at NIH and see people that spent thirty or forty years there. They all started to look alike after awhile. Very few of them took risks anymore. Even though the intramural program is one of the best place for taking risks, less than ten-percent of the scientists there do. They don't have to worry about funding; they don't write grants. Yet so many of them do mundane research that probably wouldn't be well funded if they went to a university. They couldn't compete on the outside. The good thing is that ten-percent of the scientists do high-risk research and make real breakthroughs. But, it was a difficult environment to leave and try to replicate.

DSM: I should have known when I asked you what kept you awake at night that you were going to tell me about the things that really were so exciting they kept you awake. But did you have any nighttime terrors about this?

CV: No. Not at that time. Those developed later after I got some new industrial colleagues. But no, it was just sheer excitement of a chance to expand the research, based on ideas that I originated. Here was somebody who was going to give me a \$70 million grant for my own research institute to expand on the EST method in genomics.

DSM: A glorious opportunity. Tell me about the significance from your own point of view of the colon cancer gene research and for coenzymes, the 1993 discovery.

CV: It was a wonderful breakthrough, but it's just been one of thousands that have come out of this field. What it was is a breakthrough that overcame all the negative criticism that Watson and his colleagues heaped on the method. Within a week of Vogelstein calling, he wanted to know if I'd seen anything new. I said, yes, that we found three new mismatched DNA repair enzymes and was about to call him. A week later we had them completely sequenced and mapped back to the genome, and they all mapped to regions that he'd shown were linked to colon cancer.

Within three months, we had key papers going into *Science* and *Nature*, now that we had the complete family of genes. He had already found the first one and here were three more linked to colon cancer. But these were discoveries that really put ESTs on the map. All of a sudden people quit the whining about them and realized that this was the future. And the discovery—instead of taking ten years—took three months. It didn't hurt that somebody of Vogelstein's immense stature went around talking about how he made this very key breakthrough in such a short period of time based on this new method. In fact, his cloning method was 1-800-Call Craig.

The comprehensive data that we were generating was wonderful. I wish that somebody had done that more than a decade earlier. I would have loved to have called somebody or done a short Internet search and found the adrenaline receptor gene instead spending ten years looking for it. So you see, the people that really wanted to move forward were scientists. They weren't embroiled in the politics, saw it as a wonderful breakthrough, and have utilized it intensively.

DSM: By 1994 the method was—"hot" is the only way I can describe it—and you came very close to being knocked out of the picture entirely in 1994.

CV: There was a lot of stress that came into my life. When I said that I didn't want to be CEO of the biotech company, I had to agree with the venture capitalist that they would find a CEO. The late Wally Steinberg had venture capitalists—was the acting CEO for the initial six months. But then he brought in a very caustic character named Bill Hazeltine, who was a very bright guy and was very ambitious. He was an average researcher in the AIDS field at Harvard, but had been involved with Steinberg in starting a lot of companies. He didn't like having to come in to be second fiddle to my discoveries. It was very hard for his scientific ego, even though he was now just a businessman, not doing science anymore. It was complicated. He made it his goal early on to try and destroy and eliminate TIGR, get rid of the funding obligation that he now assumed from the venture capitalists, and just sort of made our lives hell for quite a period of time. He tried to block our publication of research and threatened the funding. For a two-year period there wasn't a day that went by that I didn't have to talk to lawyers. It was just, again, the personalities driving things out of their own.

Basically, my guesstimate is he wanted credit for scaling up the EST method and applying it because he recognized how important it was. There was no question that he was smart enough to see the value of it or he wouldn't have left Harvard to come do it. But I think it's just that a lot of people end up in these positions out of sheer cutthroat competitiveness.

I think the general public has a very different view of science, that it's a bunch of nerdy benign people working away for the public good. Fortunately there is the altruistic portion of it that comes in somewhere on average, but it doesn't show up quite often at the leading edges of what goes on. It's the justification, but not the daily actions. It's like an extremely religious person in daily life acting in a vindictive non-religious fashion.

DSM: This literally almost killed you, right? How bad was it?

CV: Without knowing it, I developed diverticulitis. I was hospitalized once. They were sure it was appendicitis and they started me on massive antibiotics. They assumed it was just a burst appendix, but then I started getting better on the antibiotics before they did the surgery. I refused to let them do the surgery. I said that if it was a burst appendix, I didn't think I would have gotten better that fast. And they said, "We'll scheduled it. Why don't we take it out anyway?" But they had no idea what it was. I went to meeting in Nice, France. I was actually in Monte Carlo giving a lecture when I developed a very high fever and severe peritonitis and, fortunately, was able to get some massive dosages of antibiotics there and fly back for surgery. I had the lower part of my large intestine removed. It's now called a modern disease—a stress-based disease.

It was probably the worst period of stress I was ever in, with all the things I was trying to build and having somebody very actively trying to destroy it. Made Watson seem like an amateur.

DSM: That's extraordinary. And given the stress that you've been through, that's saying something.

CV: That's right.

## The Whole Genome Shotgun Method

DSM: On another note, 1994 is also when you met Hamilton Smith in Spain.

CV: That's right.

DM: Could you tell that story?

CV: The impact of that interaction has been of historic consequences. We were both at a meeting in Spain. It was actually an ethics meeting dealing with the genome. I gave a major lecture there and he was actually pleasantly surprised, because he said from all the things he'd read from Watson and others that I must have horns.

He told me he was very impressed by the lecture. We were talking and we ended up going out to dinner together. A number of ladies of different ages went with us and we just had a wonderfully fun time drinking and telling stories. I asked him the next day whether he would consider being on the scientific advisory board of TIGR, and he said that he would like to very much. He wanted to know if we'd considered sequencing a bacteria. He had a bacteria, *Haemophilus influenza*, that he thought he could make large libraries from that we could sequence relatively quickly, because our lab was the largest sequencing lab in the world by maybe in order of magnitude at the time.

DSM: So he thought before this that he was looking at a job that would take how many years?

CV: It took thirteen years to do the E coli genome and so the notion was to see if we could speed that up in any way. From discussions that we had, we actually came up with what we now call the whole genome shotgun method. Instead of using the large clones, we broke the DNA down into thousands of smaller pieces. We sequenced 26,000 of them and used the computer then new algorithms developed by Granger Sutton at TIGR to assemble back the genome. That took four months to do. The sequencing took four months. It actually took most of the year. The first way we tried didn't work and we had to start from scratch and develop a new method. All that happened during the course of that year, but it was still a year from start to finish of the publication.

We didn't set out to sequence the first genome in history, but we took more than ten years off the time course for doing it. In 1994 Ham and I wrote a grant to NIH on our new method, and we figured it wouldn't be funded because there's a history of not funding new ideas. But we started anyway dipping into the TIGR endowment of the money that I received from the venture capitalists. About the time we were closing the genome, we got this letter from Francis Collins telling us it wasn't going to be funded and that they were sure that the method would not work. I called him to let him that we're having wonderful success and that it was likely to work, and we were actually worried—we had a lot of affection for NIH, having spent close to a decade there—that NIH would be very embarrassed when they turned it down with severe prejudice, and that clearly worked. He was so confident that it would not work that he refused to fund it even with the new information.

A short while later, we published the first genome in history—in *Science*, I think. Surprised the entire scientific community. I think if I had to narrow my career down to one paper, I would choose that paper as probably the most significant. But the EST method has probably impacted as many scientists, just in a different way. There's now over 12 million EST in the public databases and they're growing by millions. The number one comment we heard was that when people saw that paper they finally understood what genomics was about. It was the first time in history that we had all the genes associated with a living organism.

Several departments around the world had made people stay up all night reading the paper when it came out. It was one of those rare moments that people realized immediately the impact of it. It was just very exciting for all of us, and it was totally due to that happenstance meeting and going out and drinking in Spain. And it's been a wonderful interaction. Ham's played a major role in every project through and including the human genome project. He's the scientific director now of the Energy Institute, so we're continuing our collaboration through the third organization.

DSM: Then why did you bother to apply for the grant at NIH?

CV: Number one, we had very finite resources. Genomics was clearly expensive as a field, and if we were going to build on what we were doing, we had to find ways to competitively increase our funding. With the initial commitment I got for building TIGR, that was funding for the first ten years. It gave us a chance to build the fundamental organization and, in rare cases, do the emergency experiment. Of all the breakthroughs, the EST method was only doable because I had independent unobligated funds within NIH. Because I had independent funds at TIGR, we were able to do the experiment anyway. So for every major breakthrough we've used independent money to demonstrate the feasibility of it as a way of proving to the scientific community. Instead of making arguments about it and fighting ten years of battles, I believe in doing the experiment and having the data speak for itself.

And it speaks very loudly. As soon as we published the *Haemophilus* paper, in fact even before, just from people in the DOE seeing the potential for it, the DOE gave TIGR its first really large grant and that was to do several more genomes. So while the NIH group was saying it was impossible, the DOE scientists immediately saw the potential of what we were doing and stepped in to fund when NIH would not.

DSM: Are there people at DOE, names we should be sure to get into the record?

CV: There's a number of people there over the years that have played very key roles. Dave Gallis was the initial director. When he stepped down to go back to a university, Ari Petronis took over from him. Marv Frazer has been there for a very long time and has really been instrumental at looking at these areas. I think the same group was sympathetic because Watson was severely attacking them and attacking the Department of Energy, which actually originated the human genome project. He was applying his approach of: if there's competition, you try to destroy the competition versus trying to work with them. Maybe the DOE had sympathy for our radical approaches, but it's been an ongoing relationship that has gotten some of their biggest breakthroughs.

The first genome was published; the second one that we did was the first one with government funds, and that was from the Department of Energy. The third one that was done was also with the Department of Energy. It was the first Archaea.

We had severe limitations placed on us by Bill Hazeltine, Human Genome Sciences, and the pharmaceutical company, Smith Kline Beecham. They were all very threatened about us publishing any papers and did everything they could to restrict the scientific publications for as long as they could. I got attacked by my critics for that situation. It's been typical of a number of these arrangements, where instead of trying to understand what the issues were, it was easier to continue to attack what we were doing because it was still viewed as a threat. I think it was viewed even more as a threat because nobody counted on the major breakthrough in genomics to come from this independent not-government-funded center.

I was at NIH when Daniel Cohen had a breakthrough mapping with yaks, which is a technique that probably set back genomics at least five years. But Watson and his colleagues were in a sheer panic over this because they thought they were going to lose initiative to the French. It's another example how this was not for the public good, or here's a breakthrough that's going to move things forward faster—somebody else might move ahead of us. It was always this “us versus them” type of approach. And with the success that TIGR had publishing the first genome and with the success of the ESTs with Vogelstein, instead of decreasing the attacks, it ironically increased them.

I got blamed for the limitations imposed on us by Smith Kline Beecham and HGS. Now maybe I am to blame because I accepted the funds with some degree of limitations—but some minor limitations—except it got twisted by the attorneys and tied up for a very long time. Basically we had a huge backlog of data and finally I decided the arrangement was not worth the money. So Hazeltine and Human Genome Sciences stilled owed TIGR \$30 million out of the original \$70 million, and I arranged through the attorneys to call it quits, which was probably a riskier move than forming TIGR in the first place. We had the sale of some of the HGS stock.

I think at the time we had \$12 million in the bank, which would have given us money to operate for one year. We had to turn around within one year to find a way to support ourselves, but I decided that I would rather fail on my own than succeed by staying tied into that situation. It was a very tough decision for my board of trustees, voting to give away \$30 million to get out of this caustic relationship. They decided to back me and it ended up being probably one of the best moves I've ever made. But it definitely caused some sleepless nights.

DSM: Are there some key players on your board that really helped you get through this?

CV: It's been largely the same board for a very long time—it's been sort of an odd-duck collection of people. A fellow named Ted Danforth was one of the first trustees; a guy named John Coleman, who is actually one of Watson's closest friends except when my name comes up. Ham Smith is now on the board. Victor McKusick, sort of the father of this whole field, is on our board, as is Gerry Rubin from Howard Hughes Institute. I mean that's just a few of the names, but they've taken it in a high-risk environment and every time have supported what seemed like incredibly high risk decisions.

I think that was my most uneasy period because I knew that my whole institution could go down the drain if I did not do something quickly. But it had a very nice impact. As soon as we freed ourselves of HGS, all our grants started to get funded. We were told that basically study section were turning them down deliberately because they didn't want to do in anyway anything to directly or indirectly benefit Hazeltine or HGS. There was just that kind of caustic feeling.

DSM: Did you have any idea there was going to be that consequence?

CV: No. No, I would have slept a lot better had I know that. And so the funding started increasing. But, it still became sort of a hand-to-mouth organization. Like many academic institutions it was only secure as the next grant. Part of the effort I was spending was looking for other arrangements that would ensure the long-term stability of the organization, independent of fickle funding.

We had discussions with a company called Amersham that offered to give me \$30 million to help start a new anti-microbial company that was based on all the microbial pathogens we had done as sort of a new era in microbial, anti-microbial therapy. This is an area we've looked at a lot. We've worked with Cyron and others creating new vaccines. It seemed like a possible way to ensure long-term success, but that's when the opportunity to sequence the human genome came back around.

DSM: Tell me about this new opportunity for sequencing the human genome coming around and the formation of PerkinElmer Applied Biosystems.

CV: One of the grants that TIGR had was—in fact TIGR is one of the test centers, four or five—doing test sequencing of the human genome. It was clear to us on a daily basis the approaches being taken by NIH were cumbersome, inefficient, and a terrible scientific way to try and do things. We were sure the method that we developed for doing *Haemophilus* would be a much better approach, but the government bureaucrats were set on going in the direction they were going. It was the notion that the human genome was so big, that it was such a complex problem to sequence, that not only was it beyond the U.S. government's resources and the American scientific community, it had to involve the entire world—the scientific community—over a decade or two.

Applied Biosystems was working on a new DNA sequencer and we were planning on building it into a new proposal to go back in NIH and see if they would change things. I had several discussions with Collins about this, but it was just so clear that they were set on the track they were going, and they didn't want to hear about any new ideas.

DSM: So at this stage the Collins Group is looking not at 2005 but...

CV: In fact at that time, up to 1998, there were less than three-percent of the human genomes sequenced and about a billion and a half dollars spent. People like Norton Zinder told me about memos that they'd seen that indicated Collins hadn't even requested in his budget enough money to do half the genome. The assumption was there was clearly no dedication on Collins's part to sequence the human genome. He was more interested in disease genes and it was unlikely to go forward. That was the environment in 1998.

When I kept getting calls from executives in Applied Biosystem, which had been acquired by Norton Zinder, wanting to know if they gave me \$300 or so million to sequence the human genome, did I think I could do it. Yes, I just thought they were crank calls. With the first two, I just sort of hung up on the guy, laughing, and told him to call me back when he was serious.

Finally Mike Hunkapiller called and said they were really serious and that the new machine was even better than they thought. They thought that combined with my method, it might really work wonders. I went out with a small team to evaluate the instrument and that day, while we were there, we did some blackboard calculations of what it would take to do it.

Mark Adams, who started with me at NIH with the EST work as a young post doc, is an incredibly conservative guy who is sort of the naysayer in the group. I made a math error by a factor of ten, and he was just saying it was absolutely impossible and there's just no way we could do it. It didn't matter how much money or anything. Then I realized my math error. It was still an extraordinarily large number. And he goes, "Oh, we can do it now." It's amazing what an order of magnitude will do to some people's thinking. I wish I had thought of it as an approach.

DSM: I hope you saved the notes.

CV: Well, it was just chalk on the board. Basically Hunkapiller and I sort of made a verbal agreement then that we would try and find a way to go ahead and do this. I went back and announced to Ham Smith that we were going to sequence the human genome with whole genome shotgun sequencing. They probably wouldn't fund it at TIGR, so we're probably going to have to start a new organization to do it. His statement was really classic Ham Smith. It was something like: "I don't think it will work, but if you're going to do it, I'm going to go with you." He actually started out as the original doubter of this.

The scale was something that was not intuitive. It was just beyond the scale of anybody who had experience in the field thought was feasible. The whole thinking would be how this was involving so many countries and governments and thousands of researchers that a small team doing it just seemed out of the question. It came down to our computational abilities to the new algorithms that we had developed at TIGR and scaling up computing by several orders of magnitude.

It was a wonderful challenge; it was a wonderful opportunity. But it's really critical to understand that it was done in the environment of nothing was happening with the public program. It wasn't done as an attack on the public program or a competition for it. There was no competition. There was nothing there. Everything we set up was the assumption that we would be the only source of the human genome. That's why I made it an absolute requirement if I was going to be involved, the company had to give the data away for free. And it was.

DSM: So that was your condition?

CV: It was an absolute condition. We even offered to work with the public scientists to make it go even faster. But again, it was this notion of they wanted to be the ones to do it and that's what was important to them. Not getting it done, that turned it into what ended up being a pretty nasty public battle versus something that started out just as straight forward. We wanted to test this approach and really push it and get the genome now instead of waiting another decade or so to get it.

DSM: I sidetracked myself by thinking why not just try the technique, given the cost and the time frame. Even if you tried it and failed you'd be ahead, would you not?

CV: That's right. That's what we argued, but it's not an experiment the government would ever fund because it's a risk. They wanted absolutes. More importantly, there was no independent group making these decisions, right? It's the people receiving the money...

DSM: Making decisions.

CV: ...that were making the decisions who should keep receiving the money. It was the person who was going to get credit if he team-sequenced the genome that wasn't exactly to see another team come in. It was considered impossible, not even something that anybody imagined would happen. They were all so stunned by it, that it was only because of our previous successes that it was taken so seriously, not in terms of what's for the public good, but can we do this faster.

One of the things I was attacked for was my suggestion in a meeting with Collins that we work together to get human done quickly. And if they want to do something independently at the same time with their approach, why don't they do the mouse genome? I wasn't trying to be insulting, but that's how they took it. I was trying to be just logical scientifically, because to interpret the human genome, we knew we needed the mouse genome. I was thinking, if both were finished simultaneously that science would be moved ahead at least a decade. Instead the human genome got sequenced twice and the mouse genome got sequenced twice at considerable taxpayer expense, and the expense of not having it even a year or so earlier at the expense of now not doing other science because of the consumption of that money.

DSM: I haven't asked much about computing. The PerkinElmer Applied Biosystems new sequencer obviously had a profound effect.

CV: It was one component. It allowed us to generate the data quickly.

DSM: Yes, the last time we talked about computers we talked about your new Sun systems. Were there breakthroughs in computing techniques where people literally made a difference with your project?

CV: Most of the breakthroughs were in the algorithms and just using computers in an intelligent fashion in the early stages. For doing the whole genome shotgun experience with humans, we had to build the third largest computer in the world, and we had to do it in six months. I had zero experience in high performance computing. The only two larger computers in 1999 and 2000 were the DOE computers used for nuclear weapon simulations. In 1999 we built a 1.5 TERRAFLOP computer in a collaboration with Compaq, which is an interesting story on its own. I could not sort out any of the claims between Compaq, IBM and even the other computer manufacturers. It helps to be an experimental scientist. I gave them an experiment to solve.

DSM: What did you have them do?

CV: I had a contest to see who could assemble the *Haemophilus* genome the fastest. I said whichever one works, we will probably go with. It turns out the Compaq alpha chip was over three times faster than anything IBM could muster. It took us initially two weeks, and we got it down to nine hours. The best thing IBM could do was like a three-day calculation. When you look at that difference, when we're scaling up to something the size of the human genome, doing something in weeks or months versus months or years, we weren't aware of any computer that was stable long enough to do the whole thing. I could envision getting halfway through and having to start over each time, but it was really based on the speed and success with the alpha chip.

DSM: I hate to put you on the spot about names again, but do you remember any of the names of the folks that were on the team, the Compaq team, that did this job?

CV: In fact the key person works for me now. He's our CTO, Marshall Peterson. He was actually working for Compaq building a giant data center in Sweden, I think, for Eriksson. They said there was only one guy who could really probably do this. He found out who he was and decided we needed him totally on our side. So we hired him. What happened was truly extraordinary, when I look back at it and understand more completely the history of the size and scale of computing operation we built in a very short period of time. I think the people that did it, Marshall and his team, and the people at Compaq deserve extraordinary credit for it.

## Always Look Forward

DSM: In reading about the June 26, 2002 announcement that you and Francis Collins made jointly, the two quotations that I remember seem symbolic in a sense. Mr. Collins said for the first time—to paraphrase—for the first time man knew something that he heretofore been known only by God. And you said, that there's a possibility that cancer will be reduced to zero in our lifetime. Talk about the distinctions and point of view.

CV: I don't want to attack somebody's religious beliefs, but it does disturb many of us to have religion introduced in the middle of science. Some people probably actually find relief and positive aspects of that. My approach has always been to look forward. We were in a hurry to get the genetic code because it's going to be the basis of most future biomedical discoveries. It wasn't an end product as it was deemed in this public effort. You can see why it was. It's a \$3 billion fifteen-year goal involving multiple nations. Getting to that point becomes an end in itself. I always believed that getting the genetic code was the starting point. Everybody was saying—but I think I'm the only one who actually believed it—that we wanted to use it to go forward to understand our lives.

I wanted to be able to say to myself, in reconciling things with those men in Vietnam, that we try to understand life. We try to explain what it meant. Maybe that's other people's religions, but we're trying to drive this information forward so we can understand the questions everybody asks him- or herself. Who are we? Why are we here?

I'm part of the group that thinks those questions can be answered by rigorous scientific efforts. With this information, we understand our relationship to all other animals on this planet for the first time very clearly. We understand that evolution is a fact. It's not a theory. It's not a religious theory. It's not a scientific theory. It's a fact. We know we'll have, within a decade or so, the precise evolutionary events that changed between other primate's genomes and our genetic code. We can track these back over a billion years now doing comparative genomics. This is the start of the future of deep scientific applications into the questions that have been unanswerable until now, where people have to resort to religion because there's been no other place to try and get answers. We can answer these questions and we can use the information to change our futures.

DSM: There's also the distinction between knowing the stuff to know stuff, and knowing stuff to fix stuff. I can't imagine you working on something you didn't see having some value in the end.

CV: At the same time, I liken this period to when the first power poles were going up around this country over 100 years ago. I don't think many, if any, people running electricity around envisioned a one-and-a-half TERRAFLOP computer used to sequence the human genome in a matter of months, or all the other wonders that we have today. I'm humble enough with this information to know that we can only at this stage of the game, understand a tiny, tiny fraction of it. But future generations will be able to use it to understand things that we probably can't even imagine today, but it's possible because of what we're doing now. So it can seem like knowledge just for knowledge's sake because in the future it's knowledge that somebody else can apply as we have some of the other missing pieces.

## **Making History at Celera**

DSM: Celera Genomics is a story and it's a science story. It's also a business story in the sense of it rising at the height of what's now looked back upon as the dot.com bubble.

CV: In fact, many people blame that on Celera. In Europe they called it the Celera effect.

DM: For people 300 from now reading this, can you describe what it was like growing that company to a \$14- \$15 billion in value during that period?

CV: I take no credit for growing it to that value, nor do I want credit. I think it was probably the most extraordinary basic science operation yet to date to take place in history. It was a hundred or so world-class scientists that got together because everybody wanted to take part in making history. They believed in something far bigger than themselves. Everybody came through at just absolute extraordinary levels—from building what was at the time, the largest civilian computer in the world in a matter of months, to the algorithm team headed by Gene Meyers to develop a whole new set of algorithms with a half a million line of new code in a matter of months to be able to run on this computer.

People like Ham Smith had to develop whole new cloning techniques. Mark Adams and others on the team had to get it so the sequencing machines would even work. We had a breadboard prototype device. It was actually an engineering nightmare with these machines, because most of them did not work for the first six months. That did cause some sleepless nights, but it was extraordinary people coming together. When I look back, there should have been thousands if not ten thousand reasons why what we did should have failed, but it didn't fail because at every level people made breakthroughs. They made superhuman efforts. It was one of the most exciting environments I think in history from everything I've read of other scientific events. It's sad that it was so embroiled with using the commercial basis as a competition, when it was a company that by contract had to make the data available to the public for free. But all that got washed away because the government was competing with us. It was a small startup company that we had a massive multi-billion dollar government machine trying to do everything it could to ridicule and basically have it go away. I think a lot of the extraordinary things that happened there are yet to truly be told in history.

The business side is sort of a minor sideshow. Obviously the investors didn't think so as the stock went up I think 14,000 percent or whatever it did. In fact I disliked that immensely because I knew there was no way that the technology in the matter of years would deliver on that level of promise. There was just extraordinary excitement. People were voting with their pocketbooks at what they thought the future meant because of what we were doing. That was an extraordinary vote of confidence, but at the same time I knew they would not get their payback in the next month from stock gains. There were days it went up ten percent a day, every day.

DSM: So heading in the right direction, just not the best...

CV: That's right. The enthusiasm was extraordinary. The prices had no basis in reality.

## The Importance of *Drosophila*

DSM: Tell me about the *Drosophila* (fruit fly) collaboration.

CV: When we started Celera, we had a sequencing technology we only saw in a breadboard device. I never actually saw it work. We knew we had to build one of the largest computers in the world. We had to develop all new algorithms that hadn't been built before. We had the notions of them, but it hadn't actually been done on that scale. Going from two million letters of a bacterial genome to three billion of the human genome is quite a substantial leap. It was going from 26,000 sequences to over twenty-seven million sequences in the same time period. We had a new team that came together just for this purpose, so we decided that a test project wasn't unreasonable. We also had all these attacks from our publicly-funded colleagues that were basically ridiculing the effort, doing whatever—the *Mad Magazine* version, all those things. My rationale was—if we took the largest genome that anybody had attempted or a larger one, one that's critically important biologically, and just do it instead of making it a ten-year project, it should prove what we were saying. And releasing the data.

At this key Cold Spring Harbor meeting that happened right after our announcement—where we went up to try and explain what we were doing to the Cold Spring Harbor mafia, where Watson called me Hitler and wanted to know if Francis Collins was going to be Churchill or Chamberlain, or a chambermaid, I think it was. I think I'm messing up a good quote there. I like my version better I think.

I had decided on *Drosophila*. I had talked to Harold Varmus about it, told him in my private meetings with him that I was intent on sequencing *Drosophila* as a demo project. He thought a demo project would be wonderful. This was in the early days where they were upbeat conversations, and he thought this was actually positive. He argued that instead of doing *Drosophila*, it was better to sequence another worm to compare with *C. elegans* when it was actually finished. Comparative genomics is important. I was not insulted by it. I think it was meant with the same intention as when I suggested to Francis they do the mouse genome, because scientifically it did make sense.

At this meeting at Cold Spring Harbor when we were met just with intense hostility, when Hunkapiller was talking, I took a break and invited Gerry Rubin out into the hallway. He was the head of the public *Drosophila* genome effort and a very distinguished scientist. He wasn't on the board at the time. I had not known him before or interacted with him. He is on the board now. I said, "Look, we want to do a test project. It's been my experience that *Drosophila* would be the most important species. Most of the new discoveries, for example, in my prior field of neurobiology at the molecular biology level came first from *Drosophila* and then to the human brain." I told him about my visit with Harold Varmus and that Varmus suggested that we do another worm instead of *Drosophila*; that I wanted to collaborate with Jerry; and that we would do it quickly as a joint project and publish all the data immediately. It took him probably less than 30 seconds to make up his mind. He said, "Yes, I will collaborate with you."

Francis Collins, who came out of the hallway because he saw me sneak off with Gerry Rubin, was standing there and was somewhat horrified by all this. I asked Gerry later why he agreed so quickly. And he said, "Look, you offered to get the fruit fly genome sequence." That's what he and the community wanted. If he'd turned me down and we sequenced another worm, he would have been lynched by the community. This is a community that's really science-focused and that wanted the data to do science. It was not a political action, even though he was head of this project and would have gotten largely sole credit for doing it. It was science at the level we wanted to do it. It was an extraordinary gesture by an extraordinary scientist, and that being the best collaboration I've ever done in my career. It was just wonderful. Everyday was fun, even though some of the problems were huge that we were trying to solve; they put their hearts and souls into it as a community.

There were some skeptics on the other side that were sure we would never release the data or it wouldn't work. But they went ahead and they did the experiment, and they followed Gerry's lead on it. It had the most extraordinary event because we got the sequence very quickly. It was 120 million base pairs. We had it in four months, while we were still building the facility. We only had a fraction of the facility. It took ten years for the *C. elegans* genome. We reduced that ten years to four months. We could have, if it was the whole facility, done it in about six weeks.

The next stage was, “How do you interpret 120 million base pairs of genetic code?” We decided on something we called an “annotation jamboree.” We invited top scientists from around the world to come here to Rockville to basically camp out on our computers for several weeks. It was probably the most unique scientific event of anything in this field where these scientists everyday made more discoveries that day than they had the rest of their careers combined. All of a sudden they had access to the complete genetic code of the organism that they devoted their entire lives to.

It was like kids in a candy store. They worked together; they pulled together. The software engineers wrote new versions of software everyday to solve some of the problems that came up. It was just an electric atmosphere. It was just wonderful. And at the end, we decided on who was going to do the writing. We wrote this up and published on the cover of *Science* the *Drosophila* genome less than a year after that hallway conversation. That ended up being the most quoted paper in the history of science per unit time until we published the human genome.

DSM: For graduate students three hundred years from now who will be looking at this, would you say just a little bit about the significance of fruit fly and the genetic construction prior...

CV: Graduate students will know the significance of the fruit fly. Every high school student is trained on *Drosophila* genetics and the comparative genomic aspects. Even though it's around 600 million years since fruit flies and humans diverged, there's so much that is closely resembling what's in our genetic code, it's really helping to interpret it.

We can do experiments in *Drosophila*—for example, looking at pathways in the brain or looking at neuronal development, body development. Everybody has seen these photos where they have legs coming out of eyeballs and things like that, just studying, just changing one gene in terms of body structure. Those are not good experiments to do in humans, but doing them in fruit flies where the genetics is quick, it's accurate. There is now a hundred year history of science behind studying *Drosophila*.

I actually considered doing the *Drosophila* genome far more important for this decade than doing human. Far more discoveries will come out of it. Human in the long run will take us further, but we don't have the history. We don't have the biological context that we do for *Drosophila*. Actually the *Drosophila* genome was the real winner here. It's a community of about six to ten thousand scientists around the world that work together in a cooperative fashion that just have been wonderfully supportive about our efforts and how they got the sequence years earlier.

DSM: A wonderful subjective verification.

CV: Yes, and it caused irrational exuberance to be far more irrational, because it became clear to the rest of the world that what we were doing was truly feasible.

DSM: How many showed up for the jamboree?

CV: I'm not sure the exact account. It was on the order of a hundred.

DSM: Were there any particular ah-ha moments?

CV: Everybody had them every hour. I mean it was just people who sat around solving riddles that they'd been studying in some cases for twenty or thirty years. Instantly they had the data for or had a gene they'd been trying to get, and all of a sudden it was there in the computer in front of them. It's going to go on for the next several decades before we even truly understand it. Hopefully, as future students look at this, they'll see *Drosophila* as a model system that's used where we know more about the genetic code and the link out to the biology in fruit flies than we do in any other species.

## The Media as a Tool

DSM: We talked several times about stories appearing on the covers of magazines and headlines and newspapers. Talk about the impact of media and media coverage upon your work.

CV: I think it had a big impact because I saw it as a strategic tool. I got over seeing my name in the paper back when I was in swimming thirty or more years ago. I think the impact was that it gave the team a boost on what they were doing. It was strategically important. It was the only way that we could fight back and deal with an overwhelming number of people associated with this public program that were attacking what we were doing. So it had tremendous strategic advantage. In fact, it might have too much of an advantage because I think if there was a media war, I think we won the media war. We won the public relations war. A lot of people clearly related to the plodding government program versus the young upstart idea. There were a lot of those elements, but in fact I think those so stung some of my colleagues associated with the public program that they're just tremendously bitter over it, which is very unfortunate. But I think it was important for the public understanding of what we were doing.

When I try to look at all the good things that have come out of all the media tension, there's been probably wider public discussion about genomics because of the so-called "race" than there is of any other modern science subject. Without it, probably very few of them would have heard of the term or would be using it. It wouldn't be taught in grade schools now. I think it would take a very long time to filter into the language. It's critical in my view that there is the public awareness of it because everybody has a genome. The genetic code and how it varies is going to be a very key part of the future.

In fact that's one of the scary things, just as I'm sitting here trying to think of somebody one hundred years from now looking at this tape—whether they're going to be in a *Galatica*-type world. It really depends on whether science prevails or public fear prevails. And whether it's intelligent use of this knowledge, or abuse of this knowledge that is the big determinant of what happens in our society. But my view is, the more people who have an understanding of what it does mean, the less chance we have of the abuses taking place.

Even though I've been stung by the media many times—I see it as key for getting the message out about the importance of what we're trying to do. It has sort of kept alive new approaches. Otherwise I think we would have been overwhelmed and we might have had our plug pulled. We didn't exactly have geniuses on the business side in the parent organization, and some of them just clearly had very little comprehension of what we were doing or why or where it was going. Without the public attention and feelings of importance of this, it got over expressed. We talked about 'irrational exuberance.' I think many of them would have gotten cold feet with this experiment, particularly the lead one or two people, and just cut it off. We never would have had this experiment done, which is now totally changed the way everybody in this field does science. So I think there's been a lot of good impact from it.

### Changing the “Whole Face of Medicine”

DSM: One scholar said it may be that the real significance of this human genome will be that—and this goes so back to what you were doing as corpsman—for the first time a doctor might really be able to say, "I know what's wrong with you" when he examines you, rather than, "I know the symptoms of what's wrong with you."

CV: Right.

DSM: Do you believe that's where this is going to take us?

CV: It's very much where we're trying to drive it in this field that we call genomic medicine. It's one of the reasons why we're in a hurry to get the data. One of my pet peeves has been this tendency to try and place the genome project and the sequence genome up on a pedestal and viewing it with awe instead of trying to use it as just the next advance level of information that we have to improve our lives—to change the whole face of medicine. Everything does not have a key genetic component that will tell us what the life outcomes are, but there are so many diseases going back to the colon cancer example where you can work out a likelihood and the increase probability of having a disease like colon cancer.

If you know that you have even a thirty-percent increased chance, it gives you power as an individual to do something about it, instead of waiting until fifty for you first colonoscopy. If you know you have an increase risk of colon cancer you can get checked every five years, every two years. This will lead to simple blood tests in the future for colon cancer, make it even more likely that you can detect something early. But the statistics are overwhelming. If colon cancer is detected very early, there's a ninety to ninety-five percent success rate with treating it. If it's detected after severe symptoms appear, that goes down to less than sixty-five percent. That whole difference could be in the hands of the individual, knowing that he or she has that risk and being able to do something about it with early detection versus just waiting for symptoms to appear.

DSM: Our graduate students three hundred years from now will, we hope, probably have their own whatever-the-technology-is poster, the equivalent of a poster that's on their wall with their own personal genome.

CV: I very sincerely hope it won't take three hundred years. We're trying to make it happen in ten years. Right now, to my knowledge, I'm the only one in history with that information.

DSM: Oh, that's yours?

CV: There is a composite of mine with four other individuals, but I have an individual copy of my own. It will be commonplace certainly in twenty years. It will happen within ten. I'm hoping in three hundred years it will be just a routine part of daily life that people use their genetic code in conjunction with knowing environmental factors and other key pieces of information. But instead of one or two things like colon cancer and a few other diseases, we'll maybe have ten thousand different parameters that we can get a statistic on probabilities with.

DSM: People will actually die healthy?

CV: That's what I think the goal for medicine should be. Not to intensively prolong human life. We have to look at the much bigger picture. We have a very serious problem with the population growth as it is on this planet, and being able to feed the six-plus growing numbers of people. Hopefully, in three hundred years there will be people to look at these issues and talk about the next phase of science, and it will have maybe a very stable population of around four- or five billions people. But it's key in terms of understanding what the opportunities are to prevent disease in the first place versus what we do now in medicine is treat symptoms after they appear. We don't often treat diseases. We're looking at a number of paradigms—whether it's colon cancer or heart disease, or Alzheimer's—where we are trying to have early genetic predictors of who might be likely to have a disease. What might be the cause of it? Then beginning preventive measures, whether it's simple changes in diet and lifestyle, to constant early detection, to maybe preventative drugs like the anti cholesterol drugs—the statins that many of us take today. Those are preventative medicine treatments. They're not disease symptom treatments in most cases. That's going to be the paradigm that changes because of genomics going forward with the future of medicine.

DSM: What are going to be, from your prospective, the biggest obstacles in the path of this technology achieving its full potential?

CV: I think the biggest single obstacle is ignorance. For example, the problem that happened with GMO Foods, where it was too much arrogance on the part of the biotech companies pushing exciting new technology. They had reason at some level to be arrogant, but totally ignored public understanding of the issues. The public understanding of issues is being driven in some countries by economic factors, not by true understanding. And that—just like early on in my career with genomic—we've had governments and public groups using misinformation to drive an economic argument.

It doesn't matter what the motive is, whether it's sincere or not. If it's based on pushing ignorance and misunderstanding of misinformation, society is the loser. Right now there's a lot of fear with genetics, that genetics will be used to predict everything about somebody's life and their life outcomes. One of the biggest misunderstandings about the human genome and understanding our futures, is we are wonderful genetic machines that are almost identical in terms of our genetic code. Almost identical in terms of our structure and our physiology, but extremely adaptable species where individuals with the same exact genetic code end up being very different people with very different life outcomes. We know that. That's part of our repertoire. Most of us know twins growing up. Are they easy to distinguish physically, because when you go from one cell to a hundred trillion cells? There are so many random events that have nothing to do with genetics that lead to different physical outcomes, and so many different environmental influences that lead to very different life outcomes, different personalities, different responses.

With our machinery, we can predict changes in the machinery and likelihood of disease. I don't think we'll ever be able to predict the likelihood of whether somebody is going to become a scientist or a writer or a teacher or a fireman.

DSM: So the two key words are "almost identical."

CV: That's right. Identical genetic codes, but not identical people. That's why all these fears over cloning are based on the wrong assumptions. I'm against it because it's human experimentation, not because it's going to produce armies of identical people.

## **New Revolutions**

DSM: I'm getting a little ahead of myself, but if we could go back to some of the situation at Celera, in which you left Celera and started the new three entities here under the umbrella of TIGR. Can you just describe that period of time?

CV: It was actually a frustrating period in January of 2002. I had to stop and think. I was actually fired from Celera. There was, as I have indicated, major disagreements with the management of the parent company that didn't like the information model and wanted to abandon that and turn it into just a pharmaceutical—another biotech company wanting to be a pharmaceutical company. Actually, it was a somewhat traumatic period because it was a very abrupt thing. I was not allowed to say goodbye to my team. I had to leave immediately. It was typical corporate behavior.

DSM: This was a "Friday afternoon give-me-your-keys" kind of thing.

CV: It was actually a Monday morning, I think. I can't remember what day of the week it was. The problem was I had indicated that I was going to leave. I just thought that it would be six months later and we would have a reasonable transition. But they were so worried that rumors of me leaving would negatively impact their stock value that they decided to impact the stock value very quickly by firing me. I didn't quite understand that logic.

DSM: Not good timing, I would say.

CV: No. It's gone from I think a high of \$500 a share down to \$6 a share. But that's on the economic side. The fortunate thing is most of the key members of the team that I established immediately wanted to join us in some new enterprise without knowing what it was. I had been developing plans of what I wanted to do with the future. It was clear I didn't want to stay and run a biotech company. I didn't want to do that before, and the only reason I was even in Celera was because I wanted, as most of the employers were, to sequence the human genome and really move that frontier forward.

We immediately started two new organizations, the new research institutes: the Center for the Advancement of Genomics, and the Institute for Biologic Energy Alternatives. Those are now expanded to two more organizations, the three research institutes. TIGR, IBEA, and TCAG have gotten together and decided that what we were doing in sequencing needed to be expanded tremendously, and so we formed what is now referred to as the Joint Technology Center. That's going to be if not the largest, one of the largest sequencing centers on the planet that will open in June, starting at the level of forty-five to forty-eight billion base pairs of sequence a year. It will try to help drive this genomic medicine paradigm and drive genomics into the new directions, but also to use the information to understand fundamental biology.

We're doing a synthetic genome project where we actually try to make a chromosome from scratch, a microbial chromosome, and then see if we can get a living species out of it. We're trying to show that we understand a lot of the first principals of biology and go in a new direction. We think that's going to be important for the future use of biology, whether it's for hydrogen production or CO<sub>2</sub> capture or for chemical synthesis. I predict in three hundred years when people are looking at this, it will just be such a routine that they use biological processes versus teams of chemists for doing anything, that they'll maybe understand this is the origin of some of that.

DSM: I think we're at good place here for me to ask you about the projects that excite you most. You've told us a little bit about the work you're doing at IBEA. Can you expand on that a little for us?

CV: Yes, capture CO<sub>2</sub> from the environment. Let me put it in a broader context. I started a foundation; it's now called the J. Craig Venter Science foundation. A significant amount of the value of the stock comes from Human Genome Sciences, from another company that I helped start, Diversa, and Celera went into that foundation. Even though I couldn't sell stock as the president of Celera, the foundation could. We built an independent endowment that gives me in particular, but also Ham and the other scientists on the team, probably the most privilege position in modern science history of only working on what we want to work on and we think is exciting.

We also have our not-for-profit organizations. They're getting excellent funding. In fact just in the last month, the funding was increased from over \$60 million a year by \$25 million dollars a year, just with add-ons recently. We have now competitive teams doing world class science, but they're all on projects that I decided—if I was going to go forward and not just retire and sail around the world and there are things that I wanted to devote my life to doing. I thought they were important enough scientifically and for society to do that. Looking around it's clear we're adding three-billion tons of CO<sub>2</sub> net increase into the atmosphere each year. I don't think we can do that indefinitely.

It's easy to see that political unrest in the world caused by our use of taking carbon out of the ground in the form of oil and coal and burning it and putting it in the atmosphere. We can't do that indefinitely without risking having nobody to watch this film in three-hundred years. Our environment, our atmosphere, came from biological processes. The coal and oil came from the net result of biological processes. But what took billions of years to develop, we're talking out of the ground and sticking back in the atmosphere in decades. The notion is why not see to what extent we can use biology and the modern tools of biology to speed up the reversal of that process, in terms of capturing some of the CO<sub>2</sub> back.

The notion for that came from the first Archaea we did that was the third genome, *Methanococcus jannaschii*. It came from this high temperature vent in the bottom of the Pacific Ocean. It lives at a temperature optimum of about 85 degrees Centigrade. It's not functional or frozen at our body temperature and it survives in boiling water. It takes carbon dioxide out of the environment. That's its source of carbon, and it uses hydrogen as its energy source to drive the process. That's where we got the initial notion of seeing that type of metabolism and there's probably of thousands if not millions of organisms on this planet that have unique types of metabolism, such as Methanococcus. In fact it's thought that the weight of all the bacteria type organisms in the Archaea, that the biomass far exceeds that of all things we see in the visible world, all the plants and animals.

It's hard to envision that just biomass of bacteria on this planet, that much of it beneath the surface outweighs all the plants and animals, but it's a tremendous source of metabolism. Many of these organisms are photosynthetic. In fact, we're the original photosynthetic organisms. Their energy comes from sunlight and they drive, as plants do, the capture of carbon from the atmosphere, and the carbon from the carbon dioxide gets fixed into sugars for energy stores. At night, the plants then burn the sugar and produce hydrogen. We're seeing if we can short circuit the process and engineer the cell to take the light energy and immediately convert that into making hydrogen gas.

DSM: So you could build fuel cells.

CV: So we could feed fuel cells, and the source of energy at least in human life spans is unlimited in terms of sunlight. Whether it works or not, I don't know, but it seems like an experiment that's certainly worth trying. Now people have been talking about this for decades and decades, but just trying to use native organisms. It's clear the metabolic rate is not sufficient to do that. But molecular biology has been very successful in increasing specific biological processes by as much as ten thousand fold.

We don't even have to go that far in terms of hydrogen production to make it a cost effective alternative to taking carbon out of the ground. Hydrogen—when you burn it is totally clean—you end up with water as a byproduct, which is being limited in a large part of the world as it is. We're really exploring to what extent we can do this. The long-term thing is we would use the engineered microbes as a means for doing this with high efficiency in very specific plants versus and trying to use native organisms that we know can evolve and change if they're put back into the environment.

All this links together in that regard, and we started out within I think a few months of starting IBEA with getting a \$3 million grant from the Department of Energy. Just this last week and officially this week, they're increasing that to \$12 million for the first three years and wanting to bet that there might be something. This time this is an experiment worth doing. There are no guaranties. It's absolutely basic research. In my view, we're already making the notion of doing this a viable noting in many people's minds, which means the funding could go from zero to hopefully a large number of laboratories being funded by increasing the probability of this working.

Our goal is to make the revolution happen. Obviously it would be wonderful if we can do it ourselves, but I would be very delighted to see somebody else do this tomorrow.

DSM: Because speed is of the essence.

CV: Yes. The future of our species may be hanging out there.

DSM: What do you see as the biggest obstacle here?

CV: There's not one. There's probably thousands. Even if it's low efficiency, seeing if we can change some of the structure of the proteins to make light produce hydrogen directly, I think, would be a wonderful breakthrough on its own, even if we're not the ones to make it most efficient. Creating light from scratch is kind of a daunting task as well. My understanding is that it's only been done once before.

DSM: I'm not going to go there. Although you could...

CV: You might have to embargo this for longer than twenty-five years.

DSM: We talked about IBEA. What are the most exciting projects that you have going on with the human genome, sort of the usefulness of the human genome side of the equation?

CV: We're trying to set up major collaborations with key clinical centers to drive our acquisition of specific human genomic information. We're trying to link that up into giant computer databases to clinical records and clinical outcomes. The idea and the ideal for the future—and I have been talking to every major computer manufacturer on this—the future as I see it is a very large databases on what will be extremely fast computers sometime in the next ten to twenty years of getting in the peta-op range in small boxes.

I don't think it is out of the question at all with continuing the Moore's Law kind of pace that when you go into a clinic in the future, it will be either with your CD-ROM with your genetic code or they'll just pull it up as a database. Not only will they compare your symptoms, but your genetic code and other environmental parameters to everybody else with similar symptoms and parameters.

Right now, less than half of physicians in this country practice medicine even at the agreed upon basic standard of care level. I think without massive use of computers, with all this information it's going to be very difficult for medicine to really progress where it really affects our population in a broad sense. Genetics and genomics is a very key part of it, but it can only take us so far. We need to be able to measure all the other parameters. We need to be able to understand the environment. We need to understand lifestyle changes as we get into the preventative medicine paradigm.

We're spending a lot of effort on that. We're going to be spending a lot of money on that. I just signed a purchase order two weeks ago for \$27 million of new equipment to make this the largest facility in the world, in order to drive it. It would be ideal if we had the cost lower now, but my view is if we wait until that time, then the revolution will get postponed by another twenty or thirty years. In my view, it will be driven by people having convincing data and knowing it will dramatically impact the cost of healthcare. Individuals will demand it, because I think one of the things a lot of studies—whether it's use of herbal remedies or something else—people want to have more control over their own lives. This information at least gives us all that opportunity.

DSM: And by doing it you have the same impact that the initial success had on the international human genome project.

CV: Hopefully, we'll get the major funding agencies, NIH, and others, to think about doing this now. One of the things we heard when we finished the genome is that the funding agencies weren't prepared for it. Society wasn't prepared for it. They were sure that there was at least another decade before they had to deal with this information. For better and for worse, we dropped it in their laps in the year 2000, not in the year 2010 or 2012.

### **“Whence Cometh” Innovation**

DSM: There are some questions that I try to ask everybody I interview. I'd like to ask you a few of these, and we've touched on some of them. The first is about innovation. You've worked with some of the most brilliant people in the world and are one. Whence cometh the innovation? Is it bringing together lots of bright people? Is it having great questions to work on? Is it Kuhn's breakdown of the traditional problem solving structure, and it just drives people crazy? Where does it come from?

CV: I think it has all those components, probably in different people. One of the things that I learned from the late Nate Kaplan, my mentor, is he thought ideas were a dime a dozen. He probably had ten or twenty potentially Nobel Prize winning ideas a day, but he was able to execute on very few of them.

I think a lot of good ideas float out there, and we probably could have ten times the level of innovation if people didn't talk themselves out of the experiment or let other people talk them out of it. Look at all the experiments that I've done. Almost every one is one that somebody didn't want to see done or were sure it would fail. I think it's having a society, a reward system that doesn't so severely penalize people trying, that they're afraid to try anything new and they want to stay in an area. In my cases, they've come from actually thinking about problems. I've had them be individual things. The EST idea I got on a plane flying back from Tokyo where I ran out of reading material and had nothing to do for twelve hours but think about all the lectures that I was giving in Tokyo—people I was talking to and the fundamental problems that I was talking about. In this case, how to interpret the human genetic code. I actually got the idea on the plane and went back to the lab and actually had difficulty convincing anybody to try the experiment in my lab. The old guard was totally against it. And it was only because Mark Adams was a brand new graduate student—a post doc—who showed up the week before and didn't know any better. He took it on.

Then I've had other things and interactions with Ham Smith and others, where the inspiration has really come collectively. One of us will throw out an idea and the other will build on it, and then in a short while we have a whole new approach. I think it comes from not being afraid to try new ideas, because I think once you get rewarded for it you get—the cliché is “out-of-the-box” thinking. I've never been allowed in the box, so it's been pretty easy and I'm becoming more and more grateful for that every year.

It's a way of just looking at life. You try to look at everything with a different point of view. Examining “does it make sense. Is it logical?” Inspiration is not so difficult. The first thing I did in my first papers in undergraduate was just asking simple questions. How does adrenaline work on the cell and where does it work? It doesn't take brilliance to do that.

DSM: It's the execution.

CV: I think it takes brilliance to know how to execute, and it takes courage of conviction to be willing to do it.

DSM: We've talked about a lot of successes. Is there a failure that stands out in your mind that has been particularly instructive or valuable that we should add to this record?

CV: One of the things I've argued is that I learn from all my mistakes, and therefore that I know a great deal now. There are lots of them along the way. Nothing that I would really go back and do over, though. I think I've been fortunate in not having the types of regrets of wishing I had taken a course of action and either talked myself out of it or let somebody else talk myself out of it. Had I not taken the risk and it cause a lot of not only personal turmoil, but a lot of turmoil for people at TIGR and other people I've been closely associated with, just to pick up and leave in the middle of one revolution to start another one. I think if I had not done something I always would have regretted it.

I wish there was a way to go back and do it without all the personal acrimony that developed. Looking back I'm not sure how to accomplish that even in retrospect. So I regret a lot of things that have happened and I paid a toll for that in terms of stress and problems. You quoted Kuhn's book, *The Structure of Scientific Revolution*. The EST revolution and then the whole genome shotgun sequencing and what we did with human are textbook things you can take right out of there and look at every event that happened, and it was sadly predictable.

DSM: Paradigm overloaded.

CV: Paradigm overloaded, yes.

## Honor and Integrity

DSM: The next question I always ask is personal, although we talked about a lot of personal things. It's become a question that we started asking fifteen years ago that became particularly relevant over the last few years. And that's about one's sense of honor and personal integrity. Where do you get your sense of honor? Is it something that came from your family? Is it behavior you owed to folks who were counting on you? Where does your sense of honor and integrity come from?

CV: It's a good question, and it's one that I've given a lot of thought to because I've run down a lot of blind alleys out of a sense of honor and taken a lot of routes that were far more painful. My father, people who knew him, was probably considered one of the most honest people almost to a fault of certainly anybody that I've ever known in my life. But it also comes—I've referred to it as my inner compass—of going in a direction that I feel is right and is done being true not only to my integrity, but the integrity that I think my father would respect and other people that I care about would respect. As I say, it would be easier a lot of times to go a simpler route than to try and stick with the integrity of the situation. But I've never had trouble sleeping at night with any decision I've made, other than just worrying about what the outcome will be, but not from an honor and integrity point. I think people that have worked with me—it's interesting that the same ones keep working with me over years because I think the programs we built have incredible integrity. Sometimes it takes a while to demonstrate that to people with other agendas, but I think it comes through.

Kaplan had a saying that the truth will always be out. Talking about fraud in science, an incident early on, he had a heart attack. He and I wrote a grant. I was a young graduate student. And while he was in the hospital, this woman scientist who was married to the chancellor at the time took the grant that I had largely written, taken my name off and Kaplan's name off and submitted it with her own name on it. I was stunned and horrified by this. Kaplan told me the story about when he and Lipman discovered Coenzyme A. Kaplan wrote this paper for JBC. This was in the early 1950s and Lipman decided to send it to a colleague for review before sending it in because this was one of the seminal findings in biochemistry. They didn't get the paper back until they were sent the paper from JBC for review, where this guy took off Lipman's and Kaplan's name and submitted it with his own name on it.

It was hard to understand people being that extraordinarily stupid or that dishonest. Kaplan had a saying, "It all comes out in the wash and the truth will be out." That's been the case. Sometimes it takes longer than others, but I've been associated with just some of the most extraordinary scientific teams. You won't find a smarter, more decent person than Ham Smith. Here he is in his 70s. He's like a kid in a candy store and working at the highest level.

DSM: It must give you just inordinate pleasure.

CV: Oh, it does. Every day here is a thrill because I don't have to be here. We're here because we want to make a difference.

### **At Jefferson's Table**

DSM: I ask people about having dinner around Thomas Jefferson's table at Monticello. Who would you invite? If we could have four or five people around Thomas Jefferson's table to talk about this new revolution in genomic medicine, who would you put around the table?

CV: Two of the most fascinating Americans that I think I would relate to and probably enjoy what they did were Thomas Edison and Ben Franklin. Both were very eclectic. It's amazing that Ben Franklin chartered the Gulf Stream by going out in a small boat with a thermometer and measuring this massive ocean, river within an ocean, amongst all these other things. You sort of wonder if Edison was alive 100 years later, would he be working for Intel? What would he be doing? They were people that had extraordinary impact on the thinking of the times. It would be interesting to have an updated conversation with them about those things. If you can arrange that, I will come.

DSM: I have a couple more questions. One is: if there was one object that you can pick that ought to be in the Smithsonian as a symbol of your work, is there a thing that you would put there? A sequencer, a test tube, a poster?

CV: It is a tough question. I think what would be nice, to capture the scale of the facility, is to recreate this room with three hundred of these machines in it and the scale of the computer facility. That I think will be viewed as extraordinarily primitive in the not-so-distant future, let alone three hundred years from now.

DSM: We do that with our watch.

CV: That's right. We'll probably have boxes in a decade or two that we can hold in our hands that can do what it took this football size field to do. I think appreciating the scale of it has been lost in almost all the news coverage because it just happened. It's hard to envision reading three billion letters of genetic code. I think a real copy of the sequence, a more complete version of my genetic code will be publicly available sometime in the next few years.

It's hard to envision when I look back at key scientific events. What I've often marveled about was how much was accomplished with so little. I can only imagine that future generations will view what we consider extraordinary tools as so incredibly primitive that there will be wonderment about how we were able to get anything done.

DSM: That is almost exactly the inverse. It's not in how much was accomplished in so little, but how much it took to map something so incredibly small.

CV: That we can't even see it with our own eyes.

## The Patenting Process

DSM: From your experiences with all this, tell us about your own thoughts on the patenting process.

CV: The patent question is one that's always been a difficult one for me because it was used as a weapon against me—first by Watson when the U.S. government filed for patents on my discoveries, and second by Francis Collins and his colleagues when they used the fear of patenting the human genome when we made very clear public statements in a written article that we wouldn't do that. It's been used in a very dishonest, corrupt fashion. It's an area of important public discussion because the whole biotech medical revolution has depended in part on patents. My original notion when I developed the EST method and we were publishing our paper in *Science* actually broke several federal laws by refusing to disclose our invention to the U.S. government. I wanted the data just to be freely available.

I had the same naïve assumptions everybody else did and I didn't want the government to file patents on them. The only way they ended up getting patented by the government—and I'm lucky that I didn't get in trouble for the way it happened—was a senior executive from Genentech who had heard about all our discoveries. He called the head of the tech transfer office at NIH and said, "What are you doing about all the Venter's discoveries?" Of course, he didn't know anything about them. We had our paper accepted to *Science*. It was going to come out in two weeks and I almost made it. I was informed that the person who did that is Reed Adler, who is now our general counsel and actually a wonderful man who was doing what he was supposed to do on behalf of the government. More doing it in trying to raise the question that I hadn't thought of and very few other people had is what led to the so-called "By Dole Act", where the government changed from no patents to mandating that patents get filed on inventions. That was the finding looking at all the scientific discoveries that have come out of NIH and out of places like Harvard—how many made their way after their publication into benefiting the public, and the answer was almost zero.

That led to the By Dole Act, which mandated that discoveries be patented to encourage that there would be commercial development of these. But this has always been a hot potato with the academic community. The typical thing that happens at a university is, if you make a discovery and talk to a patent lawyer, they want to slow down the publication. They want to have time to write things up, so people associate secrecy with patents.

Patents go back to the age of Thomas Jefferson. They're part of the early part of our constitution because there are two approaches with new ideas. One is you keep it a secret, and that's called the trade secret approach. In general that does not benefit society, but that's how a lot of pharmaceutical companies act even if they have tried to get patents on things. Until the patent is issued, they try and keep things a secret in an anti-competitive type of mode.

Patents actually were designed to ensure that the data was published and available to the public. That was the tradeoff, the society tradeoff that the government made that said, "we'll give you a period of exclusive rights for commercial development of your discovery, idea, invention, in exchange that you have to make all the details about your idea, discovery, invention available to everybody so they can build on it and improve it and have better ideas inventions built on that." That's how much of our society has moved forward.

When it gets down to human genes and human proteins it seems to evoke an emotional response. In another field in science, chemists brag about how many patents they have. They list them on their resume. They get promoted by how many compounds they patent. It's only in biology. When Genentech started—it's about 20 years ago now, with human insulin—the University of California and Genentech patented the gene for human insulin. On the surface that sounds terrible. Do they own your gene for insulin? Do they own mine? What does that mean? We've certainly seen major corporations trying to abuse things in the past, so this was very controversial from the beginning. But human insulin is available for people with diabetes now because of that patent. The pharmaceutical industry won't spend the half billion dollars or so to develop a drug without a patent.

That part of things is just very clear-cut. It's just unequivocally established. That's the law in this country. That's how it works. When Amgen had these huge patent fights over producing a multibillion-dollar drug, erythropoietin, that increases red blood cells, the courts ruled because they had the patent on the early partial gene sequence, that they had the right over these other companies to be the one to produce that. There were multibillion-dollar consequence decisions made by the courts that have driven this field, but that hasn't stopped people from having this gut response and from people using that for their political benefit.

What happened with companies like Human Genome Sciences and Smith Kline Beecham and Insight and the U.S. government is they developed this mantra of one gene, one protein, one drug, one billion dollars, because the early ones—with insulin, erythropoietin, GM-CSF, and a handful of others, growth hormone—were very lucrative. A gene produced a protein. That protein was a very useful human therapeutic. Companies made a lot of money off it. And so they thought with all the new genes that I was discovering that it was going to be just billions of dollars were going to fall out of the sky. I never believed it.

I think a lot of people didn't believe it, but companies invested a huge fortune in it. That's what, in fact, drove the stock market up, even though every day we would tell investors we're not patenting human genes. Nobody wanted to believe it because it just didn't make sense. Everything I've ever said about patents has largely proven to be true. The U.S. government's huge stock of human gene patents, Insight, Smith Kline Beecham's are virtually worthless.

Human Genome Science, which claimed huge numbers of them is now basing its new drugs not on human genes. They're looking in other venues. But companies spent millions and millions of dollars on this.

It caused huge controversies. People argued what was patentable, and there was a huge difference between the U.S. and Europe, because the U.S. allowed patenting of discoveries as well as inventions. In Europe they made a clear distinction. Discoveries were not patentable. Inventions were. So there were all these debates of what was ethical to patent. Is it ethical to patent the human gene? With the cases like insulin, creating a new therapeutic to save people's lives, to me is unequivocal. Of course it's ethical because that's how you get the new drugs out. But the vast majority, probably ninety-nine percent of patenting that takes place, has either been worthless or even inhibitory to developing new drugs. Because a small biotech company or university has a patent on a gene or a protein, they try to restrict other people use for that, where it would be far better if there were no patents at all on that level and patents only issued on a new therapeutic. That's not how the court's ruled so what I and other scientists can come up with as social ideals is not quite how the court works, right? That's not how patent law works, so there's been big divides there.

On the question of what's patentable, that has been a question from the beginning. A naturally occurring substance basically is not patentable. Even though my genetic code was sequenced, my genetic code as it exists in my genome is not patentable. We tried to make it non-patentable by making it publicly available. In fact, an early statement I made in my goal was to make the human genome not patentable, but that didn't fit with what people's view of commercial goals were. They just ignored it. All the things that are patented are human made constructs. cDNA clones are artificial constructs. They're not the natural mRNA. They're a chemically stable form of DNA. So man-made constructs are considered by the courts to be inventions. The insulin gene that's in your genome and the one that's in my genome is not patentable.

DSM: The construct.

CV: The construct, the artificial construct is. But does that mean Genentech owns your gene or owns my gene? The answer is no. They have a right to commercially produce insulin for a certain period of time. There's more generic drugs off patent now on the market than patented ones. I think when you look at the big picture of society, it's a pretty good deal. We have people whether they're motivated by pure greed or altruistic reasons invest to try and develop new therapeutics. In general, they only get a payback financially if they do something positive for society and have a new drug that will treat a disease. That's not bad. Our other choices depend on the U.S. government to develop all new drugs. If you want to shortened lifespan, increase the death rate and lower the population, that's a good approach to go. But it would not be effective. It just would not happen.

It only happened once, and that was with producing penicillin. Because there was not a patent on penicillin, no pharmaceutical company wanted to produce it. That's why we didn't have penicillin at the start of World War II and it was only because the government mandated its production that we got penicillin. I mean it's incredible. Here one of the most important lifesaving drugs in the history of humanity, and it was not going to be developed because there was not a patent on it. It is a sore point, as I say, because it's been used as a weapon to attack me and discredit what we've been doing in a very false and usually spiteful fashion.

## **Remembering J. Craig Venter**

DSM: I think you may be beyond that now. Last question and this is a hard one, because if you keep doing what you're doing, we've all got another eighty or ninety years to keep doing this. But as it stands now, how would you like for your role in the remarkable revolution to be remembered when your grandchildren's grandchildren look back on the crude time and this crude technology?

CV: It is a question I've been asked before. It is one that I've given thought to. One of the most rewarding things to me as I've been traveling around the world, and I was recently in India with scientists there, young people particularly, as they're trying to build their lives out of some of the most intense poverty in the world. They have opportunities to use their intellect to go into science that are inspired by my success. The irony is, instead of the ends justifying the means, the means of the approach that I've taken might be one of the more important lasting messages than any of the actual science that I've accomplished. If it inspires a lot more people to do things they wouldn't otherwise do. I think the science will be remembered. I think that will be a bright line the history of biology and medicine before and after having genomes. I think 1995 will be remembered as a very important date in history, and I think I'm honored to be part of a key team that made that revolution happen.

DSM: Thank you very much. It's an honor to have interviewed you.

CV: It's been a long, interesting discussion.