Confronted with an apparently deadlocked and frustrating situation, actors have a number of possible courses of action. The economist Albert Hirschman developed an elegant typology of such options. The first is one of “voice”: the actors remain in the troubled situation but actively seek to propose alternatives. By so doing, they affirm their fundamental loyalty to the current order of things but express their dissatisfaction with it. By affirming their loyalty, they legitimate their criticisms as being in the interest of the organization, product, or party. A second alternative is to remain loyal to the organization, product, or political party and simply endure the strain of the current situation, hoping that it will change. The third option is “exit.” This option usually is chosen only after attempts at voice and loyalty have failed. Exit can be a kind of voice, as it makes a statement of an informed kind, addressed to those who have the power to change things, about what the actors take to be an untenable state of affairs. Exit can even be a kind of loyalty, in the sense that it may well affirm commitment to the fundamental principles or modes of operation that moved the actors to join the organization, buy the product, or work for the political party in the first place.

The future directors of Celera Diagnostics proceeded haltingly and with much reflective, even agonized, soul-searching, down the paths of voice, loyalty, and finally, exit. In some situations, stasis and patience may well be
a plausible option. One can imagine political loyalists waiting through a rough period until better times arrive, but in the domain of genomics there is no such thing as long-term stasis. On the one hand, as the investments, stakes, and pressures are so high, decisions need to be carefully weighed, especially as they are being taken in uncharted waters. (No one knows how to best do genomics.) On the other hand, the investments, stakes, and pressures preclude excessive delay or procrastination. Everything turns, therefore, on what one considers to be “excessive.”

In addition to differing judgments as to what constitutes a “reasonable” or “prudent” weighing of options—over which actors might well differ in good faith—there are other factors that affect the dynamics of loyalty, voice, and exit. These include the legitimacy accorded to those making decisions. That legitimacy rests on multiple foundations, from a simple respect for hierarchy to a sense that even decisions one disagrees with are nonetheless being taken in good faith and are being applied in a spirit of equity. When the latter affective or emotional ties are eroded, they become very hard to repair. Honest differences of opinion are easier to adjudicate and overcome than the erosion of trust. Once the latter process advances, the proverbial exit door beckons. Of course, upon exiting one must go somewhere else. Hence conditional planning and increasingly divided loyalties (even if the letter of the law is strictly followed) almost invariably precede leave-taking.

The leaders of Roche Molecular Systems—Kathy Ordoñez, Tom White, and John Sninsky—during 1999 and the first half of 2000 found themselves in a situation that fits Hirschman’s typology. To show them facing the fork in the road, we first present a summary of the situation as seen from the outside, including an interview with Michael Hunkapiller, president of Applied BioSystems, and then, two interviews with Tom White, as well as interviews with Kathy Ordoñez and Gabriella Dalisay, White’s executive assistant.

Holding Pattern: Turbulence and Stasis

A line of developments with direct consequences for our chronicle took place in 1998 when Hoffmann La Roche acquired a German company, Boehringer-Mannheim. The merger was announced in April 1998 and officially started in April (or May) 1999. Mergers are complex affairs
requiring multiple levels of negotiation to bring about and many more steps to bring to fruition. Among the possible complications, and in this case an apparently unanticipated one, is cultural friction between the merging companies: German, Swiss, and American styles of management and personal relations did not blend easily. This cultural friction was linked to the power dynamics any such situation entails. The German representatives jockeyed hard for increased authority and power in shaping and running the new organization, and over time they were making advances in achieving their goal. There is no need to explore here the typical corporate and bureaucratic politics involved, only to underscore that they existed, and that they set other things in motion that do concern us directly. Among these factors was the interpersonal and intercultural dynamics between a company run in an American style and headed by a woman and a more bureaucratically oriented company staffed in its upper echelons by men of a certain age and style.

Thus, for the key players at Roche Molecular Systems, it was during 2000 that future career options became an object to reflect on. Equally, as we have seen, it was during this period that the developments in genome mapping were coming to fruition as the race to finish the initial sequencing accelerated.

We interviewed Mike Hunkapiller at Applied Biosystems on July 7, 2003. He explained the events that led to the departure of Venter, in January 2002, from the company that he had helped make famous and the arrival of Kathy Ordoñez onto the scene.

MH: Celera Genomics was started as an information and bioinformatics endeavor, and its initial goal was to use the sequencing of the human genome to establish a position in that field. It was not just sequencing for sequencing’s sake, and it absolutely wasn’t to build a huge patent portfolio around the human genome as such. It really was to lay the foundation for an information business, and from my perspective, it got a little bit ahead of itself as being seen as a business built around a proprietary set of information, and it was always intended to be an informatics tools business. The value lay in helping people understand what the human genome was. Celera Genomics had envisioned, even early on, taking some of the information tools applied to the sequence data and pulling out bits of information that they would exploit themselves, either as therapeutic targets or as diagnostic targets.
They didn’t have the expertise built up to do either because things moved so fast on the sequencing side that the company got ahead of itself.

PR: So Celera’s strategy of challenging the public effort worked almost too well?

MH: Almost too well, that’s true. They chose to focus initially on the therapeutic side. And partly because that’s a long-term research endeavor you do internally, we decided that the best way to do the diagnostics was to create a joint venture between two of us, and that provided a good vehicle for bringing Kathy and her group in.

PR: So there was no resistance from Celera Genomics on any of this?

MH: No, I think Craig would have probably preferred to do a lot of it in Celera Genomics, but he really didn’t have the people and the expertise to do it, and if you’re going to bring on somebody of Kathy’s caliber, they have to have a coequal position in the overall management scheme for the purpose of arguing for resources. So the resistance didn’t last for long.

PR: She speaks only glowingly of Venter, which is what one would expect.

MH: [laughs] Well, I mean, Craig has had a history of successfully challenging conventional wisdom as to what’s possible scientifically. And he likes to play the role of a maverick in that process, there’s no doubt about that; he’s been right on many occasions when the traditional wisdom wasn’t so correct. While Celera was in the formative mode of really having to challenge what was thought to be the pathway to get the human genome sequenced, Craig was really into that. Once he had to step back into a more traditional, longer-term role of managing a business, he was less well matched for the job and the role in the therapeutics aspect. Being a maverick may sound good but it doesn’t work with the FDA or the whole procedure of getting things through a long, drawn-out process. And so he was just less comfortable with doing that. I think it was a natural parting point. Had things moved more slowly in the sequencing, he would have had the time to build up an organization that would have brought in the relevant expertise to take that over, but there wasn’t time.

PR: And therapeutics is sexier than diagnostics too?

MH: Well, I’m not sure I would argue that that’s the case—some people might. It has bigger payoffs associated with it in some cases, but I
wouldn’t argue it’s any more valuable or interesting scientifically. But Craig hadn’t done the diagnostics either. He just hadn’t built the biology up commensurate with the science associated with generating large amounts of information, which is what the expertise of Celera Genomics was initially—bioinformatics. And they had begun to do a little bit on the protein side, mostly from the perspective of coming up with protein targets for therapeutics. But it was still research, not research directed toward specific disease indications. It was kind of broad: How do you generate a lot of data and then begin to pick the cream off the top of that? So when he left, Tony [White] looked to bring in a seasoned pharmaceutical executive who could mesh the research endeavor and engine that was there with the opportunities in therapeutics. In the end he decided that maybe that wasn’t the best position for us to be in, because it’s a rough road—it may be sexy, but it’s also risky, and the failure rate is very high. Is there a way that we can take advantage of the fact that we’ve got a pretty successful beginning to a genetic diagnostics business and the right team there in Alameda running it? So we decided to try doing the clinical diagnostics and the clinical therapeutics development together in areas where there could be synergy between the two.

PR: So it was very intense?
MH: Sure. Celera had taken advantage of the big spike in market capitalizations to go out and do a secondary offering and raise money. We had the resources there. We didn’t want the resources sitting idly.
PR: And then, given that thinking, it was, as you say, natural that Kathy and her people would be a good choice?
MH: Well, Kathy was brought in to run the diagnostics business before Craig left. Although they’re separate entities, having Kathy oversee both of them could maximize the synergy between the two.

Initial Plans: Interview with Tom White, October 15, 2001

TW: Today is the anniversary of the date I accepted the job offer from Applied Biosystems. The same applies to Kathy and John. Four to six weeks later we left Roche and joined Applied Biosystems.
The first few months were spent analyzing the AB technologies; we were somewhat familiar with them as AB was Roche’s partner in the research field. We spent close to three months working together by driving down to Foster City a lot. We would meet in the morning at Kathy’s house from eight to ten until the traffic died down, then head across the bridge and try to leave there by three o’clock, when the traffic got impossible. So it was a chance to look at things without the encumbrance of having the Roche business going. We were essentially developing a strategy for analyzing what we were going to do. At Roche we were so busy we were not able to devote the extensive time to do this analysis.

We began with a clean slate about AB and then developed a plan about what to analyze. The existing molecular diagnostic business in infectious disease tests is Roche’s business, and that is the one we built; we know the competitors (Abbott, Bayer). They are still thinking about how to take Roche’s business away from them today rather than thinking about how to proceed over the next ten years. They have had trouble competing against Roche, rather than leaping into a completely unknown area. This is not a good strategy since Roche’s competitors had not done well in the infectious disease area. Other companies approached us because they had been competing against us at Roche, and they were now thinking it might be useful to work with us as a way to compete against Roche. For us it was more a question first of figuring out what we wanted to do. We didn’t want any more encumbrances; we felt that those companies’ limited success in this field was not a plus. We left to do something really different. We are focusing on molecular diagnostics, a totally new field that is still only a small part of the diagnostics field as a whole, which is mostly clinical chemistry. Molecular methods have increased to about a billion dollars a year over the last ten years, but that is only 5 percent of the diagnostic product market. There are only four or five companies that are in that. Since those companies also offer the full range of diagnostic tests, a new, small company can’t really compete in hospitals, medical centers, and big labs unless it offers the full range of products. That is the flaw of most of the biotech companies; they think, “We have hot new technology or a hot new test for a specific thing,” but they don’t realize how diagnostics are delivered to the worldwide medical system. Even when we were at
Roche, we had R&D, manufacturing, regulatory, et cetera, but we did not actually sell to customers; we sold to another unit of Roche. We wanted to discover what was useful medically, develop it, and then have someone else sell it. And then we can go on to the next medically important thing. We felt that we don’t want to get into the end stage business of marketing and sales to customers. This meant we had to partner with one of the big companies like Roche or Bayer or Abbott, BioMerieux, GenProbe, or Johnson & Johnson. It was always an element of our strategy to figure out who was the best company to distribute the things that we develop. Because of our past relationship with Roche, our former employers, we were not inclined in that direction. At the same time, they own more than half of the molecular diagnostic business and they are more than five times more powerful than any of the other second choices. We wanted to explore the thoughts of the other companies; by the end of the year 2001 we intended to finish our discussions. So that is the strategy of establishing the downstream part of the business that will allow us to feel more comfortable about focusing on what we are calling “the front part.”

The Front Part

We began by thinking about what were the areas that Roche had not analyzed. Roche has described their genetic projects in a number of areas, such as heart disease and certain inflammatory diseases that are tied to Roche’s pharmaceutical interests. Since founding Celera Diagnostics, we have analyzed over two hundred complex diseases for unmet diagnostic needs. It is the most comprehensive analysis I have ever seen. I am aware of no other diagnostics company anywhere has done this kind of analysis. The quality of the analysis is pretty amazing in terms of what we have selected to do. So there is no reason to not just forge ahead and do it. We are not like Incyte, Genaissance, DNA Sciences, or little biotech companies trying to raise money by claiming they can do everything. We are prepared to methodically set up this massive thing to do disease association studies on the same scale as Celera Genomics sequenced the genome.

There have been a couple of illuminating moments. One was when it appeared in February 2001 that the total number of genes was on the order of 30,000. Whereas before we thought we could study panels
of candidate genes, 500–1,000 genes known to be useful in heart disease or lung cancer, it became clear that we could probably study the whole genome and not be limited to panels. With a different approach and a thorough calculation of the costs, we could study everything. And once we had that set of SNPs in place for the whole genome, there was no reason in the future to study only the smaller subsets of candidate genes. Kathy, John, and I had the idea at the same time, and we calculated our costs based on using the technologies at our disposal. We realized that no other company could do what we intended to do, because of this unique combination of technology that we could bring to it. It was the scale of the whole thing. We will always want to study a thousand patients for statistical power: five hundred cases and five hundred controls. This would give us the statistical power to find associations, if they exist. Then we will obtain genotypes on one thousand patients using ten, twenty, or thirty thousand SNPs. Can we do that at a reasonable cost, in a reasonable amount of time? Yes.

We then looked at every other group that was trying to do this (whether it was the public project with other SNP databases, or Sequenom or Incyte, etc.). They lacked the scale. Thirty thousand SNPs in 1,000 patients—what would it take? We were so used to thinking about budgets and their constraints. Kathy said, “Don’t think that way—think what it took to set up Venter to do the genome project; think about a lab with one hundred instruments, working twenty-four hours a day. How long would it take to analyze all diseases?” We did the calculations and decided, “This is what it would take.”

We have been trying to describe the workflow process and only recently figured out a way to present visually what we are trying to do. What was the conceptual approach? So much of what’s been done is linkage and linkage disequilibrium—having a picket fence of markers and going across the genome. Well-placed pharmaceutical people were saying that you need 200,000 markers, and soon everyone will go to the doctor and these will be measured; that will tell everything that we need to know about health risks. But such a claim ignores the reality of how diagnostics works on a practical scale, and doesn’t seem to understand the statistics involved in studying 200,000 SNPs. The
trouble is that it would cost almost $100 million. We are going to concentrate on the genes and not on the other 99 percent of the genome.

PR: What is your key question?
TW: Can it be done? It must be cheaper than other companies’ approaches. The steps are expensive; we know what the key reagents cost for most companies; we can calculate that they simply cannot be doing those studies for less than tens of millions of dollars or more. There is no way they can raise that kind of money to do this kind of study. We know our costs are lower, because of our alliance with Applied Biosystems. It comes down to scale and cost at that scale; only the big pharma companies could do this. We have no competition as far as we know.

Strategy: Interview with Tom White, March 28, 2003

PR: Let me try to characterize the situation. I am trying to identify the major factors during the year 2000. Roche was the leader in developing the molecular technology that was used in diagnostics whose targets were known. The next stage would be to move to targets that were not known. The other factor was that the human genome mapping projects were now in high gear. This would make available a radically different quantity of data to work with and set up the challenge of developing a more complicated strategy of using molecular tools to do diagnostics.

TW: Roche Molecular Systems started in 1991 with enzymes sold through Perkin Elmer. There were no PCR-based diagnostic products, although there were some services from Roche Biomedical Laboratories, now LabCorp. Between 1991 through the middle of 2000, the PCR-based diagnostic product business grew to $500 million just to Roche. The issue was to see the potential there and then to look out to see what it could do in blood screening. Roche had only been working on the genetics side on a smaller scale. We thought we would approach it on the scale of a few hundred genes picked on biological grounds, because the genome had not been sequenced at that point. You could explore the genetics in more diseases on more people. We were essentially proposing a broader scale that one would query. It
was not what we ended up doing when we came here. Once we heard Venter’s talk in Rockville, in February of 2001, we made the jump from 300 genes to 30,000 genes. There was a change of scope.

PR: In the fall of 2000, you were proceeding apace with your project but if either (a) Celera Genomics had not succeeded or (b) there were 100,000 genes or (c) Celera Genomics had not raised the large amount of money, things would have been different. The project would have been an incremental advance in the scope.

TW: Well, in 2000 we still did not know what the most important thing to work on was. We were simply too busy to do it at Roche. We never even got to the point of doing an analysis. There was no encouragement.

PR: On the other hand, no one else in the world was really doing it either. TW: I don’t think so. Even today what really counts is the question. So between April and June of 2001 (finishing up in September) we did a gigantic analysis of two hundred diseases, ten different questions. They went into the business plan in October that was approved in November, and that is what we are actually doing. The question of what to work on was as important as the genome data or the scale of the operations. The answer we decided on forms the strategy. It oriented us to get access to the relevant sample collections. There are not that many of them.

PR: Had you not been mired in the mess at Roche and someone gave you one hundred million dollars at that time, you would not be where you are today? You would not be associated with Celera?

TW: That is actually a key point. Since we had an existing business, we were totally occupied. Here, there are other ideas of equal importance to those we have already been dealing with. We are meeting the FDA at the beginning of May to show them how we could develop diagnostic products that predict adverse events that could meet their criteria for registration. These concepts have not been clearly described before. Once we left, there were only three of us. And we spent the first few months just thinking: what is it we are going to do? This was scary. The next most important thing was to think about who we wanted to attract to this new company. We looked across the whole industry for people we wanted to work with, the smartest people we could find,
who were frustrated with their own organizations, who would jump at the chance to work on the genetics of common diseases, who would bring with them a wealth of experience but also know what to avoid that caused their own organizations to sink into a cumbersome bureaucracy that prevented them from acting. It was all built from scratch.

PR: What if there had been 150,000 genes?

TW: Then we would have taken a more gradual approach. In the meeting with Venter, everything changed.

PR: The genome works this way and not that way. You seized an opportunity. But if the reality was not there, one would have been forced to go somewhere else?

TW: Yes. In early 2001, people were still thinking about the genome as if it were gene by gene. They were not asking, “Why would you sequence the genome if you were going to ignore it? Go where the genes are.” But then when you looked at the genes, there was not enough variation. So the next crucial thing was in the May-June 2001 period we realized we are going to have to resequence all the genes. There were not enough SNPs in genes that came out of the SNP consortium. We suddenly realized, “This is going to cost us eighty million bucks.” In June of 2001, Kathy, Hunkapiller, and Venter convinced the company to spend the money. It became a $100 million investment to resequence the genes of forty people to find these kinds of SNPs. This project was way ahead of its time. We were at least eighteen months ahead of the whole field, and now we have it.

Money is a critical factor. Celera had raised money in March of 2000, largely at the peak of the boom, which basically ended when Clinton and Blair said, “No patenting.” It had gone down a good deal by the time we had gotten there, but nonetheless there was a lot of money. We would have raised money by ourselves, but we would be on the verge of going out of business, like everyone else today. Smaller labs came to realize that their model was not going to work. We were looking for collaborators who would work with us jointly, and this was attractive because we could do things that they could never do. This was big science. The Celera name helped us a lot in this. There was a downside to the name, but here it helped. It helped us get established in this new game. The next stage will be the crucial one: finding the markers.
Gabriella Dalisay is Tom White’s executive assistant.

PR: One of our goals for this book is to let the people speak who actually make the day-to-day things run in this company.

GD: Oh, that’s funny, because I’ve read your book before on PCR technology, and then I went ahead and reviewed it again this weekend, thinking, “What will he be asking? What is he interested in?” The way you wrote it, the people you spoke to brought the book together, and I liked that because it wasn’t just your ideas; it was the group’s together. So I said, “Okay, I kind of get the direction.”

PR: How did you get here?

GD: Okay. I think it’s kind of interesting how I ended up in biotech, because I was raised in California in a very strong Catholic family, which is pretty common among Hispanic families. I attended Catholic schools and had that education in which everything was pushed on you—the Bible, the way God created the world, the way everything evolved. When I was in seventh, eighth grade, the teachers had a brief discussion on Darwinian theory, and I thought, “Oh, that’s interesting—why would they bring that up? That’s so contradictory to what we grew up with.” And once I resumed that study in college, and I’m still doing that (because I’ll probably go to college until the day I die), but when I went to college and I learned more about it, I found that I became even more confused. How could this be? And I became more interested in Darwinian theory, but what it actually did was split my beliefs. Suddenly it was like, well, he’s starting to bring me to believe what he’s saying, but then I still study the Bible, so that still kind of splits me in between the two theories. Our daily living was based on the Bible, and it wasn’t until I got older and I studied Darwinian theory that I became very confused. I thought, “Wow! This can’t be true! This is contradicting what I grew up with.”

PR: The religious crisis: did that get resolved?

GD: No. I could honestly say that I’ve learned to accept both, but I’m not very opinionated on either because I know there’s a lot of controversy with the church. It’s almost like a political statement, you know; everyone has their own opinion of it. And I guess, being raised in a
strong Catholic family, I’ve always respected my mom and dad’s ideas. I don’t want to be disrespectful of the way they raised me. But being in this field for twenty-five years, I have my own ideas, and I just don’t share that part. I guess I don’t want to upset my parents or upset the strong family beliefs.

PR: So your parents let you be?

GD: They would question some things. I had nine siblings. I’ll never forget, when I would come home from Cetus, wow! The studies! I actually saw the rats, the mice. I remember there were even studies on dogs, and my siblings thought it was so inhumane! They asked me why I’d want to be affiliated with that. I’m the oldest in the family, and I was in my twenties. So to them, the studies were being done on pet dogs, you know? There was some naiveté to that. I remember actually defending myself one time, “Well, what do you want to do? Do it on the humans and hurt humans?”

PR: These are the arguments taking place in society; they’re not resolved.

GD: Yeah, exactly, even to this day. But what’s interesting is that it made me think, and it kind of touched me emotionally that my siblings would feel that way, because I always had respect for family even though you’d go to college and you’d learn different ideas. I would try to challenge them, but then I could tell when it was time to stop. To this day, even my mom knows the importance of clinical trials. She suffers from rheumatoid arthritis. There was a study at UCSF that she participated in, and she saw the importance of it. It seemed to me like, “Wow, over the years, how things have changed.”

I remember when I first told my parents that I was going to work for a biotech company. I told them the study I’ll be involved in is about disease, people, their well-being. I saw it in a fuller perspective than my parents, and once I started working in it, I became so enthusiastic about what science can really do. They were trying to take care of people. [After an initial job] I remember there was an opening at Cetus, and I thought, “Wow, this sounds even more interesting.” Cetus was involved in a wider field of study. My first job was in development. Another administrator who worked for Tom used to say, “Tom’s the best. Tom is this! Tom is that!” I didn’t really know Tom that well. I kind of backed her up when she was gone, and whenever I did, he was so appreciative of anything the administrator did. I thought, “Wow,
this guy is great! She’s spoiled! She’s lucky. I mean, he actually takes the time to appreciate what everyone does.”

I spent eighteen years at Cetus/Roche and during that time period, I went through five reductions in force, so it got to be very nerve-wracking. You know, every year I thought, “Oh, my God! Another one! Oh!” I couldn’t stand that tension anymore. Plus, I had two kids, and I wanted more security. So when the time came, and the boss I was working for was leaving, it was time for me to move on too. At that point, I was doing project management work, and I took some courses at UC Berkeley, and I thought, “This is kind of interesting.” But the more I got into it, the less exciting I found it, because it was focused on one project, not various projects.

PR: So after the Cetus breakup, you went to Chiron?
GD: Yeah, and I stayed there from 1997 to 1998, when I heard of this opportunity at Roche. I started working with Kathy Ordoñez, and I eventually transitioned into working with Tom, who was the senior vice president of R&D. This was the opportunity that I wanted. I thought, “This was meant to be.” It turned out to be everything I had hoped it would be. It’s not like you’re just there to assist Tom when he needs you. He’s a true believer in communication, and the more information I have, the more I can help him. And that’s what we both learned working with each other. I do feel more involved with the science, and I’ve also learned that the higher the level of Tom’s job—I’ve seen him as a director, senior director, VP, senior VP, now chief scientific officer—the more responsibility he had to take on, and the more I need to help him, because he’s only one person. His workload gets bigger and bigger, and he needs someone who really can take a chunk of that. There are a lot of times I ask Tom, “What can you delegate? What can I do? What can I help you with?” And he has never been reluctant to hand over some work. He’s always doing something, and it’s something exciting, and that’s the thing I like about it. I love a challenge. I love doing something I’ve never done before, and if there is something I don’t know, I’ll truly find a way to learn it. I think he’s comfortable delegating because he knows I’ll find a way to get it done using available resources. I figure you can always find a resource to help you resolve it, so that’s how I get through most of my challenges.
PR: Okay. I’m often criticized for painting too positive a picture of people like Tom and this kind of organization. One question that interests me is whether you’ve encountered any discrimination. Or do you think that organizations like Cetus or Celera are better than some of the rest of the industry in terms of hiring and how they treat people?
GD: Personally, I don’t think that’s ever been an issue. As a matter of fact, the one thing I’ve really enjoyed for all the years I’ve worked in this field— with Cetus, and that was for many years, and now here—they actually appreciate the diversity of their groups. I feel like I fit right in. In fact, the diversity is not just of race but also of education, background, a lot of things. I think they see all of that as a contributing factor to the company. And I’m not just being optimistic; I’m being real. That’s how I’ve observed it in the twenty-three years that I’ve been here.
PR: So you started at Roche in ’98?
GD: I started in ’98 and worked until April of 2001. That was interesting. It was interesting because I learned what it’s like to work for a company when I saw what it did—how do I say this in a sensitive way?
PR: Do you mean sexism?
GD: Thank you! You’re making it easy. The sexism is what I really struggled with. We had a female president of the company, and when I worked with her intermittently, I saw it. I feel that certain people in the new management lacked respect for her and her role as president, and that made me nervous. That made me kind of wary of where things were going to go, if she wasn’t getting the support that she needed and she was running the company and we’re all depending on her to make these decisions. But some of these people were stomping on her ideas, and pretty much, I felt, dictating how it was going to go. I thought, “How can she run a company effectively and efficiently when they’re not allowing her to do that?” I will be honest: that made me nervous to the point where I said, “This is just a matter of time.” I developed loyalty to them [Tom and Kathy] to the point where I’d stay with them and help them as long as they needed me to stay there. I wasn’t going to leave during a critical time period when they needed someone there to help them. I could have jumped ship and said, “I’m getting out, because this is getting scary.” Instead, I had a lot of trust in both of them, so I said, “You know what? I’m going to ride it out. It’s going to be okay. These two are very smart people—Kathy, very smart business-wise. She’s one
of the most intellectual women I know in business. She has ideas and makes them work in a very confident way. I’m so confident it’s going to work out the way she wants it to end up working out, and this may just be a bias, but with Tom on her side, it’s going to happen.” And the team they had working together at Roche worked very well together. Whether or not they had different ideas, they compromised, they talked. They don’t all think alike, but they come together in their ideas and follow through on them, and that’s what made me comfortable even during that critical time. So I thought, I’ll ride it out. But I already had my mind made up that when they leave, I leave. In my mind, I knew I was going with them. I mean, I had every intention of going with them.

PR: You were in a distinctive and tough position.

GD: Oh, I’m telling you, it was the scariest time. People would look at me, ask me, “What do you know?” I couldn’t disclose a thing. All that information would have created was panic and havoc and destruction for the company, so you can’t disclose that. I remember going home and just saying to my husband, “There’s something I’ve got to tell you.” Having all that information would just eat me up, so I would share it with my husband, just brief points. I felt better getting that off my chest, and then I could go to work the next day and just know that it’s off my chest. I didn’t have to live with it on my own that way. It was a very difficult time. That’s when I realized that some people didn’t care about the pressure I was under. They would say, “I know you know, Gabi, tell me! Tell me what’s going on!” I said, “I don’t know a thing!” I said, “He wouldn’t even disclose this information to me.” But it got to the point where it was pretty clear that it was just a matter of time. I also knew that they wanted to handle it very professionally, very calmly. They were still sensitive to causing any disruption in the corporate functions. And I admired that, because I was thinking that if it got to the point where I couldn’t even wake up and want to come to work, I’d probably check out. I’d say, “Why torture myself like this every day?” But they were thinking that, in their role, they had to be concerned for the well-being of the company, and they were.

PR: So it’s a doubly tough situation for you? You’re loyal to Tom and Kathy, but you had no guarantees that they were going to be able to take you with them.
GD: Oh, exactly. That’s exactly what it was like. It’s true. There were no guarantees. They weren’t even in the position to take Roche employees. In fact, they were almost told not to, so it was a very sensitive situation. My intuition, my gut feeling, was that I would be working with them once again. So I think that when I talked to them, they knew what I wanted to do, but it was just a matter of what they could do. It’s really funny because I tell my husband that I can just look at Tom and know what he needs before he even tells me. I mean, it’s that kind of communication level. And I tease him. I say, “I’ve known you as long as I’ve known my husband. I know you well enough to know what you’re thinking and what you need.” And a lot of times, what he appreciates is that I anticipate what he needs, but only from the years of working with him. I can kind of bring him things that I know he is going to need before he even knows he needs them. It just cracks me up. I know Tom’s schedule better than anybody. This is really dramatic, but he’s got twelve hours of meetings in an eight-hour day, and yet he finds a way to just kind of smoothly run in and out of these meetings and get done what he needs to have done. But then, in addition to that, he has to account for the interruptions throughout the day: people need this, need that—right away!—as soon as possible!—teleconference! And he finds a way to make that work. I guess you could honestly say, I find a way to make it work because it’s my job, too: “Tom, you’ve got three minutes here, and I think you can do it in between. But you really need to eat lunch. Can you eat lunch in your office while you’re taking the conference call?” And it all seems to work out that way. My biggest challenge is managing his time, but he told me he depends on me to do that and somehow, between the two of us, it works out all the time.

PR: Would you say there’s a fluid line between the kind of family relationship and the kind of corporate relationship? One of the things that’s come up in what you just said, and what other people have said, is that Tom pays an almost parental attention to people.

GD: Oh, definitely! You hit the nail on the head. Exactly. I think Tom is the godfather, and actually I think that’s even been a joke here. The godfather of these families; he looks over them. But John is the same way. I see it. John has this huge group. I talk to the assistants throughout the day, every day, and by the end of the day we’re surprised: “Whew!
How did he do all of that? How did he get all of that done?” But he makes it happen somehow.

PR: But there’s an attention to personal relations that others didn’t have.

GD: Oh, yeah. I truly believe that one key to the success that Kathy, Tom, and John have had is in the way they work with people closely. They could be as busy as hell, but it’s like, what you have to say is important to them and they always make time. It just cracks me up because I’ll see people lined up outside Tom’s door, asking, “You got a minute?” And he says, “Oh, sure I do!” And I say, “Are you kidding? Do you see your calendar?” But then I see the appreciation from his staff. That’s why Tom is so well informed about what’s going on. He makes the time for the information. I have this joke: I say, “Tom, you know the reason why I talk so fast? Because I know I only get thirty seconds of the day to talk to you, and I’m going to fill you with information in those thirty seconds.” But thankfully, I had nine siblings in my family, and I know to talk fast if I want to get anything in. So he kind of knows that’s the way we both work together. At Roche, when I came in, I felt that this was a family of science. And the way I saw it, the way it worked, the success of it, I think was a result of the way Tom acts as mentor, to young scientists especially. I don’t even know if he knows this but I have young scientists that come in to speak with me. They say, “He is mentoring me to do another project, to move into another department.” And they go on, “You know what? I know I can do it, because of Tom’s guidance. I can’t fail.” I wonder if Tom even knows this.

PR: He does, and Kathy knows it. Kathy has talked about this a little bit, because one of the things that is very characteristic of her style of management is that she believes that if you put people in jobs that they’re not actually really prepared for but they can do, then it is an absolute vote of confidence.

GD: That’s what I was going to say. They have confidence that these groups of people will meet the challenge, which makes them more likely to do it. When someone tells me I can’t, I’m definitely going to try to do it, but when you’ve got a vote of confidence behind you, it’s suddenly hard to fail. That’s exactly how I feel. When you’ve got them supporting you, they’ll work with you to make it successful.

PR: The term “stewardship” comes from the Greek word for economy, meaning domestic economy, managing a household. For the Greeks,
managing a household was not the same thing as managing a business. It entails taking care of the people that are in your domestic sphere as family. And that’s a corporate management style that Tom, John, and Kathy practice and seems to work very effectively.

GD: It’s a fact.

PR: Is there a downside to it? People in the academic world are very critical of the corporate world. I’m trying to be careful not to be a spokesman for this company.

GD: Yeah, I think there is a downside, because I feel like everyone is my friend here, but I’ve learned that this is a business. There’s a fine line, because I have to be very conscientious in my work and be attentive to the confidentiality of the information; I think I’m very cautious about sensitive information. But I wonder where people are coming from when they ask me questions. Sometimes people have a tendency to want to get friendly, and I have to be sensitive to that and ask myself. “Okay, where is this going? What do they want?” I am very careful about whom to really trust with what information, and anything confidential I don’t disclose. Maybe I was raised that way, but it’s also a work ethic that I’ve developed over the years working with management. There’s a fence, and you can’t cross over that fence. But what’s interesting with Tom is that he draws that line, but he also bends back and forth a little bit either way, because that’s his way of building trust with the employees that he works with, too. It seems to only be a benefit, as far as productivity is concerned. But even when it’s Tom and me, it always has to remain professional. I love that guy like family. You know, I kind of get choked up thinking about it because he’s just so endearing. I mean, I’ve grown up in a big family, a big, large Hispanic family with friends and stuff. Tom? He took a chunk of my heart working for him.

PR: He’s the ultimate WASP, too, the quiet Protestant. Understated, careful, attentive, driven.

GD: Exactly! And I think that is what I love about him! He’s not arrogant. To me, in my mind, and I tell people this, Tom’s amazing! I mean, and it’s not just science, it’s the way he’s figured out people, the way he’s figured out how to progress in critical situations. I tell my husband, “Tom is the next Einstein.” And I did tell him just a few weeks ago that I’ve seen how he’s come around for people even when they need him
in a personal sense—he’ll be there. I’m talking about colleagues here at work, even when there’s been maybe some personal crisis. He’s been supportive, but he stays on track with professionalism and with work.

PR: Yes, he is faced with the twin demands of keeping the whole economy going but also being attentive to people and personal concerns at the same time.

GD: Yeah. But that’s like a gift, because I’ve worked in this field for many years, and you don’t see people like that. I remember at Chiron you had to go through ten people to get a decision made. It just wasted time: it was so micromanaged it made me a little bit nervous—it just did.

PR: Okay. What I’d like to know now is how things are working here with this very high-risk, exciting enterprise. How are you experiencing it as well? You didn’t step into an ultrasecure job.

GD: It was interesting, because I thought about that. I said, “Okay, Tom, number one question here is security in the company. How do you feel about this?” But he told me about all the challenges that we are about to face, and somehow, even as nerve-wracking as it could be, I thought, “That’s exciting!” When he’s telling you this, it just sounds challenging and exciting, but the big difference was that we had support from the other companies. That’s why I felt even more comfortable than I was at Roche at that time, where I had job security. I would probably still be working there, but the thing is that it was the ideas of the way the company is run. Do I just stay because it’s a steady income? Okay, I’ll just come in like a robot, work, and go home. That was my thinking about my job. I thought, “No, it can’t be that way. I’m going to take the risk, because Tom and Kathy don’t want this to fail, and if I can be a contributing factor, I feel better about it; I do.”

PR: Do you have a sense that Celera Diagnostics is over the hump yet? Or a few more months? Or a year?

GD: We’re on the hump. Yeah, that’s how I truly feel it is. I see them work like dogs here. I mean, we’ve got deadlines, and Kathy’s adamant about those deadlines. It’s not like we have some flexibility, and the teams here know we don’t. It’s a fast-working field. That can’t be emphasized enough. We just have to be faster. We have to know what we’re doing. We have to work quickly, and they’ve got that in our brains. It’s like a rat race: who’s going to get to it first? And we have to
do whatever we can, and they seem to be providing us with everything we need to make it work, because they know it’s high-risk, and we have to get some positive results.

PR: Do you think people get a sense that if it does succeed that everyone will also profit from it?

GD: I don’t think so much about that because this whole industry is risky. Five or ten years ago, everyone was like, “Whoa! I want to be rich!” In this economy right now, nah! [laughs] I don’t really see that. That’s not, like, my reward at the end of this trail. It’s a nice thought, but I guess I’m thinking more of Celera making a statement, making a mark, showing the industry what we can do and what we are. I mean, that’s the first step, and then, as we continue to do that, then we’ll reap the rewards.

Interview with Kathy Ordoñez, February 14, 2003

Kathy Ordoñez is soft-spoken, uniformly polite, yet direct in her answers. One gets the sense that she says exactly what she wants to say. The tone of the interview was both orchestrated and cordial.

I asked about her relations with Craig Venter; she responded with a series of positive adjectives. I summarize this portion of the interview. Craig was: “Excellent. Gracious. Supportive. Responsive. Terrific. Scientifically helpful.” He was restless and wanted to move on to the proteome and explore variations in proteins. It was no secret that there had been a conflict with Tony White over commercial strategies. “I prefer not to be in the media. I want to do things that make a difference. If people recognize it, that is nice. I was proud to be a colleague of his.” Tony White was aggressively looking for someone with pharmaceutical experience, as the corporate decision had been made to go that way. He called out of the blue and that was surprising because she did not have that kind of experience. They had a meeting in New York. He was “Straightforward and direct. Practical and analytic and organized and made things happen quickly.” Although Celera Genomics had been built around Venter, Tony White thought that she could pull a new organization together. “I am good at creating an environment where really smart people like to work. I can recognize big
ideas and push people to get over the hurdles. It was time for a change in my life, a new challenge.” She accepted the offer.

The Eureka Moment

KO: When we came to Applera, the sequencing of the human genome was about to be completed. Of course, there would be a profound impact ultimately on diagnostics, and medicine as a whole, once associations could be made from the genetic information. Other people who watched us in the industry probably think we crept out of Roche with some idea in our pockets, and that is not the case. We just knew we needed to be in a different environment, where we could think more freely, and it was amazing what we went through in that transition. The first couple of weeks were almost terrifying, because we didn’t have the pressures of supervising hundreds of people and dealing with day-to-day crises related to products on the market or manufacturing issues or issues in R&D. We suddenly just had time to think! It was very exciting and somewhat intimidating, because if you are accustomed to the type of jobs we had had for years—you came in each morning and there was one hundred and fifty times more to do than you could realistically achieve in one day. So, suddenly we had a blank slate. So we started reading and thinking. And we didn’t even have offices; Applied Biosystems gave us space in Foster City, but that was very inconvenient for us to reach. Sometimes we met in my living room, or sometimes we went on walks, or whatever, so we could begin to share information.

One of the things we agreed on was to come up to speed on the detection and other technologies that existed at AB. Tom and John took that on and thought about it. I began thinking about how we would work in molecular diagnostics with a focus on genetics—how could we build a business strategy? We thought there were really two different ways we could go. One would be to just jump into the next generation of testing—that would be genetic testing. Or, we could try to participate in the existing molecular diagnostics market that was dominated by Roche and was primarily focused on infectious diseases and use that as a way to leap into genetics. And there were advantages and disadvantages both ways. The new genetic tests we knew would ultimately take off and be successful, but the uptake curve for them would probably
be slower than what we thought we could achieve by taking a piece of an existing market from Roche or Abbott. So we decided that we would try to get into the existing market and use that time, while we were generating revenue in existing markets, to build a very large-scale discovery in genetics. This was important because it would impact the scale of the company and how much research there would be versus development. Our goal, which I had agreed upon with Tony White, was to try and break even in the fiscal 2005–6 time frame.

So with the basic business strategy coming together, we could see the size and scope and approximate how much money we could invest in the research effort. We came up with a pretty sizable amount. As long we were confident of having sufficient success with the existing Applied BioSystems tests that were put into the joint venture, plus being able to take a slice of the existing molecular diagnostics market, that money was secure. And with the scale in mind of approximately how many people we could hire and how much money we could spend, it was all coming together at about the same time.

Tom and I heard Craig give an internal talk about the human genome sequence in early February of 2001. I remember we were sitting in a big meeting at a table that was shaped like a U: I was over here, and Tom was all the way over there, and Craig was showing slides that he used when he talked publicly about the human genome. One of the key points that he made—that was just mind-boggling—was that there were just 26,000 genes. Up to that point we had always thought that there were 100,000 or 150,000 genes. I remember thinking, “Gosh, the magnitude of what you really have to interrogate on a genome-wide basis is really significantly smaller than what we had thought.” I filed that thought away in my mind to think about later. Several of the key points Craig made about homology and genes being reproduced around the genome were very interesting and were not what I had expected.

I didn’t get to talk to Tom that day, or I think even the next day, but we were on the company plane coming back, and Tom and I started talking about how amazing and unanticipated some of the things Craig had said were. That is how it evolved. Imagine: with only 30,000 genes, you could interrogate them with 30,000 experiments, and if you want to look at several different places, you multiply by four or six.
People who are close and work together over a long time sometimes don’t need to talk in sentences anymore. It’s like that with Tom. It’s electric: “So what about this?” and “What about that?” and “Gene chips!” and “We will do this and do that.” I just remember looking up at him and saying, “Aha! We could!” and he looks at me. We have worked together for so long, but the way we think and process information is very different: I am a very intuitive person, and somewhat mathematical and analytic, and so it was absolutely apparent to me. If the answer is there, I see it first and then I go back and derive it. You could just see Tom’s mind going; he was calculating, calculating, calculating, and he said, “You’re right.” So the two of us got so excited, and he called John and gave him the same sort of set of data that brought us to the conclusion that we came to, and John just immediately said the same thing.

We vetted the idea with an external consultant and with Mike Hunkapiller. We met with Craig, and we talked with management. Craig is a very brilliant scientist. He bought the idea of addressing the problem on a genome-wide basis. We had been thinking of this in terms of fishhooks and fishnets and how could we capture more and more. I went home that night—a Friday night, I think—and I could not sleep. I like to get up very early anyway. I sat at my computer and wrote a message to Craig to explain to him what we had thought up: Forget the fishhooks and the fishnets; we are just going to drain the lake and walk out there and pick up the fish.

We explained it to Tom White and Mike Hunkapiller and the CFO of the company, and they said, “Go. How much will it cost? How long will it take? What are the odds that it will be successful?” They had confidence in us. There was trust.

The second thing that happened was that as we were building our assays and planning the methodology that we would use for these association studies, I felt that there was something that was missing. I couldn’t exactly put my hands on it. One day I was in Foster City talking with Mike about the need to have a better understanding of polymorphism. I remember driving back from Foster City and feeling really agitated that there was something missing. We were just beginning to hire people so it was the April–May time frame, and I remember going to the blackboard and telling John there is something missing
here; tell me what it is. Resequencing. Mike was thinking the same thing. John went at it, and then Tom came in and they went back and forth on the resequencing effort that I believe will become extremely important. It will show how important it is to have identified so many novel functional SNPs that we can use now in our association studies. Association studies alone are not enough. Finding “the gene for schizophrenia” or whatever is not enough. We think we have a huge advantage. We will do our association studies with thousands of cases and controls, and we will replicate them with two or three or four sets of samples, so that we are not just looking at ethnic differences or whatever. But beyond that our whole plan was to take the information we had developed and configure it into the diagnostic product. I spent my whole career doing that, bringing products to market, figuring out how to create demand for them, educating physicians to order the tests, get the tests up and running in the laboratories. So there was a very coherent business strategy supporting the strategy for discovery.

PR: What enabled you to see this?

KO: The approach we are taking is not in and of itself that important—the scientific approach—but it is the timing of it and the scale at which we are doing it and the environment we are working in that allows us to drive to the next thing. It is the combination of the things we are doing that counts. Certain aspects of what we are doing have been published before, certain aspects of sample extraction, et cetera. So you could go all the way through and say I have seen something very close to this and very close to that—but it is the way in which it comes together and gets aggregated so that we can look at genotyping, expression, and ribotyping and do that on a scale that, to our knowledge, no one else can imagine!