This Week in Virology

With Vincent Racaniello, PhD

Special Episode: Ignorance with Stuart Firestein

Recorded 12 December 2012
Aired 29 December 2012

http://www.twiv.tv/2012/12/29/twiv-special-ignorance-with-stuart-firestein/

[0:01:20.5]

Vincent Racaniello: Thanks for joining me today. You're a neuroscientist, right?

Stuart Firestein: Yes.

Vincent: You're not a virologist?

Stuart: No.

Vincent: Probably don't you ever have studied viruses. I think you use the vectors at some point.

Stuart: We use the vectors all the time back in my laboratory. That's right. Yes. Viruses, the best little machines going.

Vincent: One of the questions I got at the Café Columbia this week is: Is there any hope for using viruses as vectors to cure human diseases?

Stuart: That's a good idea.

Vincent: Absolutely. I wanted to get you up here not to talk about neuroscience, but I'm sure that will come up, but to talk about a book you wrote which caught my eye, I don't know, months ago. I ended up reading it. I read it in two hours on an airplane going somewhere.

Stuart: Perfect amount of time.

Vincent: That's exactly the way you wanted, not to be a burden, and it was terrific. It's called "Ignorance: How It Drives Science." I thought you and I could talk about it and give our listeners a flavor and explore some of the points in your book. It's a great title and, in fact, I picked it on This Week in Virology a while ago as a Listener Pick. We do—a listener pick is a pick. We each pick something every week that we think the listeners will like—books, movies, whatever, anything—and that was my pick. So hopefully some listeners have read it.

Stuart: That will be great.

Vincent: If not, after this episode, you want to read it. So I thought whenever I have guests, I always start out with them telling their story. In fact, one of the chapters in the book is you telling your story and I enjoyed that a lot.

Stuart: Well, thanks. It's a little bit of an unusual story I guess. I don't need to retell entirely here. The idea…

Vincent: Give us the overview.

Stuart: I will. So the idea, of course, in the book, at least, the second half of the book of what I call these "case histories" or "case histories in ignorance." The book, of course, is all based on a course that I started teaching here at Columbia some years ago and we can talk a little bit more about that in a moment. Part of the course has these—I invite people in to talk and then I use these "case histories," as I call them, to demonstrate some of the points in the book. So I did three of them and I wanted to have a fourth one. It seems that there was one missing somehow or another. I kept thinking, I don't know, I can't figure out which one it is I exactly want to do. At one point, my wife—somebody who was due to come into the course, one week, couldn't make it at the last minute, I think they were injured, a skiing accident, some crazy thing—anyway, they couldn't make it at the last minute and my wife who was also a scientist, said, "Well, why don't you do it? Why don't you be the guest and I'll interview you." I said, "Well, alright, I guess we could try that and see how it works." So based on that, and then, of course, the fact that I know my life I thought, "Well"—and then she suggested while I was writing the book—she said, "Well, why don't you use yourself for a case history and see how that goes?" So I thought, "Alright, I have a slightly unusual background for a scientist in that I started life really—my professional life anyway—working in the theatre. I was a stage manager. I started out as an apprentice and a stagehand and a sound technician, lighting technician, stage manager eventually and finally a director which is what I mostly made a career with.

Vincent: Where did you grow up? In the New York area?

Stuart: Well, I was born and raised in Philadelphia and then I was sort of in New York and then in Baltimore, Washington, a little bit in Boston. I sort of consider the northeast Amtrak corridor my hometown. In those days, the days that I was working in the theatre—now this is in the, I'd say, 1970s, my God, that sounds quite a ways back, doesn't it—but in the 1970's the big thing really was to decentralize theatre in America. We had all these regional rep companies. The idea was to move theatre out of New York City and into the provinces as it were.

[0:05:05.0]

Vincent: Like baseball, right?

Stuart: Yes, pretty much. Get it out there—or the National Hockey League that hasn't worked out so well.

Vincent: Yes, baseball, we used to have all three teams here.

Stuart: All three teams here, that's right. [Laughter] So I did a lot of work in the so-called "regional repertoire companies" which was actually quite nice. It was a great way to do the theatre and a little less commercially-oriented and therefore a little less frazzle. I did some commercial work as well and I was always happy to do that. So I got a chance to do a lot of different things. Then I wound up moving to San

Francisco with a show actually. I liked it out there and I stayed there for a while and got involved in the theatre scene there and picked up another show there which I did the lighting for actually. Then they wanted me to run the show that is [BH] performance and do the lighting for the performance. It got very good reviews. It looked like it was going to run for a while. So I thought, "Alright, I have a cushy little job here for a while. A little more stability than I was used to." I always had this interest in animal behavior, so I decided I was going to take a course at the local state university. That's California State University in San Francisco. In those days you can actually be a fulltime student at Cal State San Francisco for $106.00 a semester. That's not just an inflation issue I have to say. There's a lot of other things that have happened that have made education much less accessible monetarily than it was then. I think that's very unfortunate. For me, there was no issue. Money was not at all a question of financial aid. $106.00, I mean, come on. Somebody stands up and tells you everything they know about something, this is a great idea, who have thought of this? I'm fond of saying, I think it was Aristotle, but I hadn't heard about it yet. So the good part of the story—and I won't go into the lengthy, lengthy part of it, you can read the book if you really want to hear the ugly details—the good part of the story is that I met a great mentor, a fellow named Hal Markowitz who, I'm sorry to say, died two months ago. He was a great mentor and a wonderful teacher…

Vincent: Did he read your book?

Stuart: Yes, he did. He did read the book. He knew about the book. There's a dedication to him in the book as well as two other mentors that I've had. So I've always been, I'd say, very lucky this way. I'd like to think it's not just luck. It's the way the system works. I had a great mentor in Hal Markowitz who taught this course and convinced me to become a student as you were 30 years old as an undergraduate which seemed crazy, but he said, "No." He helped me through all of that. And I did. And then I got an undergraduate degree in Biology which we all know is worthless but I didn't know that. He never told me that. So then it came down to graduate school. That's really when I had to make a decision that I was going to change my life or not. So I thought—because I could do undergraduate and still work in the theatre back and forth—but graduate school, as you know, is a commitment to a different level of what you're doing. So I applied to graduate school and said, "Well, if I get in, I'll do that. And I'll have a second career. We all live twice as long as we used to. Why not do a second thing? And if I don't, I'll go back and work in the theatre happily with my undergraduate degree in Biology." Unfortunately, I got into Berkeley which I say regularly is probably the result of a clerical error, but it's all right, take advantage of those too—where I met another great mentor, Frank Werblin, who's still a very close friend at Berkeley. He's still there. And he took me into his lab as a 35-year-old graduate student which I now recognize, running a lab myself, you have to be a little crazy if you can consider that but he did. And he was just a fabulous trainer.

Then I went on to do a post doc at Yale University with Gordon Shepherd, another fabulous mentor. People who really—it always seem to me had—my career when I was doing mostly at heart. I guess, I'd say, I think I was lucky that way because you hear these horror stories so often about bad mentoring or PIs that—from somebody in the lab had to steal ideas from people or trying to get credit or this or that. I have to say I was fortunate never to have seen that or experienced it and it's made all the difference. It's permitted me to have a wonderful career. So I'm a firm believer in mentorship.

Vincent: So after your post doc, did you come to Columbia? Were you somewhere else before that?

Stuart: So I was a post doc at Yale for two years really and then they put me up into one of this research assistant/professor-type positions. I established a lab there, more or less, independent lab for three years. Then an opportunity came up at Columbia and I came here.

Vincent: When was that?

Stuart: That was in 1993. Once again I had a great mentor actually. I came here as a non-tenured associate professor, Darcy Kelley, who is in our Department of Biology still a close colleague, brought me in. Martin Chalfie, who is also a close colleague. The two of them were instrumental in bringing me in to Columbia and then mentoring me through the whole tenure process and everything else.

[0:10:05.8]

Vincent: So you made that decision that you were going to quit the theatre and go to graduate school?

Stuart: Yes.

Vincent: So you quit—you let that play ran out? That last one that you were…

Stuart: Yes, well that had long gone actually. This was already four years later. This was now after finishing undergraduate, so I was about 34, almost 35.

Vincent: As an undergrad, were you working in the theatre?

Stuart: I continued to work in the theatre. I had this odd sort of flip thing because I would go to school during the day and work at night. There's a lot of people working during the day and go to school at night.

Vincent: You know it's funny you mentioned lighting. So one of my co-hosts on This Week in Virology, Rich Condit, his daughter does lighting. I think she's in Texas now. She's a professor but does shows. She did the lighting for "The Hood." Is that the one about Washington Heights?

Stuart: Oh, yes. Yes, the Broadway show, right?

Vincent: Yes.

Stuart: Yes. Really?

Vincent: Yes, and Jersey Boys. So she's good.

Stuart: She's pretty good. Oh, that's very fancy stuff.

Vincent: I told him if we ever do video on TWiV, can she help. He said she'll make you look like Johnny Depp. [Laughter]

Stuart: I would hire her right away.

Vincent: That's a great story. So basically—I don't know if today you could do that. I would say to people if you want to do something and make a switch, just do it if you're passionate enough about it.

Stuart: I think so. I think if you are passionate enough about it and you're willing to stick with it, you can do it but you have to find people to help you out. I don't think you're good on your own. You need good mentors. It's a responsibility. We all have to be good mentors as well. I think we're not appreciated enough.

Vincent: Sometimes we get letters from listeners who have bad mentors and they want to know what to do. So probably they have to switch.

Stuart: I think so. I don't think you'd change the spots on the leopard in that particular sense. I think you just have to jettison that one and go on to someone else.

[0:11:50.6]

Vincent: Alright, let's talk about "Ignorance." I love the first quote. "It's difficult to find a black cat in a dark room especially when there is no cat."

Stuart: Yes, is that a perfect description of science? Is that what we do every day?

Vincent: Yes, that's a great one. Let's define "ignorance," because as you say in the book there are two different ways to look at it.

Stuart: Yes, of course, I use the idea of ignorance both as a course title and as a book title to be sort of intentionally provocative I suppose and I don't, of course, mean that kind of ignorance. That's just simply a word for "stupidity" or worse than that, the kind of wilful stupidity, indifference to fact or data or empiricism. I think the ignorant, I think we all agree, are unenlightened, unaware, uninformed. Unfortunately, often occupy elected offices but that's another story altogether I guess. No, the kind of ignorance I mean I think is best expressed in another quote that I use in a book from James Clerk Maxwell, a physicist, perhaps the greatest physicist between Newton and Einstein I guess some would say, who said that the prelude to every great discovery in science is thoroughly conscious ignorance. That's the kind of ignorance that I think we mean and I think he's absolutely right.

Vincent: Was that your choice or did your editor have that title for the book?

Stuart: The title of the book is more or less my choice "Ignorance." The "How It Drives Science," was the editors' decision. They weren't sure how it would play otherwise. I think they were probably right.

Vincent: Your course had been named "Ignorance" long before that, right?

Stuart: Yes. So the course had been running for about four, almost five, years before I actually dug in and wrote a book on it. That's just called "Ignorance." I think it's called "Ignorance: A Course about Science." Sometimes I'd subtitle that so people have some idea—what's it about.

Vincent: I know you mentioned in your book that if you're taking a course in Ignorance, is it good to get an A or an F?

Stuart: Yes. That always puzzles the students on the first day we talk about grades. I say, "You want to think carefully about this. In your transcript that's going to say 'Ignorance.' Do you want to have an A or an F after that?"

Vincent: Right. That's a great course. So how does the course work? What do you do?

Stuart: Well, the course is a seminar course. So it meets once a weeks for about two to two-and-a-half hours. I usually schedule it in an evening because it seems to be easier to get people together then. So we meet from six to eight, usually Wednesdays evening, it doesn't really matter. So it's 15 times a year basically that the class meets. About half of those meetings, more or less, we discuss various bits of literature both primary and books and things like that that we read from. Questions like: are there limits to science; can everything be known; what's an appropriate question for science; what's a fact; how long does a fact last; do facts come undone; when do we think a job is finished, when do we don't; how might we decide about what questions to ask or how do you make questions. Variety of things of things like this. So it's a little bit of philosophy and history of science although I'm neither a philosopher nor a historian of science but we at least look over some of that kind of literature and have discussion about it and readings. And then more or less alternate weeks or the other half of the weeks, I invite members of our faculty, mostly Columbia, but not only. There are many other people in New York, of course, especially and many people traveling through New York giving talks or symposia and if their schedule works out, I invite them. I invite essentially a working scientist to come in and spend two to two-and-a-half hours talking with a group of students about what they don't know. Not what they do know, not the facts that they've published and discovered and all the rest of this but what they're working on right now, how they chose that question as opposed to some other question that we also don't know why this question is more important than that one, why it's more valuable, what will happen if you do get to know that question, what will happen if you don't get the answer to that.

[0:15:42.5]

Vincent: But they have to give some background to their area, right?

Stuart: So what I usually ask them to do is to suggest a sort of a review paper, a Scientific American level paper, a Discovery Magazine paper. Not even the one that they wrote but just something about their general field. Usually it's something that they wrote but it's not always. I distribute that to the class. We talk about with the class a little bit first. And then I do a little bit of a literature search on them. I get a couple of papers from them and do my best to read them. Sometimes I can read them quite easily because they're neuroscientists or biologists, at least, and sometimes I've had physicists and chemists and mathematicians and various kinds of engineers. It's a little trickier to read their stuff but you can do it. You can kind of get through it more or less enough anyway to get with the question.

Vincent: So before you have a guest in another class, you'll talk about their area, is that it?

Stuart: Yes. Usually we distribute the papers first. We talk a little bit about it at the class before and then I usually ask the students—we have all this what we call the "Columbia courseworks"—every university have some web-based thing where the class can communicate with each other where you can post various things for them to see and all the rest. So I ask each student to come up with one or two questions that they might like to ask this person based on the readings and the discussion that we've already had and to submit those two or three days before the actual class. Then I go through them and then we, in fact, do that. So we start the class off. It's a sort of a—it's like the Actor's Studio thing except I'm not quite as creepy as that guy. I don't think anyway. Well, we just sit at a table in front of the room, the scientist and myself, and we begin the discussion. Very quickly, surprisingly quickly, students join in. They have questions. They want to know this, they want to know that. I let the conversation wander more or less where it will just like we're doing right now with this one.

Vincent: Yes. Sure. How many students do you have in the class?

Stuart: So that's a good question. The class started small and was intended to be small. First year, we have 15 or 20 adventurous students who tried it. I guess a little bit of word got around. We had a few more students the next year. I typically cap the class at 30 students. We posted online as "Available." You can check a box that says, "Cap this class at 25 or 30 students" whatever it was. That's what I've done for a few years. It was getting 25 or 30 students which seemed like a good number.

About three years ago, I apparently forgot to check the box. The next day, the day after registration closed, I opened up the course site to see how many students that were all and that, there were 95 students who had registered for the class. I thought, "Oh, boy. Now I'm in deep here." So the class is only available to seniors. I make it a class for seniors and it's in the spring semester. So it's their last semester there. So I felt bad about—it wasn't like I could go through the list and say, "We'll hold the Juniors. I can write them and tell them to take it next year." Everybody was in their last semester. I thought, "If these people really want to take the class, I'll try it with 90 students," and it worked out. I was surprised actually. In some ways it worked a little bit better. The students were even more involved and more engaged in the discussion, ask more questions than in a smaller group, which at first surprised me. Then I think—I don't really know the exact reason why—but I think the anonymity of being in a larger group helps a little bit especially in a class where—a seminar class is just me for 15 weeks. By the end of the second or third week, everybody is pretty comfy with me and they're willing to engage in discussion. When you bring a perfect stranger in every other week, then the students have to sort of start that whole—"Well, if this guy going to or woman going to take any kind of question or do I have to be a little more formal to them?" So I think it's easier actually in a larger class, it seems to work. So I've left it that way.

Vincent: I always wondered because my Virology class is growing every year in number and I would like to have more discussion but I always thought that having 80 or 90 students would prevent that but from what you say you can do it.

Stuart: In the format that the Ignorance class works anytime. I also teach a large lecture class in neurobiology and it's typically 90 to 110 or 120 students. There I would say it's harder to have a discussion. It's more difficult. You could stop and ask for questions and you get one or two but it's hard to set up a serious discussion.

[0:20:04.1]

Vincent: So I could come in and say, "Okay, I work on polio and one of the questions that we don't know the answer to is how the virus gets into your nervous system." That would be okay. That's one of the things we don't know. What I say how we're trying answer the question then or is that not far…

Stuart: No. Yes, you could say we're trying these sorts of things. So these are things we've tried. We failed for how long now. I think an interesting corollary to Ignorance, by the way, is failure. The other thing students ought to learn about science. So we often talk about that: how many things have failed, how many things we were sure would work but haven't worked, how many things worked for a while and then we learn actually that's not the way they work they come undone or this or that.

Vincent: Okay. How do you grade them?

Stuart: Well, that's always a bit tricky. Mostly it's just—I assign them to write a paper at the end of the semester. The paper I insist—first of all, because they're now a hundred of them, so many of them. They're senior, so I don't have much time to read them actually because they need the grade to graduate—so I insist they write a 1,500-word paper. The reason for this is that Columbia students have become extremely good at writing 5,000-word paper. That's the standard paper. The one thing they learned at Columbia is to bang out a 5,000-word paper. So 1,500-word paper is actually is much more difficult. There's a famous phrase which has been attributed to many different people from Abraham Lincoln to Voltaire to Ben Franklin but I think it's actually Blaise Pascal, I sort of tracked this down a bit. Pascal supposedly had written a rather long letter to a friend. At the end of the letter he ended it by saying, "I apologize for the length of this letter. I would have been briefer if I had more time."

Vincent: I love it.

Stuart: That's perfect.

Vincent: We used that sometimes when we get long letters on TWiV.

Stuart: Yes. [Laughter] So 1,500 words is a little tricky. Then they're mostly graded on the paper. It's not a tough grade. One of the reasons that I teach it for seniors and do it in the spring is that the grade doesn't really matter. It's purely selfish reason. By the time they're senior, they're either in medical school or law school or business school or whatever graduate school they're interested or they have a job that they're going for and how much can the two units of the class affect their GPA anyway.

Vincent: Do you take into consideration their class participation as we call it?

Stuart: Yes. I try to.

Vincent: You get to know the people who talk a lot, right?

Stuart: Yes. Of course, as is always the case, there are people who will talk a lot and people who will talk much less. Sometimes the people who talk less wind up emailing you later on. They want to have an email discussion with you or something like that. I appreciate that. Some people just are too shy to open their mouth in a big room full of people. That's okay.

Vincent: So what's your "Beef with facts" tell us about that?

Stuart: [Laughter] Yes, well, I may have overstated it just a little bit.

Vincent: It's okay. It's for a point. The same way that ignorance is a shock title, right?

Stuart: Right. So I just feel it's a balance issue really. I think that part of the problem—one of the difficulties is that science has become, what I call, "runs on the accumulation" model. It just seems to be an ever-expanding pile of facts. It seems impregnable I think to most people even to many scientists. Nature or Science comes every week and you'll look through it and you're lucky if you can really understand two or three of the titles, let alone read the articles. So you begin to think, "Well, what can the public have to do with this? How can we provide some access to this?" I think it's wrong in the end. It's not really about piling up facts. For some reason or another, we could go in to whatever the sociological reasons or theorize about them. Science, I think, has turned this sort of encyclopedic phase to the public as though that's what we're all built about here and that's what we all do is we gather facts

and we put them in encyclopedias or big textbooks or something. We now hide the face of the mysterious part of the operation, the questioning part, which is what we all mostly care about. So I guess just to try and balance the issue a little bit, I feel that's a good idea to try and point out that science is much more about the questions than it is about the facts. A point of fact, if you pardon the phrase, I think most scientists recognize that the facts are probably the weakest link in the whole operation. Facts change, we know that. For me, this is what makes science different than other belief systems be it astrology or even some religions or things like that. That is, in science, revision is a victory. That's what we work for. We try and revise. We overturn facts or we at least revise them. Whereas it's an embarrassment in astrology if suddenly something that's supposed to have been this way for 10,000 years is not this way anymore. So that's the difference. I think facts are culprit in some way that way. We can become too dedicated to them. You can even see it I think in your graduate students probably. That we don't really teach them enough about how to put a question together. The first thing they're worried about is how to do the experiment, how to get the fact, how to get this or that, how to fill in the bits on the table.

[0:25:23.5]

Vincent: So my take on your book was there are two issues, there's facts and teaching and then facts and research, right?

Stuart: Yes.

Vincent: So we teach facts. That's what got you to teach this Ignorance course because you said you were giving them too many facts and at the end they said, "Do I need to know this for the exam?"

Stuart: Yes. It's not your typical experience. You begin to wonder: is this what we ought to be teaching them? My favourite quote about education is from William Butler Yates that the purpose of education is not to fill buckets, it's to light fires. What we're doing is filling buckets especially in the age of Google and Wikipedia and whatever is going to follow it, whether facts or click away.

Vincent: I have to tell you after I read your book, I felt very badly about the way I teach my course because I remember the first year I taught it. It was three years ago. Before the first mid-term, the student says, "I have all this material here, what do we have to know?" So I have to give them a study sheet with the questions that would be on the exam basically or areas that would be on. That's giving them facts. How does this virus get into cells? What is it attached to? How does it make RNA? Maybe I should put a few questions in: "What don't we know about this virus?" "Tell me one thing we don't know about polio."

Stuart: I think that's a great idea. Yes, I think it would. Even a multiple choice exam, you know, those little bubbles that you fill in. In addition to "A, B, C" and "all of the above" or "none of the above" or something, there should be either "I don't know" or "We don't know" and that should be a legitimate answer to the question.

Vincent: Well, maybe if you get people like me to change their courses that's a success, right?

Stuart: It's not easy mind you. I think about it all the time too. After all, of course, part of the problem is that both of us teach courses to students who many of whom are pre-med and many of whom are going to have to take an exam called the "MCAT" and if you don't teach them the stuff that's going to be on the MCAT, they're not going to pass that exam, they're not going to get to medical school.

Vincent: The MCAT is all about facts.

Stuart: That's all about facts. So you have to change it really several levels up which is not an easy trick as you know. These things have stayed in place for years and years. Evaluation I think in general in education is maybe one of the most difficult problems around. From elementary and high school education you see the problems we have with it now trying to evaluate schools and people teaching to the test and using what I call the bulimic model of education—we jam a lot of facts down their throat…

Vincent: Yes, I understand. Let's see who's the best of spitting them back.

Stuart: Right, they throw it up on some exam and then nobody gains any weight.

Vincent: It's a problem with medical school in particular because they apparently want just people who are really good at getting great grades. That's not often going to be the best physician I think.

Stuart: I think that's true.

Vincent: You need some other kind of metric and it's not just—especially, MD-PhD applicants up here—the most overachievers I've ever seen in my life. They do everything. Makes me exhausted to read their CVs.

Stuart: Yes. [Laughter] You have the sense though that having done all the stuff on the CV, they basically done it to build the CV.

Vincent: Exactly.

Stuart: That seems to be the motive. That's what these points can really…

Vincent: I get these kids to interview, and I often interview them, they're wonderful kids, they've done so many things and they're really genuinely interested and engaged but I just feel that they're not doing it for the right reasons.

Stuart: Yes. Something that really tickles them in some way that they can't do anything else. When I was back in the theatre, I took an acting class. I wasn't sure I was going to be an actor, a director, whatever. I did okay as an actor. I did a little bit of acting here and there. I remember this fellow telling me one time, he said, "There's only one way to be an actor. The only way to be an actor is that you can't be anything else. If you cannot really see yourself living without acting then you're an actor. Otherwise, it's way too frightening to do it." I think that's exactly right.

Vincent: Same as science. Yes, absolutely. That's what we've heard. We had a few people come through who have said the same thing. If you can't imagine yourself doing anything else then you can be a scientist. If you can see doing something else, then maybe you should do something else especially nowadays when it's very tough. So we really need to fix our teaching. We have to give them some facts because, as you say, you assign a review article so the students can then ask questions.

Stuart: Sure. Yes.

Vincent: Because questions come from having facts and then we use them to tell you what you need to know.

[0:30:01.5]

Stuart: For me the purpose of a fact—of course, we do science, we go after facts, we want data, that's what we go after—the question is, what are we going to use that? What do we do with those facts? I think the idea of—the best thing to do with those facts is to make better questions. That every fact really generates a few new questions but, as I say, "better quality ignorance" is the way I like to put it because it sounds so silly in a way but it's true. There is high-quality ignorance and low-quality ignorance and that's what we think about all the time as scientists.

Vincent: There's a quote you had which was: the best research leads to more questions not facts, something like that.

Stuart: Yes. I think George Bernard Shaw on "A Toast to Einstein," it's one of the quotes that I use which is "Science never solves anything. Every time it makes a discovery it just leads to ten new questions" or something.

Vincent: Right. That's the way it should be. Not all science is like that, right? Because there some scientists who just try and accumulate facts.

Stuart: Yes. You can't completely dismiss that. There is some science that works by moving the decimal point one more notch and adding something. One of my favorite examples of that kind of science, although, it's somewhat imaginative in its own way as well is Kepler. Kepler spent I think six years battling with eight minutes of arc in the sky. The planets weren't going in perfect circles. By this time, they've been reasonably well-established in everybody's mind that, in fact, the planets went around the sun and not the other way around but we still have the tyranny of the circle. People thought they went in circles and you couldn't really work it all out until Kepler figured out that the eight minutes of arc that everything was off by was not an artifact really careful measurements. When he fixed that and realized the planets went in ellipsis then Newton made sense and it's possible for Newton. Sometimes eight minutes of arc…

Vincent: But his facts led to more questions obviously.

Stuart: Yes. Absolutely.

Vincent: And that's what is important. As you've said in the book, sometimes we reward facts and that's part of the problem. So grants and talks and papers and prestigious journals are based on presenting a set of facts, right?

Stuart: Yes.

Vincent: Cell and Nature and Science don't care about the next question, they want your paper.

Stuart: They want your paper now. That's right. Of course, if you're clever somehow or another or if you're good at this or if you gain enough confidence to do it, you try and leave the paper with the question. You try and end the paper with a question or something like that or a suggestion about where it will go. I've always thought—so many of your listeners will know this as well—but in addition to the papers that come out in Nature and Science, they're often sort of what they call "commentary type articles." It was in views of this or that. Where they ask somebody else in the field to write a commentary about this really interesting paper in that particular issue of Nature. I've always felt I prefer

to write a commentary. I hate handing in a paper. Not that I get so many papers published in Nature and Science but then a couple of papers I had and I thought, "Gee, what I really want to do is write the commentary. They give me a thousand miserable words. All I can do is dump a lot of facts out on this and there's no time for me to post the interesting questions that I think it's about."

Vincent: And probably they're different from what the other people are writing in their news and views.

Stuart: Yes.

Vincent: I always wonder how often do the authors of the article look at those and say, "Well, these are good but I have some others as well." It would make more sense, wouldn't it?

Stuart: It would. Well, that's a perfect example in many ways. I would say in some ways what's exactly wrong with science. So you take journals like Nature or Science which purport to be general interest journals. Part of the deal of publishing a paper in Nature is it's supposed to be of interest to a wide audience or relatively wide audience not a narrow specialized audience. Then they tell you, "But you only have a thousand words and you only have one paragraph for an introduction and one paragraph for discussion. It should be just the opposite of anything. A thousand words is bad enough but, okay, let's go with thousand words because there's a space problem. But then it should be mostly introduction and mostly discussion and a couple of facts in the middle and if you want to look some more up go online or whatever you need to do. It's just the opposite really of what it should be for a general audience to understand it and that's why none of us can read those papers.

Vincent: I had a colleague here years ago, Arg Efstratiadis, I don't know if you know the name.

Stuart: I don't remember that name.

Vincent: He was right next to me. He used to complain that you can't write scholarly papers anymore because it has to be so short. In fact, now where everything is online, I don't see why you can't just…

Stuart: I don't see either. Space is not an issue.

Vincent: There is a new journal eLife by Howard Hughes and Wellcome.

Stuart: Oh, yes. Max Planck and Wellcome. Yes.

Vincent: They're supposedly allowing you to run wild with your words.

Stuart: Oh, that's interesting. I've had a sort of—I tried to pitch this a couple of times to one publisher. I was still hoping that Columbia University Press may do it one time. I think it would be interesting to take the ten "best papers of the year," however you want to charge that up. You put a committee together or whatever you want. Papers that were in Science or Nature or any of these others sort of high-end journals that have serious restrictions on space though. Then go back to those authors and ask them if they would be interested in writing a somewhat longer article with the help of a writer, if you want a science writer, who really let them kind of develop the ideas in a paper more, who really explains a lot about the paper, to give some background on the paper, that talk about where they hope to go with or how they came to it or things of that nature. I suspect there'd be an audience. I think it would be fascinating to have this wider view of this really interesting papers. You could bring this out once a year.

[0:35:40.9]

Vincent: Absolutely. Yes, that's a great idea. I like that. One of our colleagues in the city, Arturo Casadevall, he's a chair of Micro at Einstein. He and a colleague of his, Ferric Fang, wrote two papers about what's wrong with science and how to fix it not too long ago. "Reforming Science," they were both called. One of the issues he talked about was we have too much competition and that leads to imbalances and fraud and all the bad things in science. That's because we have competition for papers in the best journals for grants, for Nobel prizes, and other kinds of prizes. Really, those are all competitions for facts, right?

Stuart: I guess they are. Yes. That is the problem at the base of it. Yes. It seems like it used to be less competitive and somewhat more maybe collegial. I guess the reason for that is that at one time there seemed to be more money around. Maybe there were just fewer of us doing it and so there was more money around. Science wasn't quite as expensive as it's gotten now so you could run it on less money. Of course, that's always the case. When the money run short and everything else becomes extremely competitive and probably not for the best purposes. I think that's right.

Vincent: I just think that in light of your ideas about finding out things that lead to more questions, maybe those aren't the findings that always get rewarded.

Stuart: I think they're often than not. Certainly the question, you rarely get rewarded for the questions, you know that. Of course, you have people who want things settled. That's not the way science works. Science doesn't settle things. This is the one area I must say where I would write the book again. I would write another chunk of it that I think I probably left out and should have spent some more time on. That's this notion of uncertainty and doubt in science. Because it's become very important in things like the climate issue where there are those forces, for their own purposes, that were trying so-called "deny" the issues of global warming and so forth. They do it by claiming, "Well, we just don't know enough yet." The science is too uncertain or this or that because scientists are, to be honest, uncertain about this or that or this chunk even though we know a lot. I think it's important to recognize that unsettled science is not unsound science. That's real science.

Vincent: Sure. You mentioned the problem with grand proposals and prediction. You have an issue with prediction as well. Let's talk about that.

Stuart: Okay. It's not so much that I have an issue with prediction. I think the great thing about prediction is that it's predictably wrong typically. They were so bad at…

Vincent: I was going to say there had been times in science when people put a claim that something is settled, finished over. The one that comes to my mind is in the '60s. The Surgeon-General said infectious diseases are finished.

Stuart: Really?

Vincent: Yes. Because we had antibiotics. They seemed to be working. There was not much resistance and then everything exploded and now, of course, they'll never be gone. There are other areas in science and you talked about a few of them in your book where people have claimed that this is solved, right?

Stuart: Yes. Well, people today, I think, would probably say if you said geography, they'd say, "That's not really science, is it?" That's all pretty much settled. "How many times can you discover America?" as they

say. It's not at all true. We still have the geography of the oceans. We have planetary geography. We have all sorts of new ways of mapping things. Some of the most sophisticated computer programs now were actually aimed at geographical mapping of things. These things almost never seem to really close. When they become close for a time it's just because we haven't figured out what we don't know yet.

Vincent: That's the key really. Science is never finished. We never will understand everything because when you do discover something it just leads to more questions.

Stuart: That's right. It opens up a whole new tunnel, another black room with some more black cats that maybe wandering around in there. Maybe they have already left for some other place who knows.

Vincent: Okay. So back to predictions. Grant is a way of predicting what you think is going to happen, right?

Stuart: Yes. I guess this is tied up on the notion of hypothesis which I also maybe…

Vincent: You hate that too, that's right. You actually wrote that, "I hate…"

Stuart: I hate hypothesis. [Laughter] Well, I've grown to hate them.

[0:40:00]

Vincent: You didn't hate them when you started out probably?

Stuart: No, they seemed like a reasonable idea then but I think they've become something that inappropriately runs the show. They have even become misunderstood by scientists let alone the general public.

Of course, the original idea of a hypothesis is Popper's philosophy of science and the trick is to have a falsifiable hypothesis. In other words, what you are supposed to be doing is proving it wrong. That's the only way a hypothesis is really of scientific value. Otherwise, they become little bits of little belief systems, little clubs, little cults. Because, after all, a hypothesis is your best idea of how something probably works. Well, who wants to be wrong? Who gets paid for being wrong? Unfortunately, very few of us.

Vincent: You think we set it up to be right?

Stuart: Well, I think so to some extent. Even if you work against it I think you can't be completely unbiased. It is foolish to believe we can be. So naturally you think of the experiments that are likely to prove it or you look at the data a certain way, you have an excuse for throwing this outlier or data point out, one way reason or another—Tuesdays, nothing ever works on Tuesdays—whatever silly there had been. Sometimes there are good reasons. You did have a junior person new in the lab working on the experiment. They got that crazy data point so out it goes. But it may very well be because there was a junior person working in the lab who hasn't yet been indoctrinated in the way to do it that they got that interesting outlier and that's really where we ought to be looking.

So I think hypothesis are difficult that way and, of course, my personal huge objection is because I am a biologist and get money from the National Institutes of Health, as you do. As you know, NIH grants are supposed to be written as hypothesis-driven research. As you know the worse comments you can get from a review section is, well this is just a fishing expedition or this is just curiosity-driven.

I'm thinking, "Really? We are all on a fishing expedition here?" I mean who are we kidding? What's better than curiosity driven?

Vincent: So you think that we should abandon this idea that every proposal has to be hypothesis driven?

Stuart: I do, yes.

Vincent: Because look at what people are doing now. They are sequencing the microbiome of different human surfaces and cavities. Isn't that a fishing expedition?

Stuart: Absolutely it's a fishing expedition.

Vincent: But it is interesting and that's why we are doing it.

Stuart: Yes. There are going to be some fabulous fish that come out of this.

Vincent: And that's because we are going to have a billion questions come out of that, right?

Stuart: You can see. We thought the genome was going to answer a bunch of questions about genomics and genetics in humans. It has, but what it has really shown us is that what only about 10% of the genes that reside in our body. If you ground a person up as it were—I am not suggesting that mind you—but if you just ground a person up and sequenced all the DNA in them you would find out that 90% of the genes are not human—they are bacteria, viral, plasmodia, whatever they are. Somebody else is living in there.

Vincent: Yes, I think that the whole way that, at least NIH gives out money, is flawed. I see so many proposals. If you do not have everything lined up—so the reviewers can tell what is going to happen and it will work, then you are never going to get your money. That's terrible. That's not the way scientists—you should be doing experiments. You should be doing research.

Stuart: Yes. Of course, I mean, the only upside of that is that they give you the money for five years and then they don't bother you really. You can pretty much do what you want.

Vincent: So if you can play the game at the right stage then you can do it. That's, in fact, what most people do. They go off and do other things.

Stuart: Of course, so its grantsmanship and gamesmanship but it's not the way the system ought to work. It is a shame because the system is very close to working appropriately if it—we're just either a little bit better funded or a little bit—I mean it is ridiculous. What is worrisome about NIH is all the fabulous research that doesn't get done. What is the difference between a grant that is in the top 15% and top 16%?

Vincent: There's nothing. In fact up to 30% I would argue they are all really worthy.

Stuart: This is already a highly selected population. You can't put a grant in unless you are an investigator with a laboratory in some accredited institution with a PhD. At the very least it is not like a normal bell curve even.

Vincent: In your field, do you do olfaction still?

Stuart: Yes.

Vincent: I presume you write your grants in a hypothesis-driven way?

Stuart: What choice have I got?

Vincent: If you could write a fishing expedition, what is something that you could do?

Stuart: Well, we did sort of write a little bit of a fishing expedition. It was a genomics grant. When the first sequences of human and mouse genomes were becoming available, we were interested in specifically the olfactory genome. It turns out that there are this whole large number of receptors in your nose that detect all these odors. They are the largest gene family in the whole genome. They are very much like receptors that are used in many other places in the body for detecting dopamine and serotonin, acetylcholine and all these chemicals in the brain that we now think make us depressed or happy or this or that, reward, et cetera. They are very similar.

We thought this is a really interesting area to be in now. We simply wanted to fish around in the genome and pull out all these olfactory receptors and so forth. That was a grant that went through and was a very successful program because it was in the—I mean it was criticized as being a fishing—in fact, I wrote the grant and I said in the grant, "I know this sounds like a fishing expedition and it is but it will definitely produce data that will be of use. I just can't tell you what the use will be for sure." They sort of swallowed that but that is the closest I've ever gotten.

[0:46:00]

Vincent: So if I wrote a grant application to say I want to go and catch mice and find out what viruses they carry it probably would never see the light of day.

Stuart: No, because it's fishing.

Vincent: But it would be really interesting for a number of reasons that you could elaborate. You could make it compelling but still they would say, "But what is the hypothesis?"

Stuart: Yes.

Vincent: That is problematic. I don't think we should do that. I think really that grant applications need to be much shorter and they should depend largely on the investigator and their track record. Give us a

general idea of what you want to do for the next five years. Looks good, this person is productive, give them the money.

Stuart: The last part of it, I go even a step further with you. I'd say you have to spend a little bit of time and effort writing your first grant where you lay out a research vision. What you see as being—identify several critical questions that you believe the tools are available to work on and, therefore, you would work on them.

If you get the funding then you have five years and you see how productive you are. That grant should simply be renewed based on productivity because there is really no other decent measure. If you have been productive for five years then give them another five years. What is the worst that can happen? The last five years the person is not productive and then that's it.

Vincent: I agree with that. I think the idea of—at least the length of applications has decreased.

Stuart: Thankfully for that.

Vincent: The other thing that I wanted to explore with respect to funded science is this, you talk about it as a dichotomy between basic and applied research. The applied part I guess you mean "translational" which is the buzzword now.

Stuart: That is what it is called now, yes.

Vincent: We had a fellow here not too long ago, Jon Yewdell, talking about science careers. He said translational research is actually not research because you just wanted to see if something does something. You don't really do setting up a question and trying to answer it.

So, you say that they are both the same, right?

Stuart: I think they are in the best cases. He's right in the sense that translational research is not is itself at the final stage of it or whatever—maybe not research, it is an engineering kind of solution or something like that maybe—but I think what's the best kind of translational research, and I'm not against translational research, I love the things. I like having a flu virus vaccination and things of that nature. That's good by me.

But I think translational research is a kind of basic research that already decides it has a point. That it is directed towards the possibility of translation. It is devoted to a specific disease not to an underlying fundamental process of how cells work or things of that nature. How the Higgs Boson is—nobody can imagine what it will be about but who knows. It is the future right?

Charles Townsend, who was a member of the Columbia faculty in Physics in the 1950s, invented the laser, was ridiculed by his fellow faculty. I mean there are these famous stories down there of people telling him, "Will you stop—what are you messing around with this collimated light nonsense for? Get to work on something useful. You are not going to get tenure." The man invented the laser.

Vincent: There are so many stories like that—Taq polymerase, *Thermus aquaticus*—who knew what that would be? Go look at these hot areas and see what's living in them.

Stuart: Retroviruses—that was a chicken virus, right? That was a poultry experiment.

Vincent: You have to let smart people do what they think is best.

Stuart: Fish, you have to let them fish.

Vincent: Let them fish. That is the only way. You have a good section of your book where you give a lot of examples of things that happened. Serendipity that turned out to be really useful. And that goes back to prediction, right?

[0:49:50]

Stuart: Let me say a quick word about serendipity because I think it is sometimes used in the wrong way. I like serendipity. I agree that an awful lot of what happens in science seems to happen kind of somewhat unpredictably. But it is also true that it is not pure serendipity. Lawyers don't make serendipitous scientific discoveries. Scientists don't make serendipitous judicial ideas either or have them. I think you have to be on a search. You have to be there. It is more like what Pasteur said, "Chance favors the prepared mind."

Of course, you know, Pasteur was the beneficiary of a great deal of serendipity but he was right. He was thinking about it. He was thinking of something. He was out on a fishing expedition, as it were.

Vincent: I think you say it in your book, you have to be asking good questions. You can't just be randomly be looking here and there.

Stuart: You can't be just hoping for the best and thinking something will fall on your head.

Vincent: I like to cite restriction enzymes. In the fifties the people knew that if you took DNA from one bacterium and put it in another it would get digested. They wanted to know why. But they weren't thinking of making recombinant DNA. They just wanted to understand what… and maybe they get a clue about immunity or something. It led to restriction enzymes but in itself it was good science.

Stuart: Yes, the whole biotech industry and all the molecular biology, yes.

Vincent: It was good science.

Stuart: That's right.

Vincent: So that's your point. You have to have good science. You are not going to just wander around.

Stuart: There is a great story about Albert Einstein, may be apocryphal, but when he first got to Princeton he was being interviewed by a reporter from the Princeton newspaper. Somewhere during the interview the student said, "Well Professor Einstein do you carry a notebook with you to write down all

your great ideas?" To which Einstein supposedly responded somewhat sheepishly, "To tell you the truth, I don't get that many great ideas."

Vincent: That's great.

Stuart: How many do you need? I mean 1% of the ideas come into fruition would be a bounty.

Vincent: I don't know if I would have answered it that way. That's why he's a better scientist. I would have said, "Yes, yes. I keep these notebooks…"

Stuart: I never look at them.

Vincent: I think it is good to write them down even if they are not good ideas. There are so many things. Here's another one. There is a joke in your book about looking for keys under a lamp. Can you tell us that and how that fits in? It's great.

Stuart: It is sort of a classic one. I think there were many of us who tell graduate students. It is a story supposedly about a scientist, although I've heard it of others too, but there is a scientist who's standing around outside by cars under a lamp light and looking on the ground. Clearly he's lost something. A passer-by comes by and says, "Did you lose something? Can I help out?"

The scientist says, "Yes, I lost my keys. I can't find them."

So they look and look and five, seven, ten minutes goes by and they don't find them. Finally, the guy says to the scientist, "Are you sure this is where you dropped them?"

The scientist says, "No, I think it was down there." And he points to some dark corner of the street.

The guy says, "Well, what are you looking here for?"

The scientist says, "Well the light is so much better here."

This is perfect. This is exactly what you do.

Vincent: Einstein also said in a different way, "I have no respect for people who take a board, find the thinnest part and put all the holes there." It's the same idea. You have to go beyond your comfort area or what the field allows you to do, I guess. That's really it.

Another thing I wanted you to talk a little bit about which is another—"All models are wrong but some are useful."

Stuart: George Box, I think.

Vincent: That is what he said, right?

Stuart: Yes.

Vincent: Talk a little bit about models. You use a model to study olfaction.

Stuart: Sure, we all do. I guess, I always think that when you talk to students, to begin with, and then when and if you have an opportunity to talk to a wider public it's one of the most important ideas in science to explain to people because I think it is one of the easiest to be misunderstood. People think you work on the brain why don't you just work on brains? Well brains are hard. It's a hard thing to work on. It is big, there are a gazillion cells in it and they do a lot of complicated things.

So more sensibly using the light-from-the-lamp-post metaphor if you will, we work where the light is a little better, where you can do something in a somewhat smaller system that nonetheless seems to be a good model for the larger system. If you learn some fundamental things about the smaller system, you have learned something about the big system too and then that lets you move up the ladder a step or so.

We use these model systems but sometimes they can sound quite silly or strange or funny or like a waste of taxpayer money. That is kind of the problem with them I suppose. That's what we fail to communicate clearly, that choosing the right model system is one of the most critical things a scientist can do because you've chosen a system that is amenable to making discoveries, to experimenting, to manipulating and understanding. Even though it is not the thing itself, it gets you a step closer to that thing.

Vincent: Do you think most non-scientists understand that we can't do most of our research on people and therefore we have to use, say, an animal? Or is that even hard?

Stuart: I think even that may be harder. Whether it's valuable to do it—now, the idea of the laboratory mouse is sort of part of the culture. I think people do sort of understand that because you read it in the paper all the time.

Somehow or another we went from guinea pigs to mice. There was a time when guinea pig meant just that, right, an experimental sort of…

Vincent: Yes, that's right. Don't be a guinea pig.

Stuart: Almost nobody uses guinea pigs any more that I am aware of, to tell you the truth. But what I think the public often doesn't know is that there are many other interesting systems one could use besides mice that seem weird.

I started my career off studying the sense of smell in salamanders. Now it's not because I care how salamanders smell particularly. But I understand somebody can look at my grant proposal which says the molecular physiology of olfaction in salamanders and go, "This is my tax money? I am paying for this nonsense?"

It is easy to make fun of but there are good reasons to do it in salamander before you try doing it in a mouse or even a person. It is a simpler system. They are cold blooded and easier to maintain. They are not endangered. There are all sorts of reasons.

Vincent: People will not understand that unless it is explained to them.

Stuart: I think that is right. That's a hard explanation to make. I agree.

Vincent: A science writer-journalist probably won't be able to do that.

Stuart: No, I don't think they have an appreciation for it in the same way that a working scientist does.

Vincent: A real key is, let's say you discover things in a salamander, how do we then figure out if it is the same in people?

Stuart: Yes, how many times have we cured cancer in mice? I mean no mouse ever need die of cancer.

Vincent: That is the leap that is harder to make, right? I mean I personally have trouble explaining it to people, how we get from mice to people.

Stuart: It doesn't always work. Of course, one of the ways that we can explain it, and I think is a sensible way to explain it, is we believe in evolution. Part of the idea of working in mice in order to find things that will work eventually in people is that we realize that there is a certain continuity in physiology and everything else about us because that's how evolution works. We are not perfectly continuous because it has been 80 or 90 million years since we shared a common ancestor so we diverged significantly. But, in the end, mice have a four-chamber heart like we do. They have a liver. They have all these things.

Vincent: Also the olfactory genes in humans and salamanders are probably similar right?

Stuart: Yes.

Vincent: At least structurally somewhat similar?

Stuart: Yes, they're structurally they are very similar. It is the same kind of a protein. Even many of them are very, very similar. They've been retained because the same odors are out there in the world now as when salamanders were walking around.

Vincent: I guess if you want to develop eventually from your research products to help people's health, something to do with olfaction. I don't know. What's a drug that you could make that would target olfaction? Eventually you got to test it in people, that's what I am saying.

Stuart: Yes.

Vincent: Not all research goes to that point but eventually if you want it.

Stuart: Well I'll give you a quick example in olfaction. A couple of years ago, I was at a meeting, a biophysics meeting, and happened to pass by a poster. It was an anesthesiologist who was working on rhodopsin, which is the molecule we use to see with. It turns out—this is going to sound crazy and I won't bother to explain it—but that rhodopsin, this molecule we use to see light with, is very similar, the same receptors we use for odors and dopamine and serotonin neurotransmitters and all that. This was an anesthesiologist, I couldn't figure out what he was about. So I went over and piqued my interest.

We had a conversation. I said, “Let me ask you something, these anesthetics you work with, these inhalation anesthetics like halothane and isoflurane and all that, do they have odors? Because I know ether does.” Ether has—even though we don’t use it anymore.

He said, “Oh, yes. They have very distinct odors. In fact, trained anesthesiologists will often use their nose rather than their equipment to be sure that all the gas is cleared and stuff like that.” So I thought well if they have an odor they must be activating receptors in our nose. Just by accident, of course, because we have so many receptors in our nose they are binding to some of these. But if they are binding to some of these, then they may be binding to other receptors in the brain that are like olfactory receptors; that are like the odor receptors.

Now I don’t think that’s actually how anesthetics work. I mean there are lots of—it is 150 years we have had them and we don’t really have a clear explanation on how they work. It is a great area of ignorance. I don’t believe that that’s how they work. But I do believe that that maybe where their side effects come from. That binding to these particular kind of receptors in the brain and elsewhere could be how the side effects come about from anesthetics. It was kind of unexpected.

Vincent: Yes. So that is something you could eventually test but you would have to do something in people.

Stuart: Yes, so we know now that there are about ten or so receptors in mice that bind these molecules and we know there are similar ones in humans. Now we could go ahead and look for it in humans.

[1:00:25]

Vincent: I always make an argument that you can’t use results in animals to predict what is going to happen in a human.

Stuart: I think that is probably true. It can put you on the trail.

Vincent: Of course, it puts you on the trail but eventually you have to do other experiments in people. The example I use—last year there was a brouhaha about avian influenza, H5N1, in ferrets. The fact that they could be transmitted through the air in ferrets, a lot of people took to mean that they would do the same in people. That really bothered me because they are models.

Stuart: That’s right. There is no evidence that that would be the case.

Vincent: People say, “But, yes, but it’s the best model.” It still doesn’t mean that you can predict. That’s why I wanted to emphasize that you have to always take what you learn in your model and somehow figure out, if you wanted to be directly applicable to people, if you want to make a drug or a vaccine, you have to do it in people.

Stuart: Yes, you have to really do it in people. I agree. We are like nothing else.

Vincent: There is no other way around it.

There is another cool thing you said that I wanted to just bring up. Listeners will like it—"Don't ask scientists what they do, ask them what they are trying to find out."

So you are sitting on an airplane, the person next to you—"What do you do?" But don't you think that most scientists will actually say what they are trying to find out?

Stuart: Yes, I think so. The real trick is to not let them get away with that in a way. We become conditioned to do that. We just dumped a lot of data on people. That is what we are used to talking about. But if you really—I think the trick is, if you want to have a great conversation with that scientist ask them what it is that they are trying to figure out, not what they recently published or what they are doing.

The story I like to tell about that is this—I believe a true story that took place between Chaim Weizmann the first President, I think, of Israel and the namesake of the Weizmann Institute which is their big research institute in Israel.

He was actually trained, I believe, as a chemist although I don't think he ever worked as a scientist. In any case he and Einstein were on an Atlantic crossing together on a ship. I guess they were going to be on this boat for eight or nine days together. Weizmann determined that he would spend every morning—Weizmann and Einstein would spend every morning for two hours sitting on the deck and Einstein would explain relativity to Weizmann. And you think, "Well, this is a great idea," right. "Wow, if only I had Einstein available I could actually have him explain relativity to me."

So at the end of eight days, and having done this, they get of the boat and Weizmann was reported to have remarked that he now believes that Einstein truly understands relativity. But he had no idea, of course. But if you had asked Einstein the questions that were now open because of relativity: what are the new ideas, what's going on with those guys in Copenhagen and how do we understand the world differently, then I think he would have gotten an earful and he would have been fascinated by it.

Vincent: Yes, a wasted opportunity. I think that I have had some really interesting people ask me that and then said, "But, no, I don't what to know what you've done. I want to know what you are going to do or what you are doing." So it is just the same idea, right?

So to all the listeners out there who are not scientists, if you ever talk to a scientist that is what you should ask them.

Stuart: Otherwise, we'll bore the eyes right out of your sockets.

Vincent: What is it that you are trying to find out? That's the question. So get that ready. So you think that given that most scientists would be totally comfortable, right. They should be.

Stuart: I think they should be, yes. They should be. I mean after all—so people that come to my class often say to me, "Well, what should I do to prepare?" I always tell them, "No PowerPoint. For sure, no PowerPoint." "What should I do to prepare?"

I say, “You don’t have to do anything to prepare. You are prepared every day you walk into your lab, every morning, that’s how you are prepared. You are there with a set of questions.”

Vincent: Bring your curiosity.

Stuart: That’s how you come to the class.

[1:04:10]

Vincent: At the Café Science the other night, there was a high school superintendent actually from New Jersey. He says, “What’s the best thing you could tell kids in, say, high school or ever earlier to make sure they are prepared for science?”

I said, “Make sure they are curious.”

Stuart: Absolutely.

Vincent: Look around the world and want to know how it is all working. Because you find kids that say that then they are the ones that will be scientists.

Stuart: Yes.

Vincent: Be curious.

Stuart: Yes. Of course, we beat that out of them pretty well. As Peter Galveston pointed out to me the other day, I was hoping to cover—he is a historian of science and an astrophysicist at Harvard. I had a meeting with him. Anyway, there’s a sort of a discussion at the table. He said, “Well, the amazing thing to me is that in second grade about 100% of the kids are interested in science. But by twelfth grade about 3 percent are. So we have developed this fabulous system for beating an interest in science out of our students apparently.”

Vincent: We give them too many facts. We want them to regurgitate facts.

Stuart: That’s it and we select for the ones who can.

Vincent: Yes, exactly. Unfortunately we don’t teach them how the facts were obtained which would be good.

Stuart: Yes.

Vincent: Now I had a great high school biology teacher who did just that because she had done some research. I attribute to her the reason I am in science today, one of the main reasons, because she made it cool. “Wow, this is how you do science.” She told us how you would go in the lab and set up an experiment and how carefully you had to be. That’s what we need but it is hard to do unless you have actually done science.

Stuart: I think that's part of it and unless you want to take the extra time. Of course, it is hard for teachers these days because everybody gets tested and they get tested on the facts.

What I think is a more effective way of teaching a subject is to try and recreate for kids at the level of ignorance that existed when that discovery was made. Try and put yourself back in the place of a Galileo. It is an interesting story about Galileo who measured acceleration and gravity and all that.

One of the terms in his equation, which is simple but hard to remember if you don't care about it, is time. Time squared (t2) in fact as it turns out. That is all fine and dandy until you say to the kids, here is the only thing, there were no watches in Galileo's day. They hadn't invented time pieces yet. Yes, people could measure a day or a month or a year, but there was no minute. There were no seconds. There was no stopwatch. How did he make these measurements?

Oh, well, I don't know. I don't know, we didn't know about time. We didn't know about inertia. Well, it turns out he used his pulse and then he used a pendulum. So you have to be clever. Once you learn that. And then you say—well, you know those awful inclined planes? You roll a ball down an inclined plane and measure it? What is that? That is so boring. It is so dreadful. But if you realize that the reason for that, Galileo did that because he needed to slow gravity down. His pulse wasn't fast enough to just drop the balls from head height. He couldn't measure it. But he could slow it down by putting them on an incline plane. They will still drop through the same vertical distance but take much longer to do it. Then he could work out a calculation.

Well, that's a clever idea. How would you slow down gravity? When you think of an inclined plane that way, it is interesting, isn't it? Otherwise, it's just a boring physics experiment.

[1:07:29]

Vincent: That is how you have to teach it to kids and they would love it I think.

Stuart: I think so too.

Vincent: But not everybody can do that. I think one of the things we have to do moving forward is to try and get teachers at the elementary and high school levels to know more about how science is done, not just the facts.

Stuart: Yes, and to give them the opportunity to do that. The problem with it now is that they are simply overwhelmed with the requirement to get through a textbook for a test that is coming up and an evaluation that will decide whether they get a raise or get fired or something awful.

Vincent: As you said earlier we have to change the way we evaluate. We have to change the whole thing.

We do have a nice program here in the city. It is a Hughes-run program to get high school teachers in the lab for the summer.

Stuart: I had one this summer in my lab. She was fabulous. She will be back again next year.

Vincent: They can be very good. I've heard great stories of how these individuals go back and they do totally different things. I think we need more of that. I'd be happy to have someone in my lab doing that.

Do you find that having written this book you were meeting different people than you would if you were just a neurobiologist?

[1:08:29]

Stuart: Yes. I've never written a book before. It's not typical for a scientist to write a book. A few do but normally we write papers and all that. We travel in an ever smaller circle it seems. Yes, it has been kind of interesting that way. It can take over a little bit. There is a side of me that would actually like it to kind of stop. You get caught up in this sort of slipstream of the book. People call you. They want you to come give a talk here or there. The most interesting one, I suppose, was a fellow named Jeff Middleman who is a rabbi in a synagogue in Westchester, New York who wrote me and said that he had just read the book and he intended to use it as an inspiration for his Yom Kippur sermon. That's kind of remarkable.

So I wrote him back and I said, "Well, please send me a copy of it so I can send it to my mother, who will at least get a kick out of it." He actually wrote quite an interesting sermon. It was rather nice. We have since met. We had lunch together. From a completely unexpected corner, I have to say, I would not have really not have expected it from a religious corner.

But I have gotten several phone calls and emails from priests, preachers, chaplains, rabbis and artists that I would not have expected. So that is always pleasing, very gratifying.

Vincent: So you can see that the book is having an impact then, people are getting ideas from it?

Stuart: Yes, which I will say is very gratifying. One of the most interesting, I have to say very quickly maybe is that an audience that I didn't expect, since we were talking about this a moment ago, an audience that I didn't necessarily expect or I hadn't anticipated at least would be interested are secondary school teachers.

I've gotten I'd say half the emails I get and if I am on a call-in radio show half the calls I get are from secondary-school science teachers who say this is what we need to be doing with our students. How can we do this? How can we introduce this into the curriculum?

Vincent: That's great.

Stuart: I think that's fabulous. I'd love to see that happen. I'd feel so gratified by that.

Vincent: You know you can make an impact in science but when you go outside into the real world to make an impact is really good. So that leads us to the last thing that I wanted to talk. I know I've kept you more than any of your other interviews. That's my style. I like long form. I think there is a subset of people out there who like it too.

You make the point at the end of your book that scientists—well, we get money from the people so we should explain to them what it is that we're doing. They shouldn't depend on papers and other forms of the popular press to get their information. Why do you think that's the case?

Stuart: Well, I think it is the case because for the obvious reason that they pay for it and deserve to know something about it. It's clearly one of the key features of modern Western culture. I would say modern almost global culture. It is true there are, I suppose, places in the world where science is not crucial or a part of the culture.

Vincent: As far as they know.

Stuart: As far as they know, that's right. But in general I'd say science is one of the most important things in our lives. We are all quite happy to use the next gadget or take the next drug or procedure and are happy for it. We should know something about this fabulous adventure that is what it is. It is only recently, I think, as far as I can tell from an historical perspective, that science is becoming so divorced from the public that both supports and uses it and would find it interesting.

In 1800s England it was common for there to be performances. People would go to Albert Hall and pay money for a ticket to go see science demonstrations of magnetism and electricity and things like this and hear lectures on it. Darwin's *Origin of Species* was a best seller. He was already wealthy but he got quite a bit more wealthy on the sales of *Origin of Species*.

Vincent: Weren't there public debates in Paris over spontaneous generation versus Pasteur and….

Stuart: Oh, yes. They would have big crowds. There was real involvement. I think that that's healthy for one. I think when you don't do that then you—well, my favorite story to tell in this is the Galileo story which we all think we know about. I thought I knew about it. Galileo got in some trouble with the Church fathers and all that, the authorities for championing this idea that the heliocentric solar system, that the earth went around the sun and so forth. But actually it seems to turn out that what Galileo really got in trouble for was not so much the ideas, which there is fairly good evidence I gather that the Church fathers knew as well because they were the educated class as well. It was in the wind. Everybody knew this was really going to be the case but I think they hadn't quite figured out how to explain it to the populous yet.

What Galileo did was, because it was the height of the Renaissance and so forth, he published his book, *The Dialogue on Two Chief World Systems*, I think, it's called. Published a book about this in Italian, the first time a science book had been published in a vernacular or common language as opposed to Latin or something like that. That made it available to a much wider audience. That's what kind of pissed the church off. But it started a huge tradition of that. So Descartes wrote in French, and Hooke in English, and Leibnitz in German and so forth and so on.

So now the public became involved and interested in science. I gather there are numerous historians who believe that this was actually crucial in the transition from the kind of magical mysterious kind of

world of the Middle Ages through the Enlightenment to the more empirical scientific world of the Enlightenment.

I think we are seeing a reversal of that now as science becomes less available to the public, we do see people going back for a kind of magical mysterious explanations of events. So terrorist acts or hurricanes occur because there are too many homosexuals in New York or New Orleans or wherever or we are not living the right life or other explanations that are not real explanations whatsoever.

Vincent: Why are we going backwards then?

Stuart: Well, I think because science is becoming as inaccessible to the public now as it was as when it was written in Latin. And that's, to some extent, our fault.

Vincent: Which is sad because the internet makes it accessible to everyone. There are things like TED Talks and podcasts.

Stuart: You should see how popular those things are. I mean these TED Talks are amazing. They cost a fortune and they sell out overnight. Then they are available online. Hopefully that is beginning to change. And there are things—there are people like you.

Vincent: There are certainly interests out there. I think you said less than one percent of the population does science. Is that in your book?

Stuart: No, it is not but I bet that that is probably right.

Vincent: I read it somewhere and the rest of the world doesn't and needs to understand how it works. So you think the scientists are the best people to explain it?

Stuart: Well, I do. Not every one of them. We all have colleagues that we actually don't want to talk science with—never mind talk to the public. But that's true in every field, of course. But, yes, I think there are some scientists who are capable of communicating.

One of the difficulties I think is that if you—I worried about this when I wrote this book and I'm sure you get this comment to some extent too for the time you spend on these podcasts and putting this work out and your blog and all that. If you are a serious scientist, is this what you should be doing with your time? Or should you be at the bench? Should you be in the lab?

Well, I think, yes. If you are capable of doing it or you enjoy doing it and it works then I think you are doing a great service to science.

Vincent: Yes, I tell people that you don't have to do as much as I do but just do something. Do a little something and if all of us or most of us did a little something communications-wise it would probably help.

Stuart: At least, people wouldn't flee from us at cocktail parties.

Vincent: Exactly. I think that there is a big desire to understand science out there. Most of it is inaccessible. Science writing fills an important void. I think people like the Science Times once a week. People really like that because it's pretty well written science but it is not coming from the heart because they are not scientists. I think that, with a few exceptions, they are missing out.

I think you made a point in the book also that a non-scientist cannot understand the whole role of failure and how it drives science. You're fearing failure but you do want to take risks and ask questions that you don't know the answer to. If you haven't done science, you can't know that.

Stuart: My favorite quote in the book may actually be from Enrico Fermi the famous quantum physicist who used to tell his students apparently that if you do an experiment and it proves the hypothesis you've made a measurement. If you do an experiment and it doesn't prove the hypothesis you made a discovery.

Vincent: That was very good, yes. I like that very much. One of my favorites is actually one I think we should close with: "Getting comfortable with ignorance is how a student becomes a scientist." I like that a lot.

Stuart: That is absolutely the case.

Vincent: It is but how do you teach that?

Stuart: I'm not sure how you teach it. I guess you—there is not a program that I know of for teaching it you just—if you are in a laboratory, let's say it's a graduate student, which would be a little easier than teaching an undergraduate because it is very hard to teach them being comfortable with ignorance is a good idea because they are worried about a grade-point average.

But a graduate student, at least, I think if you talk to them about what is failing and you talk to them about the things that aren't working and you spend as much time and interest on that instead of demanding that they get you the data to fix this hypothesis up to put it in a grant proposal, which is some of our colleagues do. They run a tight ship. They run a lab where they expect to put data in the hopper and papers come out the other end sort of thing and that's the way they run it. I think that's not the way to do it.

But I think if you teach a student by your own patience and your own interest in everything that they do that doesn't work and not penalize them for any of those things that don't work then they begin to appreciate that that's the real fun.

Vincent: Well, I think that the book is absolutely brilliant. As I said, the length is perfect. I think I'll give it to my lab for the holidays. I think every listener of TWiV should definitely read this book. The more non-scientists out there that read it, the better they'll understand science. I mean they are not going to understand the mechanics but they'll understand the whole philosophy of really what drives discovery.

Stuart: I hope.

Vincent: So I want to thank you for writing it.

Stuart: Well, I want to thank you for this chance to talk about it.

Vincent: Like all other episodes of TWiV this will be on iTunes at TWiV.tv. If you do like TWiV and the things that we do go over to iTunes, subscribe, and leave a comment or a rating there. That helps to keep us visible so we pick up more subscribers and help explain this science that we do that is so important as you heard today.

We love to get your questions and comments. If you have any for Stuart I'm sure he would love to answer them. Send them to TWiV@TWiV.tv.

Stuart Firestein is Chair of Biology at Columbia University. What is the official department name, "Biological Sciences"?

Stuart: The "Department of Biological Sciences."

Vincent: That is such a broad name.

Stuart: I know. What can I tell you?

Vincent: That's fine.

Stuart: If you just write the Biology at Columbia that works too.

Vincent: Thank you so much for talking with me today.

Stuart: Thank you, Vincent. It was a real pleasure.

Vincent: I am Vincent Racaniello. You can find me at virology.ws. You've been listening to This Week in Virology. Thanks for joining us. We'll be back next week.

Another TWiV is viral.

- End –

Transcript by: Raphael Fernandez and Steve Stokowski