



## Stanford eCorner

### There is Always a Way Forward [Entire Talk]

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Serial entrepreneur Dr. Matthew Rabinowitz discusses how letting go of ego can empower entrepreneurs to solve problems that change the quality of life. As the founder of molecular diagnostics company Natera, Rabinowitz also shares unique financing insights, the value of being irreverent, and ways to manage your entrepreneurial destiny for as long possible.



#### Transcript

Thank you very much. I see myself with these speakers is like I'm starting a strip routine or maybe I am. Good afternoon, everyone. It's a real pleasure to be here. I was told by Tina and Co. that I should talk about past experiences, which might convey some lessons. And I had to think really hard about what I might talk about, which could actually have an impact on a group of really smart people like this. And it turns out the best lessons I have - have actually been the hardest ones to follow. So I'm going to talk about those at the beginning and then I'm going to disguise them a bit and talk about them at the end as well. The topics I'm going to talk about will firstly be being a bit irreverent not just towards others, but also towards yourself, because you and life are just better that way, makes you a much better entrepreneur.

Second thing I will talk about is how once you've given yourself that space; you go about choosing a problem that's really worthy of you and several years of your life. Third thing I'm going to say some - I'm going to give some thoughts on fundraising, which I hope will be helpful and then the last topic I'm going to talk about how they catch monkeys in Central Africa. So onto the first topic. We are surrounded by so many bright people at Stanford and in Silicon Valley there are so many successful people, some of them by luck, some of them by hard work and achievement. But there is this sub culture that's emerged of reverence. Especially at the business school, no normative judgments implied, people want to be associated with these folks who have done so well and you want to have them respect you. And you want to be up in a pedestal like they are. And I'm not saying be disrespectful. Obviously you don't have to be disrespectful, the people around here I think really do command respect. But you want to be a little bit irreverent, because it's going to help you make better decisions, it's going to give you that sort of freedom from your own ego, be a little bit irreverent towards yourself, people are going to respect you more and life is just going to be a lot happier.

When I came to Stanford as an undergrad, I had won the National Science Olympiad, in South Africa, which is this competition that all the science students take and it was kind of a big deal and I was good, but I wasn't that good. And I was really lucky. And I arrived at Stanford, studying electrical engineering and physics. I don't know where my parents were, I don't know where my academic advisor was. If my academic advisor is watching this I don't know where you were, and I had to be on a pedestal. I competed with everyone and I worked all the time. And luckily I had a couple of friends who took me out from time to time I don't know what they saw in me at that stage. But I to this day have never had anyone outside of Stanford University, look at my transcript. I have never had a job interview. And after all of this work and all of this competing, it added so little to my quality of life.

All it did is make me want to be something for other people and how they would see me. And you should really spend your time trying to work out the things that you want to do for the sake of doing them because they make you feel good not because you want to appear anything for anyone because it's very hard to find your way back after you tried so long to be on a pedestal.

And what actually happened to me is I had come out of my PhD, my first company had been sold and it was just a very stressful time and I just come out of a relationship and there was a lot of stuff going on and I had to work out my direction vector in life. And I had these two friends, this little furry Russian guy called Ilya and his very cute Indian girl friend called Seema and they told me that I had to go to Vipassana Meditation. Well somebody seems to approve of the concept. Seema said to me, you've got such powers of concentration, but you're always concentrating on the wrong thing. We are just warming up. So I thought, I'm going to give this a whirl and I went to this Vipassana retreat where you were in complete silence for 12 days, meditating nine hours a day. And it was horrific and you sit there with all of this churning in your head and for the - there is the pain of your body because you are meditating so many hours in silence and stillness and there is this serious rage, I mean for the first couple of days you're afraid you're going to die and for the next couple of days you're afraid you won't. And the whole time there is this guru, really impressive man S.N.

Goenka and he actually passed away on Sunday, which is why he is on my mind. And he is saying to you the whole time that you are in this fury, oh no your brain is a chattering monkey. Anichcha, anichcha, anichcha, which means changing, changing, changing. And after six days or so, I actually had a breakthrough. I was able to look at all of these physical sensations and all of this angst from a place that was inside of me, but it wasn't inside my thoughts. It was me but I could just watch the sensations and separate myself from my ego. And you realize that your brain is a completely dysfunctional organ. It has completely lost the plot. You're worrying about what people are saying about you and what they're thinking and whether you're on your own schedule and what you've achieved and what you're going to achieve and it's all just dust in the cosmos. All of these transient things and that's a really powerful moment that I had.

And I still try to meditate for an hour every morning many years later, because it just makes me so much more likeable. If you think I'm not likeable now, you should see me when I haven't meditated. It just makes me a very different person. And it has application to so many things in the path of an entrepreneur. So I'm going to talk about some of those things that - separation from your ego and a certain irreverence help with. One is choosing classes. You want to come here and you want to be really good, you want to be respected, you want to take the hard classes and you want to be on a pedestal. The classes that made a big impact for me are the classes around the 200 level, some 100 level classes, very few 300 level classes. The professors, I mean these are brilliant guys, but they're so enamored with their work and they have such depth in their particular class, that's sort of the late 200, 300 level series that they are convinced that you will not do anything useful unless you do this class. And the more specific the class is the less useful it's going to be to you, because once you've chosen a problem that's really the problem that you want to work on unsolved in life or in a portion of life, you're going to have to learn the things that you need to learn to solve that problem.

You're never going to take enough detail in a class that is going to give you the tools to solve the problem that's the right problem for you to work on. So be a little bit irreverent. Nobody knows what you should take and what you're good at, what you want to do better than you do. The same thing applies for company ideas. They are the world's best companies I would say have come out of Stanford, but very often professors, academics in general have a slightly distorted idea of what it takes to bring a concept out of the lab and actually have it be impactful in the real world. And this is a mistake that I made, I was a consulting professor in aero/astro for eight years and I learned that it took a long time to get things into the real world and there were a bunch of considerations that one doesn't get to in the academy setting. It also applies - the level of irreverence applies to the people that you want to put on your board or the people that you want to get as investors. It's obviously great to have big names associated with your project and that can help you raise money and people will take you seriously, but be really careful of the big swinging Silicon Valley cojones who walk around and they just kind of shoot from the hip and they pattern match and they give you quick advice based on not really thinking about your problem, they will do more harm than good. They can open doors, but really you can open doors yourself. Opening doors is not the hard part.

When you got a really big name, they will open doors that are actually distractions because the doors will open because they have got such a big name and a year later you realize there wasn't really a viable business there. So you've got to just look for those people that can really respect you and understand the particular challenges that you are facing and work with you. One of the greatest directors I - coolest guy I ever had as a director was Paul Baran. And I think he had the highest ratio of achievement to humility that I had ever encountered and that's because he invented the Internet. So he was a Polish engineer and his father was a cobbler in Poland and he always used to give these piece of advice in board meetings when we were struggling about whether we should show a demo, working through the details, he would say things like well, are these engineers bright? And we would say, well you know they are kind of bright. He is like are they creative and we are like, yeah the guys that we're talking to at this big company I don't really know, and he would say because my father always used to say never show a fool half finished work. And everyone would be like, hmmm, Paul, that's really profound and it came from his father who was a cobbler in Poland. He was just a really wise guy. And he worked on the first computer systems, the ENIAC and he noticed that the thing kept breaking because of bugs, literally bugs that were in the valves and he started to think well how do we make a communication system that is more robust than the sum of its individual parts. And he came up with this concept that you could take a message, could split it up in to its constituent pieces and you could send it into a network where each node would make a decision about what the next optimal trajectory for that message should be, that packet, and at the

end the packets would be reassembled and that was packet switching.

And he invented this at the Rand Corporation and not only did he invent it, he wrote papers in the 1960s for AT&T and the Department of Defense about what the world of packet switching would look like, And he described so much of what we do today on the Internet, really an amazing guy. And I had started my second company and I had a group of board members and I was so proud to have them be board members. And my mother was visiting from South Africa and she is the most irreverent person you've ever met in your life. So I thought she needed to meet these guys, because I was just wanting to expose things that were important in my life in California. So we sit down to lunch and I introduced these various names and they were all on the National Academy of Engineers, really big name guys. And then I introduced Paul and I say to my mother this is Paul Baran and he invented packet switching, which is the architecture of the Internet and he received the award from the FCC as the father of the Internet. And you say this to people in Silicon Valley and they start to shake and they drop on their knees and they look at the guy, my mom said why can't they make it work? I've spent a week calling my ISP in South Africa and they keep telling me that it's going to work and they keep telling it's reliable and they just can't seem to make it work reliably. And every day I get the same story and it just doesn't do what they're supposed to - what they say it's supposed to do and everyone is talking internet, internet why can't they just make it work? And Paul looked at her, I was hiding under the table and Paul looked at her and he said well, Dr. Rabinowitz, we're still working out a few kinks. And this is the nature of the guy, this is the kind of person that you want to be associated with, not a big ego, really thoughtful, really bright and really willing to work with you and work through your challenges.

And that ability to step away from wanting to be on a pedestal is also really relevant to the team that you hire in your company. One of the things is when you start a company and it looks interesting and it's going well, people are interested to get involved and it's such a true - it's so good for the ego because everyone wants to be involved with you and you want build this team, don't do it. It's not the glamorous way, but keep it tight. Make your team when you start really small and really bright and really focused. It's going to end up being much better for you as an entrepreneur and you're probably going to end up starting a much better company that way. Same things VCs will often say to you, you need to spend more money. Spend and the glamorous thing to do is to get a nice office and spend and really pursue. When you are ready to spend money in a company when there is real need to spend money, you will feel it in every cell in your body. You won't be able to keep your foot off the accelerator. If you're spending money just because it looks kind of good and people are telling you to spend money, chances are you're spending money on the wrong things or wastefully and it's not going to be good for you financially in the long-term.

Same thing applies to the people that you bring onto the team. You want these people to not be sort of glamour seekers who want to be on a pedestal. You want these folks to be tenacious. The kind of people who will stop at nothing, the kind of people who understand that Churchill quote, where he says "if you're going through hell, keep going." It's a beautiful notion that you just - there was always a path through, there is always a way. And as an engineer I think one learns over time there is always a way, there is a way around, there is a way through, there's a different direction, you just need to have a team that will stick with you to find it and not wanting to be glamorous and on a pedestal because those will be the first people who will leave the company. Okay, so those are all the topics of being slightly irreverent towards yourself and others. Once you have given yourself some space to really think about the problem that you want to solve. The message that - the main message I have learned is to then focus on a problem that is really worthy of you, worthy of you for several years because these things always take longer and consume more of your life and not to focus on a technology that you want to apply. And that's also about irreverence and letting go of your ego, because you've come out of Stanford, a lot of you are PhDs or postdocs, you've being published and you are respected in your field and you know so much about it and very often it's just difficult to pry that technology, that particular know-how out of a person's hand, so they actually focus on a problem that the market needs to be solved. It's very hard.

You got to let go of your ego and look at the market and the problems in the world and say what do I really want to work on and learn what I need to learn to solve that problem. And there are always problems to solve. Everywhere you look there is problems and as technology becomes more advanced society evolves around it and there are new problems and that process of refinement of the problem has no limits. I have a personal bias on problems that I think are important over the next 10 years because the best companies so far out of Silicon Valley have been the IT companies. They have certainly been the biggest companies. But if you look at the life we lead today, if communication networks get much faster and we get much more processing power and we're able to render all images in 3D holographically, and we find new ways of making things go ping on the Internet and making things go ping on your friends' social network pages, I just don't think it's really going to change the quality of life so much. But when you look at life, when you look at the problems of biology and health, your physical health, mental health, the problems of ageing, there are so many challenges out there that are really worth solving and are going to be solved. When you look at that world, it's like that Shakespeare quote where he says, it's Edgar in King Lear where he says, "World, world, O world! But that thy strange mutations make us hate thee, life would not yield to age." And there is so much out there that requires intellect to be solved. My background was Information Systems, Signal Processing, Physics and then I was in the Aero/Astro Department just as a consulting person for eight years and the companies that I had started initially were in

the IT space, Internet company, then a communications company and I had invested in a lot of IT areas. And then my sister had a child that was born with Down syndrome.

And I spent six days while everyone was sleepless just flying around the country speaking to experts, trying to understand what could be done, and after six days the child died and it was just a horrific thing for a family to go through. And I couldn't believe it, I couldn't understand how in the 21st century they could not know that a child had Down syndrome until it was born. And once I got into it, I learned the limitations of the testing, it was unbelievable. Either you could do these hormone tests, which missed about one in six cases of Down syndrome and had very limited coverage of all the other things that can go wrong during the pregnancy or you could do these invasive tests later in the pregnancy like an amniocentesis where they take a needle and they stick it in women's belly and they pull fluid out of the uterus and they look at the cells. And this has a chance of miscarriage and can cause harm to the fetus and this was crazy. So I started to work on all sorts of problems where we could take signal processing and optimization and apply to challenges in genetics. And very soon we focused on the problem of single cells and the reason why single cells was so important, well there are many applications, but one of the applications was In Vitro Fertilization because that's a unique intervention in medicine. You've got 10 embryos that have fertilized in an IVF lab and the one or two embryos that you choose to transfer have a direct impact on the outcome, namely the health of the born child. And so if you've got a family history of cystic fibrosis, so you got a BRCA1 mutation that causes breast cancer or you just are concerned about the chromosomal structure of the embryos because you want a high probability of implantation, about 80% of embryos in an IVF cycle have a chromosomal problem. You can take single cell from the embryo and you can analyze it to look at the DNA.

But the challenge is if you look at a single cell every molecule, every position on the chromosomes that you're looking at is just one molecule. So you can't make that measurement reliably. You get a ton of allele drop-outs where there is a molecule there that you can't see or you think molecules are there that aren't. So we came up with this approach where you would measure hundreds of thousands of positions along the chromosomes from that single cell. And that measurement was really noisy. But you'd also measure the genetic sample from the parents and you would take the data from the Human Genome Project like the HapMap database, which tells you where chromosomes crossover when the parents are forming the sperm and the egg that become the embryo. And from that very noisy measurement of the single cell combined with that prior information, we could work out where the crossovers happened in the parent chromosomes to make the gametes that became the embryo. And if you can work out where those crossovers happened, you could reconstruct the DNA of the embryo in silica. So we can look at a single cell and we can look at all sorts of things and we do this for hundreds of IVF centers around the country, around the world now actually. And there are amazing things that we can solve.

I mean you have couples who have a born child who has got a disease and they need cord blood from another child to see if they can help the born child. Now that cord blood comes from the placenta. And we will take a single cell, we can analyze that single cell for six genes on the histocompatibility complex to make sure that it's compatible and we will look at multiple disease linked loci to make sure that the embryo doesn't carry that disease susceptibility and we'll simultaneously look at all 24 chromosomes for insertions, deletions, translocations and versions and 24 chromosome copy number and they will select embryos based on that and, my God, can this make a difference to people's lives. And we've got a lot of ethical decisions we have to make with this technology because we get a lot of crazy requests. I mean, we're focused on helping with severe disease or phenotypes that are very high penetrance. In other words, if you have got the genes you are very likely to express the disease. But the other day we got a call, it was a while ago actually, to our counselor and the caller said I use a testing for my embryo with Natera and my mother is very beautiful Ukrainian woman and my husband's mother is not beautiful. I don't want a child to look like husband's mother. If look like husband's mother, so she said - she wanted the child to have blue eyes, so the counselor said yes we can do this. We actually do know the genes for blue eyes, but we just don't test for that.

And the woman was like you don't tell me what test I get, either I get the child look like my grandmother, if I'll have child look like husband mother, I don't want child. And we had to deal with this woman who was not prepared to pay for the test and as we tested the things that she wanted and obviously we wouldn't. But there are some real ethical questions here that we have to grapple with everyday and it's a really challenging problem. Those ethical questions have become more and more challenging as our tests have actually moved into higher and higher volume markets. So we offered a test in a series of pregnancy and reproduction related issues and the really big test that has probably so far the biggest test that Natera has offered that many of you might have heard of is the Panorama Test, where at nine weeks into pregnancy instead of having to do an invasive procedure, much later in the pregnancy or relying on the screening test which have limited sensitivity and specificity. We can just do a blood draw from a needle stick in the mother's arm, regular blood draw that has no risk to the fetus at all. And from the tiny traces of fetal DNA in the mother's blood, we can determine if there are chromosomal problems in the fetus and it's really cool how this technology works. We are using maximum likelihood Bayesian estimation, which is an optimization signal processing concept that is well understood in the engineering side. It's not so well understood in the biology world. The way it works is you measure thousands of positions on the chromosomes called SNPs, single nucleotide polymorphisms; these are positions where we have genetic differences.

So I might have an A, you might have the C or T or G. And from that measurement of 20,000 SNPs, we construct a whole series of hypothesis of what came from the parents to make the DNA of the child. So at a high level did I get two chromosomes from the mom, one chromosome from the dad, at a particular chromosome like 21 which would cause Down syndrome. That would be a Trisomy 21 or did I get one chromosome from each parent which would be normal. And within those very broad hypotheses of what came from the parents, we look at literally trillions of sub hypotheses describing where the crossovers happened to make each of the chromosomes that went into the kid and you calculate the probability of each of those hypotheses, given what you have measured in the plasma from the blood draw which is a very noisy measurement and also given what you know from the mother's DNA that you get from the white blood cells in that blood draw, and also what you know from the Human Genome Project. And so you do this maximum likelihood estimation technique and typically one of those hypotheses will stand up above the others with 99.99 plus percent probability and that's your diagnostic call. But if you don't have a rarely high probability call which is basically your confidence, you don't make a guess, you say look do another blood draw and will get a really reliable result and the data on this test is absolutely staggering. We have done a series of trials, the latest data that I have from one of our trials was about 1,300 samples and looking at Down syndrome and Trisomy 13 and 18 which are the most common and severe whole chromosome problems that you can have during a pregnancy. We had 100% sensitivity and 99.9% specificity, which is really impressive data. And it's not obvious - it's not a 100% because biology is just not that simple, but the performance of this test is quite incredible.

And it's changing the way people manage pregnancies all over the world. And not only are we just looking at whole chromosome problems, we're starting to look at all sorts of sub chromosomal issues, because we found that these lead to kids being born, they don't show up as abnormal in ultrasound, but the sub chromosomal insertions and deletions have children born who have mental retardation, developmental delays, organ abnormalities and these kinds of challenges. When I started in this field, there was this canonical wisdom that about 3% of pregnancies were abnormal and we didn't really know the genetic causes, but we thought most of them were genetic. Now we are actually at a point where we can explain roughly the majority of those abnormalities on a genetic basis and the question is what do we actually test for during the pregnancy. When we put 20 of the top maternal fetal medicine specialists in a room, the top guys in the country, really bright people, none of them can actually agree on what are the things that should actually be tested for during a pregnancy; that definition of what is abnormal and severe enough is a totally loose definition. So it presents us with real challenges and this has been an experience for me, which has been ethically really interesting, technically really interesting, and it was a great problem for me to choose. I was very lucky in some ways that I encountered that personal tragedy. And I'm going to just say a couple other things about the problems that one should choose leading on from that. One aspect is when you choose your problem and you're looking for your solution make sure that you pick a solution which is in your own control. Manage your own destiny as much as possible.

When we came up with this technology, can I walk by the way? Can you track me, it's cool? Okay, technology. When I - when we were looking at how to build the business around this technology, people said well you want to license the technology, because you don't want to build a lab, you're not going to be able to scale and we decided actually that it made sense for us to raise a little bit more money and build our own lab and do the trials our self and start offering these tests out of our own CLIA lab. And it was a little bit longer, now we have got this lab, I don't know if you guys see it in San Carlos, there is the old Nectile building is now the Natera building with the embryo on the top of the building, it's kind of this embryo flower, looks really cool. And we've got 300 people in that lab who are doing the tests ourselves, but having done this ourselves, having developed these tests and offered these tests ourselves we now have partnerships with all the top labs in every continent around the world, in the United States the Panorama Test has been distributed by Quest, which is the biggest lab in the world and about 10 other key labs in the U.S. We got the biggest lab in South America, biggest lab in Canada, biggest lab in Western Europe, top genetics lab in China, Korea, Japan, Russia, Africa, in Johannesburg my hometown. So and there is about 40 labs - 45 labs around the world now who are distributing the test. And now we can use that pipeline, that infrastructure that we have set up with these labs to give them our molecular protocol, they can run the samples themselves and we can run the informatics in the cloud. And there is a whole series of things that are going to go down the pipeline; a whole series of new and different tests that we are going to be working on related to personalized medicine. But we had to get to that point and to get to that point it was a really valuable that we were able to offer the test ourselves. You can spend years trying to convince some important person in some big company that they have got to change their plans and take you seriously and it is really hard to do that unless you really have the control to do it yourself.

So that's the one thing. Try to keep destiny in your own hands as much as possible. The other thing is make sure that you choose a test that's in a hot and growing market. It really makes life so much easier when you've got something which the market really wants. And sometimes it's very difficult for you to work out what that is; it's not your expertise. So one of the things that's great about Silicon Valley is there are lots of people around you who have that expertise and this is bringing me to my third topic, which is thoughts on fundraising. A lot of people will say don't take a ton of venture money upfront or any venture money. Do it with friends and family. Keep it tight until you have increased your valuation. I actually have seen very different evidence.

I would say raise institutional money as fast as you can and then spend as little of it as possible. And the reason for that is

twofold. Firstly, VCs can be very bright and they can be very dumb. I would say an equal split, but it's not quite. And I'm not going to say where the split lies, but if you can't convince one institutional investor that you have something which is suited for the market, you've got the wrong plan. And Silicon Valley has two great things. It's got a lot of capital, a lot of investors, and it's also got these folks whose job it is to work out what the market needs and what can work in the market and that's incredibly helpful for you as an entrepreneur, because it's often your blind spot especially when you come out of Stanford. So raise money, not that Stanford is used to having blind spots, most universities - all universities have way bigger blind spots I would say than Stanford. But coming out of an academic environment it's difficult to work out what really connects to the market. So convince somebody at an institutional level to put money into your project.

If you can't do that keep working on what the plan should be. The other reason it makes a lot of sense I think is you'll end up getting less diluted usually. There are a few cases where everything goes so beautifully that you raise money from institutionals at a much higher valuation than what your angels or your friends and family had, but that's usually not the case. If it is a good problem, it usually costs more and takes longer and if you're still in the process of trying to get to the key milestones and then you need to raise institutional money, very likely they're going to pay what they would have paid if you had gone to them the first time, your angels get diluted, you get diluted and it usually is a much less optimal outcome for the entrepreneur. So I would say go to the investors as early as you can. And when you go to the investors, you got to choose if you have the choice, choose venture capitalists who you like and respect and more than anything trust, because there will come a time, however you set it up, there will come a time when your fate is largely at least intertwined, possibly controlled, by them. And there are two philosophies - roughly two philosophies in venture capital. You got the big swinging cojones who invest in a company and very often they will gut the company of the founders and they free up a lot of common stock and then they put in their own management team and that can be a very good decision for them to make, and there have been some big companies built just that way. And then you've got venture capital groups who really have a philosophy of partnering with the founder and that's part of their credo. If you look at a firm like Sequoia Capital for example, I think it's about 80% of the companies that IPO or sell have a liquidity event that Sequoia Company's still have the original founders running the show.

And that's because they look for people that they really want to partner with and really want to work with for the long haul. And if you can get money from a fund like that even if it's at a slightly lower valuation, I would really say take it, it's going to make a difference. When you meet with an investor at VC, it's quite amazing. I think the lesson I have learned there is what you see is what you get. You are always wondering well, what they are going to be like and doing reference checks, just use your eyes and ears. When you go into the meeting and the guy's sitting there and he is on his cell phone and then he's kind of got all these opinions and pattern matching that are not really relevant to your problem and telling you what you should do, but he hasn't really thought it through and he is not really giving you the time, I guarantee you however big that person's name, you're going to have problems unless you're really lucky. So what you see is what you get, just look for a person who is listening to you, working the problem, thinking about the problem, and gives you that level of respect. So - all right, those are the easy things, those are the decisions - oh, actually there is one more thing I wanted to mention. I think it's a gem, maybe it will help, maybe it won't, but listen up. There is a new paradigm in liquidity over the last couple of years where you don't have to sell your company or go public in order to have liquidity as a founder, because there is all these organizations that are enabling a secondary sales in the market for investors who want to get involved in the company, but are not part of the key team.

And as a founder often that IPO is a schlep and it's a distraction, so you might decide to delay the IPO or things might just take longer in the company and you have things that you want to do. You want to build a house; you've got family commitments and obligations. When you start your company, it's a really good idea to put in a little bit of your own money, not a lot because that is going to make you irrational. But put a little bit of your own money to get preferred stock. And the reason why preferred stock is so valuable is if you want to sell it a few years down the road in a secondary transaction, you can sell that preferred stock at a high valuation without messing up the valuation of your options. They don't ruin your 409A valuation for the SEC, because you've got particular rights and voting privileges associated with that preferred stock. And that will give you the flexibility to sell your stock earlier. It can make a really big difference. When you get your initial VC's involved you need to talk to them about this. And the good funds who partner with the entrepreneurs will understand that you just have commitments in life that you want to fulfill at some point down the road.

So - okay, those are the easy decisions because those are the decisions that are hopefully mostly in your control. Now I want to talk about how one makes decisions when the underlying variable is just not in your control at all. When I was coming out of my PhD my first company had been sold, it was an Internet company, we were just lucky, it was just the right thing at the right time. The company was sold at \$30 per share. And by the time I could sell - don't knock inflation. So, \$30 per share and not that I had much control over that, but by the time I could sell my stock it was worth \$16 and I thought well I'm not going to sell at \$16, it's worth \$30. And then the stock was worth \$10 and I sold a little bit at \$10, but I thought well that's just irrational, I'm not going to sell the lot at \$10, because if I didn't sell at \$16 why would I sell at \$10? Does anyone know how they catch monkeys in Central Africa? Nobody? So what they do is they hollow out a log and they put these really yummy berries in the log and there is a hole that the monkey puts his hand through to get the berries and the monkey is so apt to have the berries

that it won't let go of them although with its fist closed, it can't get its hand out of the hole. And even when the hunters come out to grab the monkey, it still will not let go of the berries, it's just too psyched. And you look at this and you think, I mean, actually you think poor little monkey, but you look at this, you're like you stupid monkey; let go of the berries. So this happened just before the first bubble burst and was right, and I lost pretty much everything.

And at the time it was painful. In retrospect it wasn't such a big deal. It was a lot of money at the time, but it wasn't such a big deal and actually it was a really good thing for me that this happened, a really good thing. It made me work on better problems, it made me a better person, but the lesson that I came out of this with is 50%, half, it's an incredibly powerful number. If you're thinking of selling, sell half. If you're wondering whether to buy, buy half. If you are in a negotiation and you want to make an offer to the other side, but you don't know how they're going to react: offer half. Whatever you do, however it turns out, it's not in your control directly, you're going to be half right and half wrong and you're not going to have regrets. And managing your own emotions as an entrepreneur is probably the most important thing, and it doesn't just apply to these decisions. Try to find the balance in everything, really everything.

Even find the balance in irreverence, because there are some incredible things in the world and at Stanford to treat with reverence. But if you can look at things that happen and especially the bad things, and realize that there is a good side to every bad thing that happens. Sometimes it manifests right away, sometimes it takes a long time to manifest, but if you can treat every event with that sense of balance and let yourself be free enough from your ego to wait for the good side to emerge and to look for the good side. You have probably achieved the most important thing that you can achieve as an entrepreneur. And that's it. Great. Thank you so much for these inspiring words. So now we're going to open it up for questions and I'm going to ask you the first one while everyone else is getting their thinking together and their questions together. So this is really inspiring and clearly you've accomplished a lot. What are the biggest challenges that you're facing now in this company? Biggest challenges? It's like an interview question.

I want to say we all work too hard. I think the biggest challenges on the ethical side are making sure that just because we can do something, we don't necessarily do it and it's the right thing to do before we do it. And that's the one part of the business that actually doesn't scale I think is the genetic counseling. So we got a whole team of genetic counselors at the company and when we have an abnormal result they'll get on the phone with the doctor and sometimes the patient as well and talk through the details. And it's quite amazing that the doctors who are offering these tests are often way behind the curve and they don't know all of the complexity of the testing and all the things that you can and can't say from a test. So we try to err on the side of excessive information and excessive caution. On our reports we will give much more information than the doctors typically want to deal with, because they have got very limited time per patient and it can actually confuse the patients to get so much information, so we have got to spend a lot of time with the genetic counselors. And as we want to give more information, for example to look at deletions and duplications in the sub chromosomal structure; this becomes more of a challenge. So there is not much that you can really do about it except you want to work closely with medical geneticists, you want to have a lot of education of the doctors who are offering your tests, you want to make sure that there is a lot of bioethics engagement and senior doctor engagement in the tests that one offers and you want to spend a lot of time with genetic counselors to make sure that the information that we provide is actually actionable and explained to the doctors and the patients in the right way. It's a very interesting challenge, but it's a very real challenge.

A question? Yes. So you mentioned that nine weeks into a pregnancy you guys have a test for whether there is an abnormality in a baby. Say the mother finds out there is an abnormality, what is the mother expected to do at that point and what are your guys results on the statistics of what mothers or parents do decide after finding out that there is an abnormality? That is a great question. That's a wonderful question. The question is we can do this test at nine weeks and sometimes people actually do it later than nine weeks that determines if there is an abnormality in the fetus. But what do people actually do when they get that information and what are the statistics of what next steps people usually take? Great question. I have had personal experience with this, which I am not going to go into here, but I will tell you there is never a right answer in those situations. What you really care about is giving the information to the parents and the doctors as early in the pregnancy as possible. And what you previously had is people would get the information often after the screening tests in the second trimester or after an amniocentesis. And then, if they chose to terminate the pregnancy it's horrific.

It can be a two day procedure and it's really a terrible thing for people to go through. So you want to give them the information as early as you can and one of the key timings that you care about is if you get it through these screening tests, you want to do a confirmatory invasive procedure like a CVS. And you can do that CVS that Chorionic Villus Sampling is an invasive procedure you can do that 11 to 13 weeks into the pregnancy. And so you want to get a really reliable result that early in the pregnancy so that if they do choose to do a CVS and if they do choose to terminate a pregnancy, they can do it really early. It makes a really big difference to what the couple goes through. Now on the other hand, there are certain things that we test for like Klinefelter syndrome, which you actually have interventions during the pregnancy and some of the other things that we test for where although you don't have an intervention during the pregnancy you can plan exactly what you're going to do as soon as the baby is born and the baby will be born in the right hospital. And then more than anything it's a question of the

parents just preparing. It makes a huge difference if you just know early in the pregnancy rather than be shocked in the middle of the pregnancy or late in the second trimester. It really does make a huge difference if people have that information and can think about it and make considered plans. In terms of what people choose to do, it's quite amazing.

It really, as you might expect, it's very different on the coasts of America, the blue states versus the red states. In the blue states more than 80% of people will typically terminate a pregnancy for Down syndrome for example. In the red states, more than 80% of people won't terminate a pregnancy for Down syndrome, and Down syndrome is the most common one. So it's really dependent on the particular culture and mindset that people have and there are no right answers. It's such a - when you - I don't want to make this too personal, but having just seen what people go through when they get that news, it doesn't matter what people have said they were going to do in their discussions, what their plans were, so often they're just lost. And so what you really want to do is give them all the genetic counseling support and give them as much information as you can, as reliably as you can, as early as possible. Right. I want to ask a question, when you get started very early on, you don't have customers, you don't have a tracking record, you don't have anything to prove to people, how do you keep the first early customers? And how do you make them happy? When you get started you have no customers, no money, no track record, it's bleak and you have your first customers, how do you make sure that you keep them happy? It really depends on the field in which you are working. So I don't think I can really give a catch-all but I think the first answer is listen to them, listen to your customers. And by listen I mean really size them out for the things that they like and also get them involved in the design process, because your prototype is going to always be a prototype that needs to be iterated and not going to be the final version.

And if your customers feel that they are part of that process and they take a certain ownership that can really lock them in emotionally. In terms of other things that one can do, I guess sales and marketing is a big deal. Marketing is everything. This is a room mostly of engineers, the way some people dress I think they're probably marketing people, but for the engineers in the audience marketing is everything. And good salespeople are worth their weight in gold. So you want to have a great engineering team and a great technology, but you also want to have a really bright and really committed marketing and sales team and getting that message out can often be really hard and you're often competing against really big companies who have much bigger sales and marketing budgets. So you need to have people who are bright and tenacious and focused and get the sales and marketing going early. Great. Yes? So as - as you can predict better and you've been able to change hormones, where do you draw the line and how do you as a company deal with ethical issues that come up? Well, we don't change hormones. No, I mean eventually - in the future, where do you see the line being...

As we evolve? ...as we evolve? So the question is as our ability to offer different tests that are looking at more and more complex disease states and phenotypes that may or may not be really high penetrants, variables of unknown clinical significance - variants of unknown clinical significance, how do we make a decision on what to offer and what not to? And I assume you're looking for some sort of mechanistic approach. Yeah, please. We get patients in the IVF context where we have time to think about it. Sometimes people will ask for certain things and we have time to really make a considered response. For example, the -I don't want to get into examples because I don't know - just we can maybe talk about that afterwards, but sometimes couples will want certain things on the embryos to be okay when they have got a condition. And we sometimes have very hard decisions to make. So the first thing that you do is, you spend a lot of time with your medical geneticists and your genetic counselors and you've got to really understand what the issue is and more often than not we'll just say - we will give the couple the freedom to choose, but if it's a serious disease that actually in any way shortens - we will only screen for serious diseases. If the couple wants to allow for an embryo that has a condition we try as much as possible to let them make that decision unless they are doing something irresponsible. And so it's really hard. You've got to make these decisions case-by-case.

Even for a particular disease like cystic fibrosis, the different mutations have very different penetrants. So you've really got to look at the particular mutations and get a lot of advice from your medical geneticists. In terms of what we do going forward, we have a whole advisory board. For Panorama, as an example, we have a whole advisory board of MFMs and genetic experts who will come together to recommend what the next thing should be on the panel. And we've just been through this process actually and there are certain deletions for example where, I don't want to say exactly what they are because it's going to come out in a couple of months, this panel, but there are certain deletions where some doctors are just banging the table and they say I have seen patients like this and it's a problem and you cannot not tell people about this and then there are other doctors, all senior guys, who are saying you shouldn't tell a couple about this because it's a phenotype of variable penetrants and what are they going to do during pregnancy and you are going to worry them. From a genetic counseling perspective, it's just a real problem. So we just have to navigate this and do it with a lot of care and lot of time. The thing that we will try to avoid responding to is when decisions are made because the healthcare system in this country is so challenged. A lot of decisions get made because the doctors just don't have time and they say I just don't have genetic counseling time to deal with the complexities of this particular disease. When that happens, we will almost just on principle say no, there has got to be a way to get people informed and our genetic counselors can carry a lot of that load.

So I guess the answer is you've really got to follow the professional societies and when you're doing something that's

ahead of the professional societies, you've got to get the world, the national experts involved. Great. Another question, back there. Can you further elaborate on how to apply the concept of irreverence to ? How we apply the concept of irreverence to ...? Drink, drugs... Joking, joking. How do you apply your irreverence? I think I said most of what I can say except for one thing. Don't let any amount of stress or any amount of schoolwork stop you making really good friends and going out and exploring the world with them. The most important thing for me has been just a couple of people who pulled me out of a little dark corner of the lab once a week and took me out and these became - the friends that I made as an undergrad at Stanford have been really like brothers and sisters to me. And that they have changed my quality of life more than anything that I studied here. So it's a balance.

I'm not saying be irreverent. Sanford is a really impressive place, I mean, obviously one is very proud to be associated with a place like this. But don't let other people decide what's right for you. You know what's right for you better than anyone else does. And have that little bit of irreverence so you can just think about that for yourself and don't try to be on a pedestal for them. And while you are at it, try to find some time to do other things like make really good friends, spend time with people here, because they will be really important people later in life I think. I'm sure you all will agree this has been a fascinating way to start the quarter. Thank you. Join me in thanking Matt Rabinowitz.