Jacob Hanna Interview by Arjun Prabhu, 11/27/2010

Background Research

AP: When did you know that you wanted to pursue a career in science and medicine? Was this always your passion or did your love for science develop later on?

JH: Really, I've always wanted to become a doctor and go to med school from a very young age and I went on to do it after high school. It was during my medical studies, like half-way through that I found myself more and more drawn to research and just asked questions about disease. That's how I decided to do, in addition to an MD, a PhD in biology. After completing that I decided that I wanted to focus on one thing so I gave up on the idea of continuing the medical training of going on to do a residency and just went on to do a postdoc and completely dedicate my career to research.

AP: That's interesting, do you think you would have been able to do both, like would it be too difficult to do both of them then [both practice medicine and do research]?

JH: I wouldn't say it is more difficult, it's just different, I think. Also, one variable for me is that I didn't do my MD-PhD studies in the US. I started in Israel and coming here to start a medical training is much more complicated so that played a factor as well. But truly, besides these logistical difficulties, I feel that there are very few people who can really do both at a very good level and I thought I wouldn't be able to do it. I don't think I would be good enough at both and I'd rather concentrate my energies on one of them.

AP: So speaking of coming to the US, why did you choose the Whitehead Institute and why did you decide to come to the US in general?

JH: I guess the specific lab at MIT is a pioneering lab in the field of stem cells and I was very drawn to this prominent lab. The MIT environment is very cutting edge and exciting to be there. I checked other places in the US and in Europe, but coming to this lab was my first priority.

AP: I read that in 2011, you will be starting your own lab at the Weizmann Institute of Science in Rehovot, Israel. What inspired you to start your own lab there and why did you decide to go back [to Israel]?

JH: It was the toughest decision I've ever made, to be honest, and I never felt I would be going back. I just realized that I have a lot of strong bonds to the place where I grew [up]. I am from Israel but actually I am Palestinian who grew in Israel. I really believe in the place and it's a very personal thing that by doing my science there maybe there will be some kind of positive impact. Leading a normal life there would be something that I would enjoy and maybe help train the future generation of perhaps Palestinian scientists together with Israeli scientists. [The idea is to] maybe help lay the foundation of such a future infrastructure that will be an added value to just being a scientist.

[Why the Weizmann Institute?]

JH: The Weizmann Institute itself is a very multidisciplinary institute and in general I find myself to more enjoy the company of people who do science very differently, like yeast people, rather than people who just everybody working on stem cells and I think that will be really exciting to do.

AP: That's amazing then that you will be to accomplish two goals, to be able to do your research and also hopefully promote strong bonds between Palestinians and Israelis at the same time.

JH: Hopefully!

AP: So the next questions I have are just about your work with induced pluripotent stem cells. In 2007, you were the lead author on the breakthrough study which proved that induced pluripotent stem cell therapy can cure sickle cell anemia in mice. What made you first begin to work with induced pluripotent stem cell? Why did you choose sickle cell anemia as the target disease and why mice as your model? Sorry, multiple questions!

JH: So, when I joined the lab in 2007, just half a year after a major breakthrough of Yamanaka making these iPS cells. Of course this opened tens of questions which five years later now, we barely know the answers for. So this was a very obvious thing to want to work with iPS cells. Choosing the sickle cell anemia model, this is a disease that is relevant, it is very abundant. The genetic mutation is known, so we know what we want to correct. And it is a blood disease, so we can transplant stem cells to the bone marrow. It is very hard to replace a brain, right, but it easy to replace the bone marrow. So the combination of these factors led us to take this as a target.

AP: Why did you decide to choose mice as your model, I guess that is a pretty common choice.

JH: [We wanted to] have a kind of full in vivo experiment in the animal. Obviously we can't do this with humans because we still don't know the safety of the cells and working with pigs or monkeys would be much harder. Being able to do all these manipulations in mice makes it a very good, easy-to-handle experiment.

AP: What are some of the advantages then to using induced pluripotent stem cell therapy as a cure for sickle cell anemia over some other publicized treatments such as adult stem cells from [donor] bone marrow or cord blood cells?

JH: The first advantage of iPS cells is the comfort of being customized, meaning you will make cells that are genetically identical from the donors. We don't have to look for matching donors and that is the major issue in transplantation therapy. The fact that we can reprogram a skin biopsy from a patient and make pluripotent cells, and these stem cells are identical to him is major, there is no other way to do this.

AP: So essentially if you were able to do this [treatment] in humans, you could cure every single [sickle cell anemia patient] using his own cells, is this true?

JH: There are limitations, yes we can make stem cells from every patient, but we still have a way to go in the sense that we don't have a lot of good protocols for differentiation, to make different types of neurons for example to make insulin-producing cells. So there is a lot of work on how to differentiate stem cells in a controlled and reproducible manner. So this is something we will continue to work on in the field, but I believe that in many cases our knowledge is advancing in such a rapid pace that we will be at least [able to say] "this can be done in humans."

AP: Right, so I know this is kind of a tough question to answer because like you said science and research [on stem cells] is moving so quickly but do you have any sort of estimate for when you think induced pluripotent stem cells might be able to be used as a pretty common therapy for sickle cell anemia in humans?

JH: That's a really tough one. I think blood diseases are likely to be the first candidates as I said because we have a way to deliver cells to the bone marrow because of the nature of this organ, we can do this. I want to be optimistic and say five years.

AP: Wow, that is amazing. So like you said, blood disorders are probably going to be on the forefront. What other diseases in general in the future maybe, might induced pluripotent stem cell therapy be able to cure?

JH: So you can talk about a variety of blood diseases, sickle cell, thalassemia, many different types of anemia, these are obvious. Liver diseases are also likely candidates. Diabetes to produce insulin-producing cells, beta cells, are a target. Neurodegenerative diseases such as Parkinson's for example to make dopaminergic neurons, something that is likely to see some progress.

I would also like to emphasize that the advantages of iPS cells are not only transplantation, by the way, but they are a very useful tool to study human disease. As you know, it is very hard to study human diseases because not only are there limitations in biological material but often by the time a certain disease ensues, such as diabetes or Parkinson's, the affected cells are already damaged and basically done so there is basically nothing to study. So it is really hard. You can think of going to a patient with a genetic disease such as Alzheimer's or Parkinson's, make stem cells and then make these neurons in the petri dish, look at how they behave, if they are healthy and maybe use these for drug screens to affect their behavior, this is also a very important aspect that this iPSC technology will bring in advances to human research.

AP: Wow that is interesting. So it [iPSC technology] might be able to be used not only used for transplant but also used to study other diseases that it might not necessarily be able to cure?

JH: Yes, exactly. You can use it to screen for a novel drug that you couldn't do before. And you have such good and relevant biological material to study.

AP: That actually gets into my next question, which was about your study in 2008 in which you were able to reprogram fully differentiated B cells to an embryonic stem cell-like state without the use of an egg. What implications does this study have for future research?

JH: In this study we wanted to prove that we can reprogram any full differentiated cell and not just rare stem cells kind of floating in our body. We proved that a fully committed cell can do this. In this study we basically reprogrammed immune cells such as B cells and T cells. These cells are unique because in biology when B cells make this antigen receptor they have a specific receptor to identify a virus or any kind of infectious agent. These cells undergo changes in the DNA to become antigen-specific. By taking a B-cell and reprogramming it into an iPS cell and making a new mouse out of it, this mouse will have only the type of immune receptor that was in the B cell we reprogrammed. So you can select the immune cells you want to study, quickly make a whole mouse, and have a specific immune response. And you can really dissect at the clonal resolution, immune responses. So I think this is something I will be pursuing in my lab. This is a very unique tool for studying immune diseases. So this shows you how the iPS research brings sometimes unpredicted avenues.

AP: That's an amazing study, to be able to study immune diseases in this new way.

JH: Yeah, hopefully.

AP: You're sort of getting into all my next questions. In the future, what goals do you have for yourself and your research, and what goals do you have for stem cell research in general?

JH: I think the questions are almost the same, because I am trying to focus on very instrumental, important questions, because I think that is where the field should be going in a little bit of a non-modest way.

One question is to understand what molecular changes are happening when we make an iPS cell. I think it is very fundamental to our understanding how you change gene expression, how this state occurs. So this is very important.

Two, I want to really understand how to make robust differentiation protocol as in [how to make cells] into any cell that you want to choose and develop really controlled protocols. That requires a lot of work and to devise such protocols, you want to make engineer-sophisticated systems to define the best condition to do this.

Third is really the disease modeling and again this goes along with the previous goal, once we know how to make a lot of these differentiated cells this will also help our efforts to model human disease and study disease through these iPS cells. I think these are generally the challenges that face our field and I will be working on, not everything, but [some] aspects of these problems.

AP: For people who want to help but aren't really interested in science, is there anything they can do to help?

JH: First of all, we are really thankful for any moral support for people who are trying to do this despite a lot of difficulties. Second, I think for patients, [if they can] really be cooperative in studies, or providing samples, through hospitals and organized programs, this is a very meaningful way that families can really do their share to boost research. That way we can learn from sometimes their painful experiences but at the same time it will enable us to do this research and alleviate many of these syndromes. For any families, this is a very meaningful way to support research.

AP: My last question is do you have any advice for high school or college students who are interested in science and potentially research?

JH: Yes, I feel science can be the most satisfying and interesting hobby that we do. I think my advice to people who are drawn to this is to fully explore this, not to give up quickly. I think everyone can find the joy and passion for doing this research. It just requires commitment and maybe being excited in what you do. I think as long as you have that, you should be fine. So that's the advice I give.

AP: That's good advice! Well that's all my questions, thank you again so much for agreeing to do the interview!

JH: No problem. Thank you for your interest, if anything comes up let me know.

AP: Best of luck with everything I'm looking forward to hearing about your newest studies!

JH: Best of luck to you Arjun.