

Entrevistas

Dr. Fritz Bach

Foi com imenso prazer que aceitamos o convite para atuarmos como “repórteres por um dia” pela MedOnLine. Na praia da Ferradura, em Búzios, rodeado de amigos, saboreando lulas e camarões fritos regados a batidas de maracujá e cerveja, pudemos fazer aquelas perguntas que nem sempre são possíveis no dia-a-dia do laboratório e muito menos nos tradicionais congressos médicos. Aproveitamos essa ocasião para agradecer profundamente a todos aqueles que participaram do curso “Organ Transplantation – from bench to bedside”, transformando-o num verdadeiro sucesso.

Eduardo Rocha

Abreviaturas:FB- Fritz Bach; CDG- Clotilde Druck Garcia; JRCR- Jose Roberto Coelho da Rocha;ER- Eduardo Rocha
Eduardo Rocha, Fritz Bach; Clotilde Druck, Walter Garcia and José Roberto Coelho Rocha



- ER- Dr. Bach, we should have previously planned what questions we were going to ask you, but finally, we prefer spontaneity and we will ask whatever questions come to our mind, OK? So, please feel free to talk about whatever you feel like, but just to start, let me ask you to talk about your “early steps”. What were the steps that have taken you from Austria to finally become a Harvard Professor? When have you decided to become a medical doctor?
- FB- I was born in Vienna in 1934, I’m Jewish, and around 1938-39 it was not “healthy” to be in Vienna as a Jewish and so my family left, in fact...
- JRCR- You had doctors in your family?
- FB- No, no doctors in the family... and, as you’ll see, it was not my intent to be a doctor. My father left first, my brother and I left (he was 5 and ½ years older than I was, he was eleven, I was 5) and we traveled in a cattlecar (carro de boi). What they did is, they built these cages in the corner, so you’d get air (it was the air of the cattle, I’d like to remind you) and we took along a certain amount of water and my brother who was eleven could understand that this had to last three days until we’d get to the coast of Holland where the ships could take us away...
- JRCR- So, you actually escaped...
- FB- Absolutely, and my mother’s parents never got out, and they died in a concentration camp....which I’m convinced that totally affected my mother’s life, from the day she heard in 1943 from the International

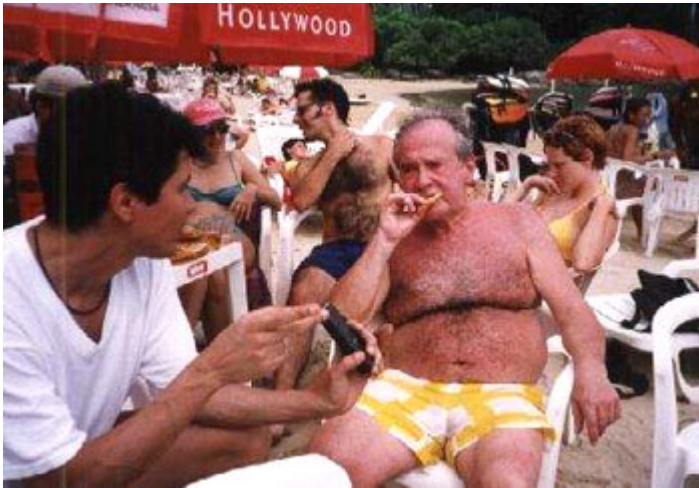
Red Cross until the day she died. And I think it had an effect in all of our lives, maybe in a positive way as well as in a tragic way. England was wonderful, you know, the English men had been killed in the war by Germans as well as Austrians - there was no difference between them, the Austrians were as bad as the Germans – and yet they allowed me to get an education. They didn't allow my brother, who was much smarter than I am, he was a genius, but at age 14 they said to him: "basta! We will not educate you further"... very interesting.

- JRCR- What was your brother's name?
- FB- Bert. And then my father said, because my brother could not get an education, " we have to leave England". We have to go to America; there we will have a chance. You know, I'm not a tremendous chauvinist at all, but America does give you tremendous opportunities. We came there as a family with U\$ 200.00 total...
- JRCR- Four people?
- FB- Yes, 4 people: my mother, father, brother and I. They allowed us to get educated, they allowed us to do our professions. My brother is immensely successful, he's a genius, a consultant who gets paid more for a day than what I get for a month.
- CDG- On which field or fields does he work?
- FB- Almost in every field. As I said, he's a genius... He reads and has an absolutely great memory. You can ask him something he read 15 years ago and he still remembers. You can see it. You go to him and say: "I just got this new device... do you know how it works?" He'll say: " Of course, I know how it works!" He's amazing...
- JRCR- Were you at New York by this time?
- FB- No, we went to Burlington, Vermont, because we had met an American soldier who spent every evening for three and a half years in our home in England, so he invited us to go to Burlington, Vermont. A lovely little town, but then, after three years I went to Harvard College. I didn't realize that getting into Harvard was a significant barrier...
- ER- Excuse me...how old were you by this time?
- FB- 17.
- ER- So at seventeen you started at Harvard College...
- FB- Yes, and I applied only for Harvard. It didn't occur to me that they could say: "we don't want you".And I think that it was naïveté of not being an American, of not being brought up in a system that is very highly competitive. I was interested in Mathematics and Physics... and I loved it! Theoretical Math is very close to Philosophy (and I took a lot of Philosophy) and then in my junior year, my third year of college, my father was diagnosed as having a very bad cancer. He had cancer of the head of the pancreas with metastasis... This surgeon, who was one of the famous professors of surgery at Harvard Medical School - Jacob Fine - operated on him, came out of the operating room and said: "your father will be dead in six months"... He sat with my mother for three hours... this very great surgeon...until she was calm... while I sat on the corner and watched this and I will never forget what a great physician can do! He sat there, holding her hand, just talking to her... and discussing, until she stopped crying, could discuss the future, what had to be done (we didn't have money or anything else) and.. he... as we were walking out of the room he said to me: "I want to see you in my office tomorrow morning at six o'clock".. (pausa)... You didn't say no to Dr. Fine, he had this unbelievable, overwhelming personality. So, the next morning at 6 o'clock I was in his office and he said: "I have only ten minutes for you, but you're going to change from Mathematics and Physics, you're going to pre-med and you'll go to Medical School. We need people like you to have a quantitative thinking ..in Medicine". And I said: "Think about it, Dr. Fine, you know, I know what I like it, I've been thankful to you..." And he said: "I don't have time to argue with you. I've already spoken to your advisor who is a good friend of mine and you should go and see him today." And he just left me there...
- ER: That means you take medical advice?
- FB: Yes, I take advice... and of course he made me the greatest favor anybody could ever do.Many times he invited me to his home...
- JRCR: So, you did go to medical school more or less against your will?

- FB: No. no... he was unbelievably kind. He invited me to his home and invited some of the great people around Boston, not only in medicine, but, in general. And what he kept saying was: "this next century (this was 1952) is not going to belong to Physics or Mathematics, it's going to belong to Biology". And if you look back, he was right. Totally right! And so, slowly I started saying: "he is right!". I mean, this is going to be revolution, you know, one of the first talks I attended was on DNA. This had been just published, you know... Do you know the famous sentence that Watson and Crick ended their paper with? "The structure of DNA..." (for which they won the Nobel Prize and is perhaps the most important paper of this last century. It described its structure!). The last sentence says: "...the biological implications of our findings have not escaped our attention". There's nothing like such a wonderful statement... and I went to Medical School and ... I loved it!
- ER: When you say you "went to Medical School", medical students at our time have one idea of what Medical School is like. What was Medical School back at your time?
- JR: Yes, what was "Harvard Medical School" like?
- ER: Did that mean that you were going to be closed in a place where you had to study 24 hours a day?
- FB: No, strictly not... In fact, you were given tremendous freedom outside the major courses to spend time - I spent significant time during Medical School in research....
- ER: When were you first introduced to that?
- FB: My first lecture was actually with Dr. Fine before Medical School, between college and Medical School, and I'm not sure it was the best introduction to research... I remember one time he sent a paper to the Journal of Clinical Investigation, he got it back and they said: "We like your study very much but we would like you to analyze your data statistically and tell us how significant the data is" .. and he read this and said: "I can't believe it! I told them this is significant and they are gonna ask me about the statistics... I'm going to send this somewhere else!" (risos...) It was his view of the world.
- ER: Just as a curiosity... do you keep this paper listed in your curriculum? We know your CV is a very extensive one...
- FB: (smile) J. Too many papers!...
- JR: Tell me before you go on... What makes Harvard ... HARVARD? What's the difference? What's the point?
- FB: Harvard is a great college and a great Medical School... but it's not unique. It has gotten a feeling that it's unique, because everybody in the world knows Harvard but how many people know Duke?... Duke is a great college! In fact, a couple of years ago it was ranked ahead of Harvard academically. But, how many people here in Brasil know about Duke University? Harvard is a name like Oxford and Cambridge, you know, and it's just a name, it's old... the other thing which makes Harvard, HARVARD is that they have an endowment of fifteen billion dollars (U\$15.000.000.000,00). I suspect that's a little more than...
- JR: Many, many donors?
- FB: Yeah!... Different corporations donate...
- JR: Every year?
- FB: More than that! A lot of the people who used to go to Harvard – I think they went there because they had the great names - like Rockefeller, Vanderbilt, lot of Presidents have come from Harvard – and I think they give vast amounts of money. I mean it is not at all weird these days to have people who give 50 or 100 million dollars, 75 million or something in that range, so they have enormous money. I'm not saying that they buy people... but I think they do!
- JR: They do offer so much opportunity that the best brains go there, isn't it?
- FB: Absolutely!
- JR: That's the idea...
- FB: Absolutely, yes.. but the point I want to make is, yes, the best brains go there but there are other places that also have the best brains .
- JR: In the 1950s perhaps Duke University was the great university...

- FB: No, Yale was very good already at that time, Stanford was very good at that time, really coming up, ... many. Harvard has a unique reputation, it deserves it, but others should have something which is very close to the same thing. I mean, I'm delighted to be there but I'm delighted to be there because that environment is... I think that is unequal. I don't think there's another place in the world where you have such an amount of intellectual power available to you. Between M.I.T. and Harvard, B.U. and Tufts University, it's incredible...

(pausa para pedir uma porção de camarão, outra de lula, uma batida de maracuja e uma cerveja...)



- ER: Just to continue the "Harvard" issue... How much does it cost now to get into Harvard University?. We all know that it is not only intellectual selection, but also an economic one. There is a price to pay to be a Harvard Medical Student...
- FB: Yes... but if you are very good scholastically and you have no money you can get into Harvard.
- Dr. Eduardo Rocha and Dr. Fritz Bach
- JRCR: Scholarship?
- FB: I was on a private college national scholarship. They paid for everything.. I earned money, you have to have a job and the money, but they pay for almost everything...
- JRCR: Everything?
- FB: Everything.. I mean, they didn't pay for me to go out to fancy restaurants,they paid for my schooling, they paid for room and board.
- ER: But the thing is, if you're not a good scholastic you cannot go to Harvard. How can one select among the good scholastics?
- JRCR: Even if you're rich?
- FB: All right... That's a very difficult thing. There are families... I want to tell you something... There is a story, which I know...
- JRCR: A Kennedy would go into Harvard...
- FB: Let me tell you a story. I have a very good friend in Boston, I won't tell you the name for obvious reasons, he's actually in transplantation... His great-grand father was president of Harvard College. His family and her family includes Jackie Kennedy, one of the houses of Harvard is named after one of his relatives. He and his wife are both full professors at Harvard. His daughter, who had straight A's, applied for Harvard and was turned down. Well, the name was not Kennedy but it's a very well known name...
- JRCR: Why was she turned down having straight A's?
- FB: Because you cannot get into Harvard just based on grades. Ninety percent of people who apply to Harvard have straight A's. I think they look – and I like that – they look for unusual people. I think they admit people with straight B's. I don't think they admit many who have many C's. They look for interested people...
- JRCR: Through personal interviews?
- FB: Oh yes! Very strongly! They have to take the college aptitude test. I think they put a lot of weight on that. That's more measuring a

person's ability to think and such... They look at what they have done at High School outside of being a good student...

- CDG: Like social life?
- FB: Yes, social things...
- ER: Talking about social activities... You know, you are in Brasil and the national sport here is soccer, or football. I heard you were a good soccer (or football) player.
- FB: I was not that good, but I was a heavy soccer player...
- ER: Tell us a little bit about football and Dr. Bach.
- JRRCR: Could you have made professional?
- FB: Oh, no!... The first thing I always think when I think of football, which is how I call it 'cause I lived in England, is that I scored a goal against my own team. It's the first thing I think of. I don't think of all the goals I scored against the other teams. I always remember, drifting back – I used to play inside right forward – when we were being attacked, I drifted all the way back and the ball deflected on my left ankle, right passed our goalie!
- ER: But I've heard you were a good player... Is that right?
- FB: I was a decent player...
- ER: I'm sure you're being modest. And besides football, what other sports do you enjoy? Winter sports?
- Nisso o grupo é abordado por um vendedor de artesanato de Buzios. Após uma olhada nas obras e uma pausa para renovação da porção de lula, sob o comando do experiente JRRCR...
- ER: We were talking about sports. Are you a good skier?
- FB: I am a decent skier, yes.
- ER: And where do you find time to practice sports? Do you consider practicing sports such an important activity?
- FB: Eduardo, it's very important in the field of medical sciences, to know how to choose the meetings you will attend. I have 2 meetings a year, which I go to every year, that are ski meetings. We also do science, of course. We meet for four hours between 3:30 PM and 7:30PM, and we ski all day, the rest of the time.
- ER: Is that productive?
- FB: very productive! A lot of science is done on the lifts. There is also a lot of science done while we are having – this is in Austria, and there's a wonderful drink called Jagartee, that means the drink of the hunter. The first time I had this, it was almost like our boat trip yesterday, where we had caipirinhas. It was 10 o'clock in the morning, it was gray outside, it was cold, we went to sky but it wasn't a perfect ski day. Then, someone said: "let's go in and have some hot drinks". Someone ordered Jagartee – to me it was like English breakfast tee, maybe a new kind of tee, and I had three! By the end of the day, I remember walking out and feeling very warm and wonderful, I said: "I've skied better today than I've ever skied in my whole life!" I had skied the most difficult slopes, and I remember it was just fantastic! And everybody burst out laughing, 'cause Jagartee is $\frac{3}{4}$ schnapps and $\frac{1}{4}$ tea – it's straight alcohol, but it was sweet – and of course I had fallen down in most of the slopes, but I didn't remember and had a wonderful time! (risos). Anyway, I love to ski.
- JRRCR: Now, you are such a well-known researcher, but who is your boss, actually?
- FB: I've never had a boss.
- JRRCR: Never? Not even Harvard?
- FB: Well, I am in a department but I've never wanted to be head of the department. I've always wanted to have my own research labs and I think, as Eduardo will tell you, I am not the boss. Christiane (Ferran) always says: "he's my boss", but I am not anybody's boss! Because I have a more senior position I can do certain things, but I never tell anybody what to do. We've developed people, so that they learn to make their own decisions, and in research too... I give them "strong advice", but I encourage them to go against my advice, because I think that's faulty, and some of the best discoveries we've made were made out of my vociferous objections, like: "this could not work"... or "it makes no sense"...and somehow, indeed, we had great results. So,

you know, I have a boss, the head of my department, but as one of them said: "I didn't want to be your boss nor I would admit I am your boss". You know, I've never had a boss.

- JRCR: Is it getting harder to get grants in the U.S. nowadays?
- FB: No, no, it is getting easier now! The budget of the N.I.H is increasing and they are going to double it in a period of 5 years. I think it's the best system for grant reviews that exists in the world... no, I shouldn't say that... I think it's a very good system, I think there's still a lot of politics, a lot of envy and a lot of undesirable aspects to the grant review. I've never had problems getting money – I've been very lucky – and I think we've done interesting work. Money is increasing. I mean, I don't want to go back to the sixties... I remember one time in the early 70's – and I think at that point already we had a million and half dollars a year – I was one of the best funded investigators and one day I get a call from someone at the N.I.H. saying: "Fritz, I have an overrun, I have money we've not spent and if I don't spend it by this or this date, the next year I won't get it." So I said: "I don't need it!". He said: "You don't need any money?". I said: "no, I have all the money I need." Then he said: "Fritz, do me a favor: write a few lines and I will send you a check of U\$ 100,000.00". I wrote 5 lines saying what I could do, reluctantly sent that to him, and 2 weeks later the university got one hundred thousand dollars! I don't want us to go back to that, that's a waste of money when that happens, but I like the fact that we need so much money in research and I think we'll have that. We are in an incredibly lucky position...
- ER: You made a point which I think it's important to make clear to most people who don't know the American system for research funding, you said: "...the university received U\$100,000.00", not you. How does this relationship goes between the Government, private universities – since we know that most universities in the U.S. are private – and researchers? When you say you have one million dollars, do you have that money or the university has it?
- FB: They should have given it to me, but they didn't! (risos). No, public and private universities get the money. They are responsible for spending the money properly within the guidelines of the National Institutes of Health or National Sciences Foundation, but more and more authority for the decision making rests with the university. I do not have that money, but they cannot spend it with anything other than my research. So, I have total control of spending it within the guidelines of the university, the N.I.H., the N.S.F. or whatever agency, but it's not my money.
- ER: That means that, as important as the scientific reports are the reports on how you are spending your money?
- JRCR: Paper work!
- FB: I have been singularly successful in being irresponsible in terms of the administration. I do not do it. I've never had to. I've always had somebody who is really good in that. We have somebody now, I had a wonderful woman before...
- CDG: Do you meet and discuss?
- FB: Yes, we discuss the general rules and we meet once every 2 or 3 weeks, I've never done administration. In fact, when somebody wants to travel abroad to a meeting I don't think I often have to make a decision about it, she knows more or less what I think that should be done and she decides that! So, yes, there is paper work but I've never done any of it.
- JRCR: Do all of your ideas for work and projects, have to be submitted to the administration at Harvard?
- FB: No, I apply to the N.I.H. for a grant, the university and the hospital (Beth Israel Deaconess) looks at the demand to be sure that it is fiscally responsible, that it covers the right salaries and all the benefits, that it meets all the regulations such as animal rights and the use of radioactive materials, and they send it to the N.I.H. The N.I.H. has a study section, my colleagues, my peers, to look at it and to decide how good the work is, should it be funded or not and, depending on the score they give it, that is or is not funded. The money gets sent to the university but it is for our research.

- JRCR: So, if there is a censorship that is done by the N.I.H., not the university?
- FB: There is no censorship.
- JRCR: I mean, if you don't get the money...
- FB: Yes, but that is solely – hopefully – based in the quality that my peers think I have.
- JRCR: Never from the university?
- FB: No. In fact, there is tremendous insistence of freedom... Once you have the grant you have a certain amount of right to do something slightly different, if you think it's going to work.
- ER: Dr. Bach, leaving the “money talk” behind and going into the scientific talk... I could not interview you without asking about two major contributions you brought in different times of your life: the mixed lymphocyte reaction and xenotransplantation. Would you briefly comment on that?
- JRCR: The mixed lymphocyte reaction was a turning point in transplantation...
- FB: Yes, I think so.
- JRCR: Which year was that?
- FB: 1964.
- JRCR: You and Amos* , I believe...(*Bernard Amos, ganhador do premio Nobel em 1980)
- FB: No, actually that was from my lab alone, but 3 years later the important paper from Amos and myself in Science came out.
- JRCR: I had the opportunity to meet him.
- FB: Really? He is a wonderful man. I have been incredibly lucky, and I mean that very sincerely, in two ways... and I'm sure that is in part due to my personality... I have met remarkable people who have been kind enough, even though they were 20 years older, to adopt me, to extend their friendship to me, and they've been many. Luigi Gorini, who is Italian, who was head of the Italian resistance in world war II, heavily decorated, worked with Jacques Monod in Paris, the Nobel Prize winning work at the operon. When Monod gave his Nobel laureate lecture he said: “this would have never been done without the genius of Luigi Gorini”. I have worked with Luigi Gorini for 3 years. I mean, I can name so many people who have been magical in terms of being teachers, being mentors. I don't think many people have had as many really great friends, mentors, whatever you want to call them. The mixed culture, as I told you the other day (primeiro dia do curso “from bench to bedside” em Buzios), was a very funny story. I had never met Sir Peter Medawar, but I was an intern with Lewis Thomas at N.Y.U. and Thomas and I – we were not friends at that time, later we became friends – we had a good relationship, because he wanted me to come to N.Y.U. and I admired him perhaps more than any of the scientist positions I had ever met. He told me I should go and listen to Peter Medawar's lecture, and as I told you, listening to his lecture and afterwards I was asking this question of how could he possibly solve all of this by working in mice? It's too complicated... He should work it out in the test tube! And as I told you, he said to me: “you know young man, you're right, you should do just that”. And I remember like... there are few moments you remember in your life – everybody in the U.S. remembers exactly where they were and what they were doing when J. F. Kennedy was shot, I do it, everybody does– I remember my feeling at that moment as he said that, I didn't realize how ridiculously, presumptuous and arrogant I was being, telling him how to do his research. As he said that the amount of embarrassment, the feeling of total stupidity... it was very great. I walked away and I said: “I'm gonna do it! I'm going to put it in the test tube.” And, again, there was so much in the literature to help, at that point, because of the work of Brent and Medawar, something known as a normal lymphocyte transfer test, it was clear that lymphocytes, leukocytes from the blood, carried the transplantation antigens. It was also clear from Gowans's work and Medawar's work that lymphocytes could respond, they weren't just dead end cells, they could respond to antigens, and that had already been a publication showing that somebody who had had tuberculosis, when they were immunized

against tuberculosis, if you mixed their lymphocytes with p.p.d. they would proliferate. So I said, "it's simple!" (after 2 years of reading and thinking, of course) "...if they have the antigens and they can respond to antigens, we should just mix lymphocytes from 2 individuals and ... there we are!". Now, how naïve I was. What we knew was that when somebody was sensitized to the antigens they would proliferate, it never occurred to me that when you're not sensitized maybe they would not proliferate! So I went in the lab, and Kurt Hershin at that time was doing chromosome analysis, and I said: "could I work in your lab? I want to try mixing lymphocytes using your culture medium because lymphocytes grow if we stimulate them with phyto-hemagglutinin and then do the metaphase chromosomes". And the first experiment I did, I sat there everyday looking at the cells, in day 3 I started seeing blasts, by days 3 and 4 I started seeing mitosis and there was a mixed culture! First experiment!... He had all the technology, he knew how many cells per ml to culture, what the medium should be...

- JRCR: You mixed lymphocytes from 2 different people, no transplantation in mind?
- FB: No, just mixed them! I saw these blasts and I figured...
- ER: When you thought about the experiment, from the start, weren't you thinking about transplantation? Or any diseases in mind?
- FB: I was interested in transplantation because I had heard Medawar's lecture. Medawar's lecture was on transplantation: what was recognized and what responds. Of course he was talking about histocompatibility antigens, although that was not what he called them, and he was talking about lymphocytes that responded. I mean, it sounds ridiculous, but I remember, it seems so simple to me when you looked at all the work that Medawar and his colleagues had done... I was very lucky, because I didn't realize that the mixed culture would have a reaction because of the very high frequency of responding humans that you didn't have to sensitize, I mean, all of that just escaped me...
- JRCR: What did you do after this first culture, I mean what did you think?
- FB: You've got to realize that at that point, and you do, we didn't know about T lymphocytes. So, our level of understanding was very low, very naïve. Lymphocytes were just cells that recognized antigens, we knew about antibody production, of course, but this was not antibody production that we were looking at. What I thought about at the moment was, I remember thinking about quantitation, 'cause sometimes we saw lots of blasts and sometimes we saw relatively few, but it was clearly aimed at transplantation. It was a model that I told Peter Medawar he needed if he was ever going to understand this. I don't think I've worked much beyond that, and in fact that year, after we made these pediatricians get all excited about diseases and a whole series of papers were published that I had very little interest in. It is very hard when you come from mathematics and physics into biology, if you like numbers, if you like to be precise, if you like to quantitate what happens in your life, biology is not the place to be. And so, I've always been very interested in genetics, it's a wonderful biological quantitative science – I'm talking about classical genetics, not molecular genetics – and so I thought maybe I could learn something about the genetics of histocompatibility and immune response by looking at the mixed culture. One of the first things in fact that we've noticed, which is one of the two or three incidents of my whole career (!), where my philosophy of ... I would talk to anybody about anything I'm thinking, any result that is my data – I could never do it with Christiane's data, for example, that's not my data – but if it's my data I will talk to anybody... I gave a lecture at the N.I.H. showing that you needed adherent cells, which behaved more like macrophages to, in order to get a mixed culture reaction, and in fact we had the first description of IL-1 (interleukin 1), although we didn't call it that, but we haven't published it. That was not my main interest, so we were in no rush to publish it, and one of my... now friends, stole the idea! The reason I know that is one of my classmates from Harvard Medical School was working with him, he came to me and said: "... he came back after your lecture and said: drop everything! We're gonna fall off on this." And he published it before me. I was interested in the

cells, I think more than anything I love cells, I love the way cells work, I find an incredible challenge to think that maybe we can engineer cells, and it scares me at the same time. I'm scared that we're going to put on a gene that we know very well what that gene does, and at the same time the gene is going to do something we didn't know it does... It's going to be in the cell where it doesn't belong, it's going to meet a new "friend", it's going to say: "you and I could tango", you know, and suddenly the cell is going to be doing something that should not be doing. But I love to look at cells, I still like to look at the microscope and look at cells and the lymphocyte is amazing. I was taught in medical school that – you're all too young, you included (olhando para o JRCR) – I was taught that the lymphocyte was an end stage cell, it had nothing to do! These beautiful little "dead" cells, like everything was nucleus, and not until I think 1959 that someone showed that...

- JRCR: Do you still look at the microscope today?
- FB: Not as often as I would like too, but, yes! At least once, twice a week.
- ER: Or we show him the pictures...
- FB: I took seven months of pathology during my internal medicine residency .
- CDG: This explains...
- FB: Yes... I love it!
- ER: Since you are now more than ever a scientist how important, if you think it's important, is your MD background? How important was it to go through an internal medicine residency? Or how important is it to be a MD and a Ph.D.?
- FB: I don't know. I feel very strongly that if you have one doctor degree, you don't need another one for intellectual reasons. You have to get trained, if you have a MD you're not trained as a scientist, these are two different things. But as a Ph.D., I think you can learn the medical issues. I like to think that my medical training helps me, but I'm not convinced that's right. I'm not sure that there are not enough Ph.D's that have much more insight then I do into the disease processes.
- ER: So, you really see Ph.D.'s and MD's as different professionals in different fields?
- FB: I see them very much different. I think they have a totally completely different way of thinking, I think medicine is based on needing an incredible knowledge base in your mind, not in the computer, in your mind, and being able to sort through that very quickly as you look at a patients' symptoms, history and everything else. I'd like to think that in science you need a knowledge base, but what you really need to is to have... I hate to use the word but there's not another one to define it... creativity, to say what is important, what do I need to do to get more knowledge. I think they are really different. Luigi Gorini, as I mentioned earlier, said to me: "stop medicine, you're ruining your mind! You'll never be able to think again, you'll be so loaded down with facts, you won't have space to think." (risos). He was a very funny character... I do think these are very different.
- FB: So, xenotransplantation...
- ER: That was going to be my next question... Since you are stubborn, as you admit it, I'm sure that people told you that xenotransplantation would be impossible, but you persisted. Tell us about xenotransplantation.
- (Nesse instante o grupo atende a sugestao da Clotilde para uma pausa... mais camarao, lula, batida de maracuja e cerveja...Apos a pausa o tema em debate é New York City.)
- FB:I have worked in NYC for a while, with a great clinician, a man named Max Gelfein. Max Gelfein had one of the largest private practices in internal medicine in NYC, he has added me very much. He would take me on rounds and in one-hour see 35 patients. When you later went into the patients and you asked them: "how did you view Dr. Gelfein's visit this morning?" and they would say: "you know what I really love about him is that he always sits down with me, he will talk to me and he'll listen to me. He really cares, he spends time with me". He had just seen 35 patients in one hour! But he had this golden gift, I spoke about Jacob Fine earlier, and I think there are people who have

that gift to, just in minutes, to give a patient total attention, total respect, and I loved it. I loved to make rounds with him, he was a great clinician. I remember years and years later I went to NYU to give a lecture and I ran into Max Gelfein and he said: "Fritz, come over here!" He didn't say hello... "Come over here! I've got to show you something!" He showed me an X-ray and asked: "Do you know what that is?". And I said yes, that person has a tumor... there was a pretty obvious image at the lung. And he said: "No, it's not just a tumor. It's this and this kind of tumor, my whole life I wanted to see one and as soon as I saw the X-ray I made the diagnosis". And the radiologist said: "Only Max Gelfein could do it". He was just a massive clinician, and I had a lot of debt, we had no money, I got scholarships for college and I had to borrow money, even at medical school I borrowed money. So, he let me take care of his practice. Just to give you an idea, as an intern I made 25 dollars a month. I was living in New York City with a car that my brother had bought for my wife – a brand new jaguar – the car was in the garage. The garage cost me 65 dollars a month, this was not good economic planning. So Max Gelfein said: " I'm going out on a 4 day weekend, why don't you take care of my practice? I have good nurses, don't worry, they will help you." So I asked Lewis Thomas if I could take a Friday and Monday off and he said: "sure". I went down there and he said: "you can have all the money that the patients pay me". In four days I made U\$1,900.00! I couldn't believe it. Can you imagine? Making U\$25.00 a month, not being able to afford the garage – my brother was paying for the car and the apartment – and suddenly you spend four days and you have a couple of grants! You know, I loved practicing with them, mainly because I've enjoyed watching them both, for their astuteness, for his incredible ability to be a good doctor. And he let me take care of his patients, I saw 35 patients but it took me 3, 4, 5 hours....

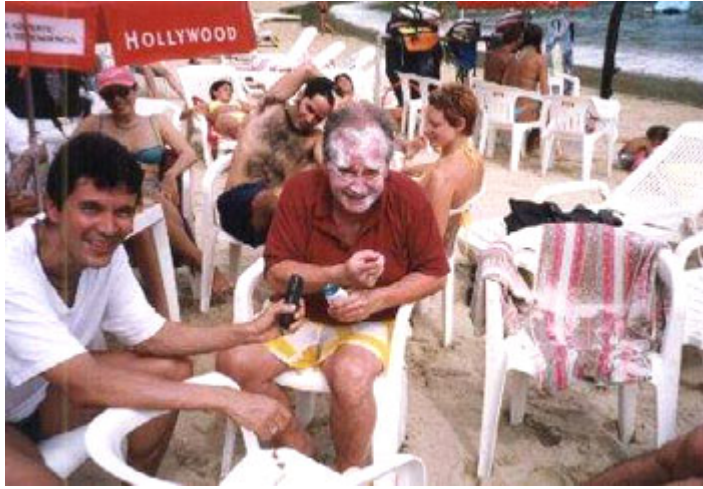
- ER: How old were you at that time?
- FB: Upper twenties.
- ER: How come that, having this opportunity of going into private medicine and making good money, versus going into research and having this "empty field", how come you chose the other way?
- FB: You know the answer to that... There's nothing like research to me. The chief of medicine at the Mass General said to me once: "you will never make more than U\$25,000.00 a year."
- ER: And you made it?
- FB: I'm almost at U\$25,000.00 a year now... (risos)
- Nova pausa para troca de lado da fita...
- ER: So, xenotransplantation... How did the idea came up?
- JRRCR: But before that, let me ask you one more question, a clinical one... Do you think that every researcher should go into clinical rounds and ...
- FB: See patients? No.
- JRRCR: I mean, not to see patients, but at least be in contact...
- CDG: ...be in contact with the clinic...
- JRRCR: ... be in contact in conferences and with clinical problems.
- FB: If we're speaking about every researcher as such as in the U.S. my answer is no. I think it's perfectly all right to have researchers who want to understand the mechanisms by which genes get spliced. But if we speak about Brasil, I personally think it's very important. To do that level of basic research is going to be reserved to very few. You have great labs here, but for the average person, I would think that the more they can relate to clinical problems, the easier it will be for Brasil to fund that kind of thing and to recognize it. I mean, I'm flabbergasted by the fact that I heard this morning that your health care budget is U\$ 48.00 per person per year. If you are faced with that you can't afford a lot of very basic research. I would think... I mean, you've heard, you've got to keep your bright people here. You've got to have a good number of labs here like yours so that if they want to do very basic and need a place to go you will do it. But I think it's very important to see the relevance.
- ER: Xenotransplantation, now?

- FB: (risos). In 1987, I think, the University of Minnesota was looking for a new head of the cardiac unit, the heart institute, and the man they've interviewed was a man by the name of Stewart Jameson, a very good cardiac surgeon. He came to meet me, just as a part of meeting some of the senior faculty, and he said to me that one thing that was persuading him very much to accepting the job would be if I would commit to work with him; to try to see if we could do clinical xenotransplantation. I had been interested in xeno problems, but it was largely genetic problems and the recognition - very basic problems - and I didn't really have any good ideas, but I had at that time been working with and learning from a man by the name of Gregory Versolatti, who was an endothelial cell expert. I knew very little about endothelial cells, except from what I had learned from Greg. So, I don't like to... I hate to admit this but... I don't like to read the literature a lot, but I went to the library for 2 days and I read all the old papers on xenotransplantation and reading them in the perspective of what Greg Versolatti had taught me, I said: "I know why the xenograft is rejected so vehemently! It's because the endothelial cells are activated, and they are probably being activated by antibodies and complement."
- ER: So, you knew it just like that... you knew it.
- FB: Yeah! I have always had faith. I've been wrong many times, but it's OK to be wrong, as long as you do good experiments based on a good hypothesis. So I went back and on a Friday afternoon I met with him and said: "if you come here I will work with you on that." I had suddenly realized that to me the endothelial cell was much more interesting than the T cell, with which I had lived for 20 years!
- ER: So, that's when you abandoned immunology or are you still an immunologist working with different cells?
- FB: No, as a matter of fact, I've abandoned immunology (risos). No. I don't know... I think it all comes together but, anyway, I got fascinated with that idea. Of course we showed very quickly that antibodies and complement can activate endothelial cells and from there... You know, this was just at the time that people were learning that there are magical switches within cells, switches that really control the whole aspects of a cell behavior. They were finding single gene products that were essential for differentiative behavior, so I said: "we have to find in endothelial cells a target that we can turn off to prevent endothelial cell activation". That led eventually to NF-kappa B. I was very lucky to have Hans Winkler joining the lab at that time. His whole passion was NF-kB, his only one! Then Christiane Ferran did the first big study showing that if you turn off NF-kB, you turn off virtually the entire pro-inflammatory response...
- ER: Like a main switch, as you often refer to...
- FB: The main switch. That's what we were looking for, and it was interesting from there because some unexpected things happened but, again, I think it's... once you have a hypothesis, and my hypothesis was that endothelial cell activation was the prime target, I think the rest was... the field was available, I mean, how to engineer, how to think of inhibiting the switch...
- ER: Excuse me, but you're making it look easy. We don't have clinical xenotransplantation yet and some people even make jokes about it saying that xenotransplantation is the future of transplantation... and it will always be! How do you see that? How can you continue despite all this adversity?
- FB: It's not adversity, it's just different opinions. I like to tell a story, I'll tell who it is, which is a very famous professor in transplantation. I gave a lecture in 1990 at the International Transplantation Society meeting in which they asked me to speak about what I thought the future was. I talked about xenotransplantation until a first time presented idea of blocking complement by genetically engineering the pig endothelial cell with a human gene with one of the complement inhibitors, which is now reality. That was our idea, despite what some pharmaceutical companies and their people would like to play. I think at that point this man came to me, after my lecture, and he sat down with me almost like a grandfather (we have the same age), and he said: "Fritz, what is wrong with you? How can you propose that xenotransplantation is the future? I mean, it's an impossible problem to solve. In the 60's and the 70's they couldn't solve it, it's just too difficult!". And I said: "you may be

right but I think, you know, we're learning now, maybe with genetic engineering of endothelial cells"... And he said: "No..." I think he was almost sad that I'd lost my mind, you know, sad that I had had a good career but had blown that. Two years later I was invited to speak at his home university in Europe and who gave the first lecture, about the tremendous promises of xenotransplantation? Himself! The guy who 2 years later, a very famous man, was saying all that. Ridiculous!... In fact, now I think it's gone too far the other way. I'm not sure we will ever be able to do effective clinical xenotransplantation from pigs.

- JRCR: You don't think so?
- FB: No, I said I'm not sure. I have serious concerns. I have concerns..
- JRCR: Because of the risk of disease transmission?
- FB: No, no. That's a separate issue, I think. Will we get out of rejection factors? I think so, but I'm not sure of it. I think we need additional genes. Will we be able to get pig organs to function in a human at long term? Physiology? I don't know. I mean, I think this is a very difficult area and I just don't want it... you know, at first everybody says: "you're crazy!" And I wasn't the only one, I don't want to act as though I was the one who restarted the field, I was only one of the people. And now everybody says: "we're going to have xenotransplantation soon". I'm in the middle, sort of saying: "Wait a minute! You've passed me by, how did you suddenly say that this is going to be a successful enterprise?" I don't think we know. But I think it's well worth the effort.
- ER: Do you think that molecular biology has added a lot to the progress observed in xenotransplantation research?
- FB: It's been the breakthrough. Without molecular biology I think we'd have no chance of solving this problem. Eventually we would have found drugs that block endothelial cell activation, block monocytes, but that's too much.
- ER: Can you compare the revolution that is occurring at molecular biology with that in informatics? I recall your precise science background.
- FB: I don't know how to compare the two. I think that, in terms of the impact in society, it will probably not. The impact of informatics, of the computer revolution, is so vast that you can't compare biotechnology or any new therapy to it. Will it be one of the great things of the first decades of this century? Absolutely. Will we have genetic engineering as a part of medical therapy? I think so. Especially if we can make it cell type specific, and we will be able to do that. I think that what we have available today is going to stun us. There are some people who have a vision of where we will be in 10 years, but even they cannot be sure. I've been dealing recently with a man who has become a multi-billionaire, has started one of the great computer companies. His vision of the future just shocks me, it's science fiction, but I know he's right. I know it will all happen, or at least it all can happen. But what will happen, how this will develop, I'd be glad to be alive to see it. I think it's going to be incredibly exciting. I don't think you can compare the biology to that. The impact of being able to genetically fingerprint individuals is vast and not all good.
- ER: Dr. Bach, coming from the 30's – that's where our interview started – when the issue of selection and human "purification" was present, and now into a new century facing the same problem, maybe just put in another way... Do you see any resemblance between all that with the science that is being performed now? How do you see this?
- FB: I think there are huge ethical problems. Huge. They vary from relatively unimportant... - I shouldn't say unimportant - relatively small problems like the one you know I'm very involved in (ética e xenotransplante, ver MOL 5), and that's far from unimportant, that's very important... to huge ones. When we will be able to fingerprint somebody and say what is in their future from a genetic point of view, who's going to have that information? Who has the right to have that information? Are we really going to try to genetically engineer at the genomic level? The answer is yes! It will be done, just as I said. We have cloned a mammal – and I won a bottle of champagne from one of my best friends because of that – before the end of the last century, and I think we will do genomic engineering. And that scares the hell out of me!

- JRCR: Do you think researchers have the right to patent genes?
- FB: Absolutely not! I think it is a horrendous thing to be able to patent a gene. I think that to use a gene for a very specific purpose is another matter.
- JRCR: Is there a law against that in the U.S.?
- FB: There is a general consensus developing because Clinton and Tony Blair have agreed there should be no gene patenting. In fact that's the reason why the NASDAQ, the "gene" stock exchange, tumbled a few days ago, because they came out and said: "there will be no gene patenting".
- ER: Talking about a few days ago, we have recently celebrated the cloning of pigs, a scientific achievement that was announced as the breakthrough that can bring xenotransplantation into the clinic. You were interviewed 3 days ago at "Good Morning America" and by other TV and newspapers, what did you tell them? What is your position about the cloning of pigs?
- FB: I have no problems with the cloning of animals. I think there are some things that have to be taken care of...
- Nesse instante o Dr. Miguel Soares, pesquisador belga/português do laboratório do Prof. Bach, vem oferecer creme solar para o Prof. Bach...
- Miguel: Have this...
- FB: Does it look that bad?
- Dr. Eduardo Rocha and Dr. Fritz Bach
- Miguel: It looks terrible! (e na verdade o sol de Buzios já castigou a pele do Dr. Bach)
- FB: Thank you... I have no problem if it is done for the sake of helping human disease, or better nutrition, whatever. I have problems with human cloning but I don't go as far as saying that it should never be any human cloning. I can think of situations that need a lot of discussion before we do that. As far as I see the way transplantation goes, this is a major breakthrough, I think. I think it is incredible! So, I am excited that they've done this, they've done this for all the right reasons. We will be able to test whether we can use different genes...
- ER: Do you really think that people who are investing in this type of research are really looking for the "right reasons"? Or are they doing it for money?
- FB: Well, of course they are doing it for money. The companies are doing part of what they say to raise the stock prices, and it's all right! Well, the world is a globalized world and companies will have altogether too much power – the multinationals – as far as I'm concerned, but that's the future, we're not gonna change that. What we have to do is to develop the ways so that their goals, which are largely financially driven - which is not all bad - I mean, it's all right to have better employments, it's all right to expand the economy, it's all right to have more food potentially. If it's applied in a good manner, in an ethical manner...
- ER: I was not going to touch this subject, since our interview is basically about medicine but... I've been reading this book about genetic engineering at the agricultural level. From what I see, companies are not doing the best they could in terms of solving the world's hunger problem... What we see is the opposite, now we have seeds that cannot be kept for a following season, forcing agricultors to buy a new pack of seeds from these companies each year. How do you see all that?
- Nesse instante o nosso sempre bem humorado JRCR aproveita para pedir a permissão para tirar uma fotografia do Dr. Bach "lambuzado" de creme solar...
- FB: Do you speak French? That's méchant (maldade)!
- (risos). Após a foto...



- FB: There are two things that relate to that. One is, I think, the reason we've had so much problems with genetic engineered foods. It's because we did not properly, at the right time, involved the public in the subject. I think we need to learn how to involve the public more, so they can have more faith on what we do. The other thing is that we cannot do genetic engineering of foods and forget about the developing world. Monsanto has now backed up from that, but they've proposed something known as the terminator gene, you know about it, so that no crop could be used a second time. That means that instead of doing what has been done through the ages where you save some seeds from one year to plant next year's crop, you can't do that, 'cause it will not replant. You might say: "why is that so bad? That's part of the market." The reason it's bad is that we will get more resistant organisms since these plants are genetically engineered to prevent the organisms that we have now from destroying them. We will get more resistant bugs, the "super bugs".
- ER: As we've seen with antibiotics?
- FB: Exactly, the same thing. And what Monsanto at a New York Times interview said, one of the scientists said: "don't worry, just trust us." If there's one thing no company should say is "trust us", nobody trusts the companies. The danger is... OK, so they'll come up with something else, let's assume that, that's fine for the people who can afford to go back to them, but in central Africa, for instance, 95% of agriculture is carried out by women – the men sit around, drink and smoke while the women do all the work – they can't afford to go to the companies and by the new crops... and these "superbugs" will get to Africa and bite them out. So there are huge problems here and one of the things we're gonna have to learn in this world is that, even if the economy is going to grow, these companies will have to consider the developing world. As you know, in our ethics project the developing world is fully represented.
- ER: Is this the main reason why in your project you propose that the public should be consulted before we move forward into clinical xenotransplantation?
- FB: Yes. And I don't think we can consult only the U.S. public, or the English public. We have to talk to the Egyptians, we have to talk to the people in China, I mean this is a worldwide problem if we have an infectious complication.
- ER: Who would you like to talk to in Brasil?
- FB: Our view has been that for most countries you... I don't even like a referendum, I don't like the population voting for that. They make terrible decisions in politics, they will make terrible decisions in science. We need an informed public and the view has been to have committees of 20, 25 people who can understand the problems, who have the time to devote to become informed, and who do not have an overt conflict of interest. I would view myself as having a conflict of interest.
- ER: Why?
- FB: Well, I'm the most sensible person in the world, you know that (risos) but my whole life is devoted to xenotransplantation at the moment. I think somebody could look at me and say: "if he helps

solving xenotransplantation he has visions of winning the Nobel Prize.” That’s a conflict of interest, and it’s appearance as much as it’s the reality. Big thing for us is that we’ve got to find a group where once that group has made a decision on behalf of both patients who need a transplant and also the people who would be put at risk, the public has to say: “we trust them. These are people we can trust”. If they truly thought about themselves just as we would think about ourselves.

- CDG: Do you know that in Brasil we have a TV program, very famous called “Você Decide”, where they show a story and the public decides which way it goes. Recently they’ve shown a story about a man who needed a transplant and there was an opportunity to perform a xenotransplant - a fiction story - and the public voted around 80% in favor of the xenotransplant.
 - FB: Was the public told that there is a risk, which nobody can quantitate, of an infectious outbreak?
 - CDG: No.
 - FB: You see, that’s one of the big challenges for the future. There are going to be a lot of technologies that will have a tremendous potential to patients, but that carry a risk for the public, and I don’t mean only an infectious risk, I mean an economic risk, any kind of risk. Somehow we should inform all people but you should think consult with people who will really inform themselves. We have to move forward.
 - CDG: Like an informed consent?
 - FB: Exactly, in fact that’s the analogy I use, informed consent to the patient. In a way we have to develop a method to get an informed consent from the public. The patient is informed when he or she makes that decision, but the public or someone who represents it should also be informed.
 - ER: Dr. Bach, you have mentioned the Nobel Prize just a few minutes ago. You have recently received the Medawar Prize from the International Society of Transplantation, you are a Lewis Thomas professor at Harvard and you have friends who won the Nobel Prize. Many people think you are probably one of the next Nobel winners. I know you’ll probably say that’s not important but, how important is it really to win a Nobel Prize?
 - FB: Well, I think it varies with the individual enormously and it really isn’t important to me. My first wife was an immensely intelligent woman, I don’t mean only intelligent as a scientist but intelligent in general. One of the things I remember her saying is: “Fritz, be very careful, because your goal is to win the Nobel Prize and you’ll win it, then you’re going to say to yourself: - Am I one of the great Nobel laureates? And then if you decide, yes, I am one of the great, then you’re going to say to yourself: - Am I the equivalent of... and it never ends.” I have gotten enormous recognition. I have incredible friends; I live the most privileged life anybody can live (I actually make more than U\$25,000.00 a year). I even have had a degree of financial success, which I never would have imagined. When my first three children went to college, which is what we were talking about earlier, we never mentioned the number but today Harvard College costs almost U\$ 30,000.00 a year. That’s U\$ 60,000.00 year firm, ‘cause that’s after tax money. When my first kids went to college and graduate school, every year, for their three lives, eight years each – seven years for my daughter who went to law school – every year I borrowed money. Then I paid it back before I had to pay the next thing and then had to somehow earn that money, then I had to borrow again in November. Every year! Now all the money for my three young kids is in the bank for them. I am incredibly privileged. How many people can say that? That they can educate 3 kids in the best schools of the U.S. to 8 years and the money is in the bank?
 - ER: How many kids do you have total?
 - FB: Six. Three of them are in the 30’s and 3 are not teenagers yet.
 - JRCR: That’s the best work of your life!
 - FB: Absolutely! When I gave the Medawar lecture, at the end I spoke about my two families and showed their pictures, the pictures of my ex-wife and my wife. Then I said: “I’ve done six unequivocal perfect experiments”.
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