



Interview

Working for a cure for Type 1 diabetes

Alan J Lewis, PhD, joined the Juvenile Diabetes Research Foundation (JDRF) as President and CEO in January 2009. JDRF is a leader in setting the agenda for diabetes research worldwide, and is the largest charitable funder and advocate of Type 1 research. Prior to joining JDRF, Dr Lewis served as President, CEO and Director of Novocell, Inc., since 2006. Novocell is a stem cell engineering company dedicated to creating, delivering and commercializing cell and drug therapies to treat diabetes and other chronic diseases. Previously, Dr Lewis served as CEO and Director of Signal Pharmaceuticals before its acquisition in 2000 by Celgene, a biopharmaceutical company focused on the discovery, development and commercialization of small-molecule drugs for cancer and immunological diseases. He then served as President of the Signal Research Division at Celgene. Dr Lewis previously held the position of Vice President of Research at Wyeth-Ayerst, where he spent 15 years leading research efforts in diabetes, CNS, cardiovascular, inflammatory, allergy and bone metabolism diseases. Dr Lewis currently serves as a Director of BioMarin Pharmaceutical, Inc., Cytochroma, Inc., BIOCROM, and the Scottish Stem Cell Network. Dr Lewis received a BSc. in Physiology and Biochemistry from Southampton University, Southampton, Hampshire, UK, a Ph.D. in Pharmacology from the University of Wales, Cardiff, UK and completed his postdoctoral training at Yale University. He is also an Honorary Fellow and Chair of the Life Sciences Department at the University of Wales in Swansea, UK.



Alan J Lewis, PhD

Juvenile Diabetes Research Foundation
International, 120 Wall Street, New York,
NY 10005-14001, USA
Tel.: +1 212 785 9500;
Fax: +1 212 785 9595;
E-mail: alewis@jdrf.org

■ **How did you initially become involved with stem cell research?**

I first became interested in stem cell research while at Celgene, in San Diego, where I ran the Signal Research Division. Celgene had acquired a stem cell company that focused on cord blood banking and placental cell delivery, and that sparked my interest in the field. San Diego at that time was a hot-bed for stem cell research, so I connected with many of the researchers in this field. Around the same time, in 2003, the proposition that led to the California Institute for Regenerative Medicine (CIRM) was introduced, with Bob Klein driving a state-wide initiative to create a fund for regenerative medicine and stem cell research.

At the end of 2005, I was approached by Novocell, a stem cell engineering company that was focused on creating a cell therapy for diabetes. I took on the CEO position there in February of 2006, and we worked on islet cell technology. Cadaveric islet transplantation has been possible for some time as an experimental therapy for Type 1 diabetes, particularly for people with brittle diabetes; however, the

transplanted cells do not last long, and the patient has to take high doses of immunosuppressive drugs to prevent rejection. Novocell was taking a different approach. They were taking those cadaveric islet cells and encapsulating them using a polymer that protected them against being attacked by the immune system. The aim was to eliminate the need for immunosuppressive drugs. In the meantime, we were also developing a proprietary differentiation protocol to coax human embryonic stem cells (ESCs) into insulin-producing cells. This was my first entry into cutting-edge stem cell research, and I realized immediately that this was the future of medicine.

■ **You have been recently appointed as the President and CEO of the Juvenile Diabetes Research Foundation. What attracted you to this position?**

I had been aware of the work of the Juvenile Diabetes Research Foundation (JDRF) for many years. Having been intimately involved in cell therapy for Type 1 diabetes, I was convinced that the goal of

.....
 “...we hope to become the go-to organization for information related to Type 1 diabetes for everyone involved with this disease: researchers, physicians, patients, and our supporters and donors.”

future
medicine part of fsg



treating and curing this disease was very important. However, I realized that there were things happening in Type 1 diabetes research that Novocell could not address, because they were very focused on cell therapies. For example, I was aware of the research progress being made in regeneration, immunomodulation and immunity, creating an artificial pancreas, and treating the complications of diabetes. Because the mission of the JDRF is to cure the disease and its complications, they have invested in a very broad portfolio of science, so joining the JDRF allowed me to be involved in several important programs that will contribute to overcoming Type 1 diabetes.

In addition to JDRF's leadership role in diabetes research, I was very impressed by their government relations and advocacy function, which played an important role in driving the stem cell initiative in the USA. I think they have done a remarkable job in keeping stem cell research to the fore and we are hopeful that with the new administration, the funding limitations of the previous administration will be overturned, allowing more scientists to enter this area of research. The JDRF have also done great things with healthcare insurers, in encouraging them to cover things such as continuous glucose monitors. Finally, they have a very interactive relationship with the US FDA, in order to create a path for drug approvals in this field.

The final factor that swayed me to accept the position was the incredible passion that the board of directors, volunteers and staff have for the mission of the organization. Many of these people have been touched by this disease and I have never met so many people that have the knowledge and willingness to make sure that this disease is cured. They have been a delight to work with.

All of those factors together convinced me that JDRF was a great organization and the right place for me to be.

■ What do you hope to achieve in this role?

Ultimately, the mission will stay the same: to cure the disease and its complications. The core areas that we focus on are autoimmunity, replacement, regeneration, complications and metabolic control.

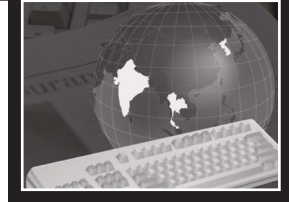
One thing that I am going to focus on is making certain our research considers the patient in a slightly different way: what we refer to as the 'person-centric' approach. Type 1 diabetes is a disease that affects people from infancy through to the elderly. This gives us different constituencies of patients and their loved ones: parents who not only want to help their child who has diabetes, but also want to know if it can be prevented in their other children; teenagers or college-aged young adults who want to know how to handle the disease in a social context; and people who have had diabetes for years, in some cases decades, who want a cure but are also concerned about complications. We want to identify which different therapeutics and approaches to therapy would be most beneficial in each of these patient groups: this will enable us to have better outreach to these groups. Eventually, we hope to become the go-to organization for information related to Type 1 diabetes for everyone involved with this disease: researchers, physicians, patients, and our supporters and donors.

Another area where we are very active is encouraging the government to make sure that Type 1 diabetes is supported financially through the NIH. It is critical that money is funneled into this disease, as it is an area that doesn't get as much attention from large pharma companies, who tend to focus their research investment on Type 2 diabetes.

■ How advanced is regenerative medicine research in diabetes compared with other diseases? How close are we to the clinic?

I think that diabetes is very high on the list. Novocell is anticipating that they are approximately 3 years away from entering a clinical trial. In terms of when we might expect cell therapies to be available commercially in the USA, that is difficult to say, as it will depend on approval from the FDA. The first ESC therapy to enter clinical trials in the USA will be Geron's therapy for acute spinal cord injury, which the FDA just approved for a Phase I trial. We hope that if that trial goes well, and the FDA does not flag any problems, further ESC therapies will be able to enter clinical trials.

“The core areas that we focus on are autoimmunity, replacement, regeneration, complications and metabolic control.”



■ A study last year by Doug Melton's group at Harvard demonstrated reprogramming of adult pancreatic exocrine cells to β -cells *in vivo*. Do you see advances in reprogramming and induced pluripotent stem cells shifting the focus away from embryonic and adult stem cells in future?

The question often comes up about how reprogramming and induced pluripotent stem (iPS) cells will impact the field of stem cell research. The work that Doug Melton carried out was remarkable, going beyond what most people thought was possible by reprogramming directly from one cell type to another. However, it is not currently applicable to clinical use, since cell reprogramming is carried out using viral vectors, injected *in vivo* into the pancreas in the case of Dr Melton's work. That would not, of course, be acceptable in humans. But this is an exciting aspect of the stem cell field. Back at Novocell, in fact, they have teamed up with Dr Shinya Yamanaka, one of the pioneers of iPS cells at Kyoto University, to establish whether iPS cell technology might be useful, especially in countries such as Japan, where human ESC research is difficult.

At present, ESC-derived cells are the only source of cells that are scaleable. If you look at the numbers of patients who could benefit from cell therapy, it is clear that you cannot convert sufficient numbers of adult cells to β -cells. That is what makes ESCs so special. It is far too early at present to say whether iPS cells are identical to ESCs – recent gene fingerprints show quite a large discrepancy; and we do not yet know whether they will act in exactly the same way as ESCs. However, if you can produce vast numbers of pluripotent stem cells using the iPS technology it will accelerate research in the field immensely, since many people will be able to carry out that work. At the moment, very few people can derive ESCs. Availability of embryos is limited and deriving the ESCs is an art as well as a science, fraught with a very high failure rate. On the other hand, most scientists in the field have the capacity to carry out the procedure to produce iPS cells. So I think that iPS cell technology will open up research in the field immensely.

If researchers can develop a small-molecule strategy to produce iPS cells, that could be what transforms the technology into a meaningful approach to treat patients. However, in my opinion, it is not an either/or proposition: iPS cells, ESCs and adult stem cells are all likely to have a place in future research.

■ Novocell entered into collaboration with Pfizer in December 2008. Do you see big pharma getting more involved in regenerative medicine over the next few years?

I think this is already happening. They realize that this is a huge opportunity. In particular, regeneration using small molecules is something that they are keen to get into, as it involves areas with which they are already comfortable. It is not as easy for them to become involved with cell therapies, as they are not familiar with that platform and have little expertise in the area. Now that the baby boomers are getting older, regenerating tissues, organs and cells is a huge market and they see this as a window for entering the regenerative arena. They are encouraged by early successes, such as erythropoietin to stimulate production of red blood cells, and want to move into regenerating pancreas, brain, heart, kidney, bladder, liver and so on. Clearly, they are looking into it very aggressively and they are a strong presence at meetings in the field. Pfizer has been exceptional in that they have created a regenerative medicine division, led by Dr Ruth McKernan, a passionate scientist who believes strongly in this work. It will rely on receptors and enzymes, targets researchers in big pharma are comfortable with, but the ultimate aim is something we would not have even dreamed of 20 years ago: regenerating tissues and organs.

In terms of cell therapy, we know that companies such as Johnson & Johnson and Novo Nordisk have had an interest in this field, as they realize that cell therapy is going to have a value in treating disease. Other companies are waiting to evaluate progress. As big companies, they do not need to jump into new technologies. For small companies it is frustrating, but realistically, big pharma have the check books and can decide when they want to make the investment.

“Despite the economic climate, the fact is that Type 1 diabetes does not go away, and the need to move science towards cures and therapies is as great as ever, so we are trying to reach out to our donors to encourage them to give what they can.”



JDRF has done a fantastic job in nurturing some of the technologies from small companies: overall we have invested US\$29 million in companies. Venture capitalists (VCs) are also funding companies, but the VC community has been a little slow to adopt this technology: moving the science into commercially viable products is a slow process and they are looking for a quicker return on their investment.

■ **Will the research funding role of the JDRF become more important as the global economic downturn continues?**

VCs are slowing investments in early-stage platforms and there needs to be someone filling that void, otherwise the USA will lose dominance in the biomedical field. The nonprofit organizations with a disease focus have to some extent been filling the gap. There are a range of organizations in the USA and around the world who

are working to move science forward. JDRF invested approximately US\$156 million in research last year, a good proportion of which went towards early-stage research. However, like every organization, we have been hit by the economic downturn and the money available for research will be less this year than it has been in previous years. Despite the economic climate, the fact is that Type 1 diabetes does not go away, and the need to move science towards cures and therapies is as great as ever, so we are trying to reach out to our donors to encourage them to give what they can.

This area of science has never been as exciting. Scientists like Doug Melton have been flagship leaders, and now they are starting to see their hard work pay off, and are making great progress. It would be a real shame not to be able to support that progress as we march towards the clinic and beyond.