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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Developing Lines of RBCs From Stem Cells

Scientist and medical experts hold grand ambitions for the emerging role of human embryonic stem cells in medicine. One of the first gains realized from these cells could be the production of red blood cells for transfusion, but several key obstacles remain; what are these challenges and how long will it be before the future of erythrocyte production is now. You are listening to ReachMD radio on XM160, the Channel for Medical Professionals. Welcome to a special segment focussed on future medicine. I am your host Dr. Mark Nolan Hill, Professor of Surgery and Practicing General Surgeon and our guest is Dr. Eric Bouhassira, professor of stem cell biology at regenerative medicine and director of the Einstein Center for human embryonic stem cell research at Albert Einstein College of Medicine.

DR. MARK NOLAN HILL:

Welcome Dr. Bouhassira.

DR. ERIC BOUHASSIRA:

Thank you for inviting me to your show.

DR. MARK NOLAN HILL:

What are the most important reasons to pursue stem cell based production of matured erythrocytes?

DR. ERIC BOUHASSIRA:

Well, there are few reasons. A well known reason is to produce red cells or rare blood groups that are sometimes very difficult to procure, in particular for people who have been transfused multiple times or who have had accidental transfusion and that are now reactive to variable antiviral antigens that makes them difficult to transfuse. Also people with genetic disease such as sickle cell disease that are transfused very often, it can become very difficult to transfuse because it will become reactive to minor antigen on the blood cells. Another reason is right now the blood is very safe. The blood supply will be released very safe because it is cleaned appropriately and old potential pathogens are eliminated, but there is always a risk that some new pathogen would emerge that would be undetected at least for initial period of time in the population and then again the blood supply could be contaminated with a new pathogen and there would be a major issue, so if we could make older cells efficiently all of these problems would theoretically not exist. There could be much more <_____> to chicken pox.

DR. MARK NOLAN HILL:

Now do you focus primarily on human embryonic stem cells or induced pluripotent cells or both?

DR. ERIC BOUHASSIRA:

Well, we are doing both. I mean for the purpose of making red blood cells actually you can only use iPS _____ cells. It is more <_____>. The iPS actually, the advantages with the iPS is that they you do not require _____ obtaining embryos you can make <_____>. In fact, we were making them from single halves. Actually, it is quite amazing.

DR. MARK NOLAN HILL:

They can come from fibroblast?

DR. ERIC BOUHASSIRA:

Well, what an iPS is basically is it is induced from a new technology that was developed 3 years ago in Japan and it is really unbelievable. What we can do is take a fibroblast or take, in fact right now a single half. You can take a single half from a parent cell and put it in <_____> fibroblast of keratinocytes that are in the hair as well as the roots and you can inspect these cells within a few hours that cuts our genes that nobody <_____> only in embryonic stem cell and you can reprogram the fibroblast into cells that are color-induced pluripotent stem cell and that are in fact very very similar to embryonic stem cells. So, the point of this manipulation is that you don't have any more <_____> embryonic stem cells. So, right now the technique is so new in fact that there are some technical issues that they are not identical to embryonic stem cell. In particular, they do have the warehouse that you use to produce them that do not exist normally and reprograming that occurs during this procedure may not be perfect but to make red blood cells in fact they are very a good source of cells.

DR. MARK NOLAN HILL:

As physicians, I don't think we always remember how many cells are in a pint of blood that we transfuse, how do you plan to make those numbers of cells for a large scale production?

DR. ERIC BOUHASSIRA:

The major issue is the cost. There is a scientist who actually scale out what we can do in the lab to an industrial scale, so that is the problem we have not quite addressed that is fund, because we feel that there is another issue, which is the cells we are making from embryonic cells that is not identical to the adult cells.

DR. MARK NOLAN HILL:

What do you mean by that, sir?

DR. ERIC BOUHASSIRA:

During development what happen is blood is not always made the same way. There are at least 3 cans of red blood cells that are made. The first red blood cells that are made in the yolk sac, which is the membranous sac that is undeveloped young or only during development. This says that you make at least a point in your life experiencing an embryonic hemoglobin, very big in fact three times as big as the adult erythrocyte and they do not lose their nuclei, they are like <_____> in adults they always have a nucleus and then they will lose their nucleus and cells that you make during the development are exactly the same in 6 or 7 or 8 weeks gestation. The fetal level of stems starts to form and there is another wave of hematopiesis of blood formation and in fact it takes place in the fetal level and the cell that you are while making at the fetal level were again different from the cells that you find in an adult. They express different kind of hemoglobin called fetal hemoglobin and they are bigger than the cells you find in the adult and they differ by the hundreds of genes in fact, which you compares them in detail, and only on this you stop making these erythrocytes that are transfused older type.

DR. MARK NOLAN HILL:

Well, the cells that you are going to produce will they be these nucleated cells or the enucleated cells?

DR. ERIC BOUHASSIRA:

That is the challenge. So, when you stop receiving an embryonic cells, we can even say that we know can make any cells in the body. They can make either all of the embryonic cells, fetal cells, and these adult cells. So we cannot do this experiment in humans and when we take the set of cells into mouse cells, we can take these embryonic stem cells and inject them inside <_____> a very early embryo and they will contribute to every tissue of the mouse. So that's why we know that these set of stem cells they can become any other cells because you can take them, put them back into an embryo and they will recreate on <_____> that is when you do it in vitro. What we are trying to do in a way is to reproduce its development. We know that the stem cells we have in addition they can make embryonic fetal assault and then what we have to do is to force them to do that in addition, so what we have also found is that we can make these nucleated red blood cells fairly easily infected. We can also make those cells that are normally found in the fetal that you find during let us say the second month of gestation, older way to build. Right now we are working on techniques to actually make such that would actually be the same as the one you find in adult.

If you have just joined us, you are listening to ReachMD radio on XM160, the Channel for Medical Professionals. I am your host Dr. Mark Nolan Hill and our guest is Dr. Eric Bouhassira, professor of stem cell biology in regenerative medicine and Director of the Einstein Center for human embryonic stem cell research at Albert Einstein College of Medicine. We were discussing stem cell based production of erythrocytes.

DR. MARK NOLAN HILL:

Doctor, how do you deal with the matching of blood types when you make these cells?

DR. ERIC BOUHASSIRA:

What we have done, in fact we have made some of these inducibly but on stem cells form in people that are O negative. So that we would have cells that actually could be used for lot of transfusions. If you will want to make that there would be any blood group or we could just start from stem cells on people with different blood groups.

DR. MARK NOLAN HILL:

Now, other stand that the military is very interested in this. Could you really make cells quickly enough to meet the needs on a battlefield?

DR. ERIC BOUHASSIRA:

Well what the military is hoping is that you will be a machine that could be transported not really under front line, not far you know somewhere in the <_____> there and that the machine could produce red cells sort of look early but to make red cells going to take a month the process of going for embryonic stem cells to red blood cell or even you would freeze these cells half way of it. So you don't have to do the whole thing in the machine where you would have some sort of frozen <_____> and that process would take probably a week, so that it is not sufficient. I do not think you could easily generate red blood cell on the spot, but you know you could have sort of machine made closer to the battlefield than having to fly blood all the time.

DR. MARK NOLAN HILL:

Let's talk about the practical aspect of this, now when someone donates blood they may do that entirely for free and the entire process is reasonable on cost. How much would it be, let's say to produce a pint of blood using this type of research?

DR. ERIC BOUHASSIRA:

You need the blood. I think right now the blood is given for free as a result of processing and testing that has to take place before it can be used, so that the cost of a unit of blood, I think is about $200 and so that is <_____> right now we are very very far away from all this. We don't even know how to make a whole unit of blood, but you know if we could get either a bit close to that cost and if we are <_____> I have to say that initially at least people that will be very difficult to transfuse and have rare blood groups and that is what actually we economically do, I mean <_____> as we are not seeing that we will be able to compete.

DR. MARK NOLAN HILL:

Are you optimistic that in the future that you will be able to complete that you will be able to solve these problems?

DR. ERIC BOUHASSIRA:

Yeh, I do not think that the cost to some degree or lot of the cost of the involved <_____> have to intellectual properties. Actually, the cost of the re-exams that are required is not that expensive.

DR. MARK NOLAN HILL:

This research that you are doing, does it help you better understand erythropoiesis and diseases of the blood?

DR. ERIC BOUHASSIRA:

This is very important when I am at work. We are learning a lot actually about early erythropoiesis than we did before. We did some of our working, so we did not compete on the stent like hemoglobin will produce to our development and these stem cells give us a good unique viewing to view because you can follow a very fast set of blood formation, which is very difficult to do in humans without enough cells. Also we are using these cells or the cells we produce in vitro either from embryonic stem cells or other stem cells to test the dogs, and to test <_____> to treat the people with sickle cell disease or to try to understand the <_____> mechanism of a variety of blood cell disorders.

DR. MARK NOLAN HILL:

Doctor, when we think about stem cell research we certainly think about other things than producing red cells. What made you get into this particular area involving red cells?

DR. ERIC BOUHASSIRA:

Well, I have been trying to find a cure for sickle cell disease for a very long time. So that was our initial idea that if I was to use that type

of system to test dogs and understand and <_____> that could be used to cure sickle cell disease and I have moulded a system to study that, and then we realized that red blood cells are in fact very very good. One of the easiest thing actually one could do with embryonic stem cells is that would have quite good application because the white blood cells do not have a nucleus, so that initially you would produce in vitro form of stem cell is that they might cause cancer and you might have done something to the cell and that has profoundly that would have made them become a potential source of cancer. White blood cells do not have a nucleus and you can in fact irradiate them which is a process used currently now is to irradiate this to eliminate or shoo away white cells that might cause a problem. Not having a nucleus is a pretty good guarantee that these cells could never produce cancer.

DR. MARK NOLAN HILL:

That's a very good point. Now can we ensure that these stem cell based red cells are free of disease?

DR. ERIC BOUHASSIRA:

The question is can we make sure they are safer than the existing cells. You know that that existing blood supply, there could be problem in the production, there could be several other issues but the <_____> should be was they are safer than the existing alternatives. I believe this is going to be the cancer that will have to be tested.

DR. MARK NOLAN HILL:

Do you think there will be a time when blood donations are no longer needed?

DR. ERIC BOUHASSIRA:

Yeh, I think in long term that might happen. I do not think that the research we are doing, you know, there is a thing we are trying to do with stem cell. You could also use alternative strategies with adult stem cells. There are many other ways, you know there is a novel of groups in the world in fact doing immune research using alternate strategies of the same type. I believe that some one, some group or some company will eventually develop cells in vitro that will be competitive with the general based T stems.

DR. MARK NOLAN HILL:

And finally doctor where do you think you will be in research 5 to 10 years from now?

DR. ERIC BOUHASSIRA:

Well, I am hoping that we have a lot of research activities right now in trying to make these adult cells. We will have these issues that we are making cells that are not exactly the same as the one we want to make. They are the fetal phenotype, and we are hopeful that within the next 3 to 4 years, we will have cell death problem and then we will be left with the genuine issues of just making a lot of cells and you know the cost issues.

DR. MARK NOLAN HILL:

I want to thank our guest Dr. Eric Bouhassira. We have discussing stem cell based production of erythrocytes. I am Dr. Mark Nolan Hill and you have been listening to ReachMD radio on XM160, the Channel for Medical Professionals. Be sure to visit our website at ReachMD.com, featuring on-demand podcosts of our entire library and thank you for listening.