Towards new cures for diabetes type 1

DCTI

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Introduction

Felco de Koning
DCTI PROJECT LEADER AND PROFESSOR OF DIABETOLOGY AT LUMC LEIDEN UNIVERSITY MEDICAL CENTRE

DCTI has given an enormous boost to the field of cell replacement therapy for patients with diabetes. The sound collaboration between academic partners, biotechnology companies, and the Dutch Diabetes Research Fund enabled us to conduct research and thereby develop new therapies. Collaboration is a strength of these Dutch partners, and we have every reason to be proud of it. In addition, we have created awareness about the necessity of developing new beta-cell replacement strategies among doctors, policymakers, and patients.

Thanks to DCTI, the research into islet biology and beta-cell replacement is recognized as an important step towards new therapies, which gives patients hope. People notice that we strive for more lasting solutions and not only treatment of symptoms. We are now working towards a real solution. The project allowed us to create new biomaterials, isolate more and, above all, better islets, and identify the factors that can improve the survival of insulin producing islets. These are all important steps towards the next phase, which should follow, for DCTI is only an intermediate step, not the final destination. In the next step, we aim to test the biomaterials in patients and create large numbers of insulin producing cells with the help of stem cells. In that way we will be ready for the future in beta-cell replacement therapy.

In front of you lies a splendid book about the groundbreaking results that have been achieved within the Diabetes Cell Therapy Initiative (DCTI), a LSH–FES project. LSH stands for ‘Life Sciences & Health’, or rather the application of life sciences to the benefit of our health, and FES for the ‘Fund for Economic Structure Enhancement’, financed by the so-called natural gas profits. DCTI started its activities in 2010 after the Dutch government’s approval of a joint proposal. This proposal was submitted by a combination of many partners – including small and large businesses, multinationals, academic and medical research groups, patient organisations, and the ministries of Health, Welfare & Sport, Education, Culture & Science, and Economic Affairs. The FES grant was used to achieve a public-private partnership: for every single euro subsidised by the government, the partners also invested one euro. After six years of hard work, the results can be directly applied in the treatment of patients or used for research that is closely linked to patients.

The consortium has hereby proved that it deployed the research funds to contribute to the improvement of our national public health and boost economic activity in the Netherlands. A vast number of these results are presented in this book. The most recent developments in this exciting field will astonish you time and time again. I therefore trust that you will greatly enjoy reading this book!

Herman Verheij
LSH-FES SECTOR COORDINATOR
Type 1 diabetes: on the way towards a cure

Diabetes has the reputation of an invisible killer, since excessively high blood sugar levels will eventually lead to complications. In patients with type 1 diabetes, the blood sugar level is sometimes difficult to regulate, as their insulin producing cells are defective. So far, these patients have nothing else to turn to but insulin injections. Sometimes a transplantation is considered. The Diabetes Cell Therapy Initiative (DCTI) research consortium searches for improvements in, and alternatives of transplantation.

The body converts everything that we eat into glucose as fuel for the cells. However, the cells cannot simply absorb glucose. They need insulin. It is the pancreas that produces this insulin. This takes place in the so-called islets of Langerhans: clusters of different cell types that excrete a wide range of hormones. The beta cells in these islets are responsible for the production of insulin.

One million
In people with type 1 diabetes, the own immune system attacks the islets in the pancreas. These islets thereby suffer so much damage that they cannot produce insulin anymore. Without insulin, glucose can no longer enter the cells and stays in the blood. Chronically elevated glucose in the blood can lead to complications like blindness, kidney failure, heart problems, and amputations.

Type 2 diabetes is a completely different story: type 2 diabetes is a metabolic disorder in which the body slowly becomes insensitive to insulin in combination with failure of insulin production – which may lead to the same problems if it remains untreated.

Approximately one million people in the Netherlands have diabetes – 900,000 have type 2 and 100,000 have type 1 diabetes. DCTI has, nevertheless, chosen to focus on type 1 diabetes. Project leader Eelco de Koning explains why: “The glucose regulation for type 1 diabetes is generally more complicated than for type 2 diabetes. Patients with type 1 diabetes need to inject insulin immediately after diagnosis, whereas patients with type 2 can usually start off with adjustments to their diet or pills.”

Transplantation
As a result of the constant risk of a too high, or too low, level of glucose patients with type 1 diabetes are aware of their illness all day. Type 1 diabetes has a dramatic impact, as patients continuously need to make calculations. What am I going to do today, what am I going to eat, and how much insulin will I subsequently need? Even if they strictly adhere to insulin therapy, there are times that it turns out to be very difficult to control glucose levels.

Some patients may undergo islet transplantation. In this procedure, which could not be performed in the Netherlands until just a few years ago, the Langerhans islets are extracted from a deceased donor’s pancreas and injected into the patient. In virtually everyone who has undergone this transplantation, glucose control is far more stable. Some people can even do without insulin for longer time periods, whereas others will need to keep using insulin or will have to start reusing insulin shortly after the transplantation.

Cell encapsulation
Transplantation is not as efficient as we had hoped, and that is for several reasons. Both during the transplantation and directly after injection, many insulin producing cells are lost. Now, in order to improve islet function for longer time periods DCTI has worked on various biomaterials. De Koning: “By encapsulating the donor cells, an environment is created in which cells feel more at home so that the islet loss may remain limited.”

Alternative sources
Apart from the efficiency problem, the shortage in donors also plays an important role. With the current number of donors, 50 to 100 transplantations can be performed each year, whereas we have 1,600 newly diagnosed patients each year. That is why DCTI focuses on alternative cell sources from which insulin producing cells can be produced – with one key question in mind: how to culture cells in such a way that we will eventually be able to treat all patients with type 1 diabetes in the Netherlands?
DCTI in a nutshell

The body of a patient with type 1 diabetes no longer produces insulin. This seriously interferes with the blood sugar system. The Diabetes Cell Therapy Initiative (DCTI) is hunting for new treatment methods.

The body regulates the blood sugar level with insulin. This insulin is produced by beta cells in the pancreas.

If the pancreas is defective, transplantation is a (scarce) option. In order to keep the pancreas in good condition during the transplantation and to increase the success of the operation, a special pump has been developed.

Instead of transplantations in these times of desperate shortages of donors, and rejection symptoms to boot, the culturing of new insulin producing beta cells would be ideal. Since, unfortunately, these cells are hardly culturable, DCTI went searching for alternatives and other methods for culturing.

More recently, the transplantation of islets of Langerhans, where the insulin is made, is also possible. However, the quality of the islets often diminishes rapidly. Clever tricks, such as a protective wrapping, should make these transplants more successful.
Wanted: cells for insulin production

There is still no cure for people with type 1 diabetes (whose pancreas no longer produces insulin). Transplantation of the pancreas is a possibility, but it is a drastic operation and there is a desperate shortage of donors. That is why DCTI sought a small-scale solution: transplanting the insulin producing cells only. These are scarce too, but the Leiden researchers reasoned that you can culture them.

In type 1 diabetes patients, the beta cells that are responsible for the insulin production are either defective or have been destroyed. To make up for the lack and to keep their blood sugar at an adequate level, these patients take insulin by injection. That boils down to the treatment of symptoms: it is not a solution to the underlying problems. Once beta cells are wrecked, they cannot be repaired.

However, you can replace them. A patient can receive a donor pancreas, including islets of Langerhans with beta cells that do function. The problem is, that a complete pancreas transplantation is a major intervention and there are very few donors. Some 250 pancreases become available each year – far too few for the 100,000 type 1 patients in the Netherlands. Moreover, the organ can still be rejected after the transplantation.

Since 2008, the islets are sometimes transplanted separately. They are injected into the liver’s portal vein. The pancreas itself remains untouched: the pancreas is sensible to inflammation and the liver has proved to be just as fine an accommodation. There is, however, still a great shortage of donors and the patients must continue with their medication to fight rejection symptoms.

Culturing beta cells
Leiden researcher Françoise Carlotti and her colleagues are, therefore, seeking another way of making insulin producing cells without having to rely on donors. Their goal: cultured islets containing beta cells, ready for transplantation. There may be several ways to get there, says Carlotti, Assistant Professor and member of the Diabetes Group of the Department of Nephrology at LUMC Leiden University Medical Center. The easiest is to extract beta cells from a healthy donor, multiply them in the lab and then implant them in the type 1 diabetes patient. Maaike Roefs, PhD student, concentrates on this possibility: further culturing of a small amount of beta cells from a donor until you have enough new ones to transplant. Culturing beta cells is not as easy as it sounds. They do not want to multiply, nor in the body or in a petri dish in the lab. Moreover, the cells that you try to culture change their identity. They start off as insulin producing beta cells, but spontaneously transform into another type of cell that no longer produces insulin.

“The good thing is that we can multiply those cells,” Roefs says. “However, now we have to find a way to make them change back again into beta cells.”

The idea is that the cultured cells must be suitable for insulin production because that is what they originally did.

Growth factors
Research into turning this process around is ongoing. By allowing the cells to group and adding various growth factors, the researchers have managed to make them somewhat return to their original function. What they have not discovered as yet is the exact trigger that makes them transform back into insulin producing cells.

Roefs collaborates with the biotech company Galapagos to find this trigger. The company has the capacity to test the effects of various medications on tissue on a major scale. For this study, it comes in handy: the effects of substances that may be growth factors can be tested on cultured beta cells within a short space of time. This quick first screening of substances helps the quest for factors that qualify as effective in helping the cells return to their beta origin.

If the quest is successful, it would be the breakthrough that Roefs is hoping for. The cell could be placed in a scaffold (see also Transplanting islets in an artificial pancreas) and a patient with diabetes could receive new islets without any chance of shortages of donor material. Of the 250 pancreases that are available in the Netherlands each year, some are transplanted in their entirety into one single patient. Other pancreases are used to extract islets, approximately one per cent of the whole organ, which are then transplanted. The rest of the pancreas is often considered to be of no value. This is a waste, the
researchers believe. The rest of the material might actually come in handy.

**Other candidates**

One of the chief elements of the pancreas is its extensive network of corridors, which collects all the digestive fluids that are produced by the organ and leads them to the bowels. Those corridors are formed by so-called duct cells. It is these duct cells that are important in the formation of beta cells: when the pancreas develops in the womb, the Langerhans islets emerge from embryonic duct cells. “This embryonic development might be mimicked in a petri dish,” says Tim Dielen, member of the LUMC Diabetes Group, who collaborates in this project with PhD student Jeetindra Balak.

**Embryonic development**

We already know how to isolate pancreatic duct cells. These adult cells now have to be enticed to behave like embryonic duct cells so that they can subsequently specialise in the direction of a beta cell. Dielen: “It is quite a puzzle. We use all of our knowledge of embryonic development. You have to identify the genes that are necessary for the development of beta cells and chart the chain reactions that take place as a baby grows. This information can then be used to give the cell a push in the right direction.”

The researchers have experimented with different growth factors. It is now possible to culture duct cells for the long term in a special type of gel, in which cells seem to create corridors all by themselves — as in the embryonic pancreas. The next step is these cells’ development into beta cells. The researchers have managed to show proof of concept: a small percentage of the cultured duct cells are now producing insulin.

**Bioreactors**

A third option for the culture of insulin producing cells is to start from alpha cells, which can also be found in islets, but produce insulin’s counterpart: glucagon. There are approximately four times fewer alpha cells than beta cells. The research group at LUMC discovered that beta cells sometimes change into alpha cells spontaneously as soon as you disintegrate an islet and allow the cells to regroup. The idea is that if this spontaneous transformation can be reversed so that an alpha cell becomes a beta cell, then this opens up a new perspective for an alternative source for insulin producing cells.

The work by Carlotti and her colleagues is special in that the researchers focus on human cells. “Many research groups that work with animal cells publish great results — but these usually say little about the way it works in people.” Working with human cells is essential when the findings are to be translated to the clinic. However, it does have a negative side: it limits the speed of the study. This is not only due to the stricter rules, but also because there is so little material to work with. Approximately eighty of all the pancreases donated each year can be used for research — provided that the surviving relatives give their permission.

No wonder that Carlotti and her colleagues use the available material as efficiently as possible. In order to upscale the cell culture, they collaborate with biotech company Xpand, which is specialised in culturing cells in bioreactors (see also Assignment: culture millions of beta cells). Carlotti: “If we want to translate our work to the clinic, we need a great many cells. Our collaboration with Xpand makes the culturing less labour intensive: in our own lab we culture cells on a two-dimensional surface and it requires quite some work to feed them. With the 3D cell culture developed by Xpand we can upscale the culturing far more rapidly.”
Assignment: culture millions of beta cells

The transplantation of islets of Langerhans that contain good-quality, insulin producing beta cells requires an enormous amount of them, but the culturing of these cells has proved to be a perilous undertaking – even for specialists.

Xpand is a biotechnology company specialising in the culturing of mesenchymal stem cells (that can later specialise in, for example, fat cells, bone tissue or muscle tissue). Ruud Das and Wendy Tra at Xpand want to use the same technique to culture beta cells, using a special bioreactor that they developed themselves and where a great many cells can be cultured in a plastic bag in a controlled environment requiring far less need of medium. The same technique should work for beta cells, they figured.

Summer 2012
The whole idea behind DCTI is to transplant healthy, well-functioning beta cells into patients who no longer have any of their own. Naturally, this requires a sufficient number of beta cells. There is a shortage of organ donors, so the researchers are searching for ways to create new insulin producing cells (see also: Wanted: cells for insulin production). This is not the only challenge, however, for the culture should not only be successful in a test tube, but also on a large scale. A healthy pancreas has around a million of islets of Langerhans, containing for sixty per cent beta cells. In other words: there is plenty of culture work to do. That is where Xpand comes in.

Autumn 2013
The first batch of cells from Leiden arrived at Xpand. Since adult beta cells do not divide spontaneously, the Leiden researchers had changed them: the "stripped" cells no longer produced insulin, but they could divide. Both the stripped beta cells and the duct cells must be prepared for culturing. It was now paramount to find out as soon as possible under which circumstances the cells thrived best. Unfortunately, disappointment came soon after. In order to culture the cells in the bioreactor (and stop them from being flushed away with the medium), they needed to attach to a so-called microcarrier: a marble with a diameter of two hundred micrometres covered with proteins that would serve as a good base for cell growth. When Tra added cells to the medium with microcarriers in a culture dish and removed the medium after a while, there were hardly any clusters of cells: alas, they did not want to attach.

Winter 2014
Growing duct cells seemed to be a good alternative. However, they proved to be quite difficult customers. The population of cultured cells was not pure; they were difficult to sort. Moreover, they needed quite some medium. After a few months of experimenting, Tra pulled the plug. Duct cells are no longer a priority. Xpand will focus on beta cells from now on.

Spring 2015
A breakthrough for the stripped beta cells: a new batch of cells, provided with a fluorescent label, proved to attach properly. Microcarrier CellBind glows with fluorescence as soon as Tra prepared it. The success was short-lived. Betas do want to attach to CellBind now, but they never let go again.

Summer 2015
The cells of two donors were growing in flat culture flasks. They seemed to be doing well: the correct microcarrier, the correct growth factors, and fifty per cent of the cultured cells could be harvested. The yields are not great, however. Das and Tra were not prepared to give up on half their culture. There certainly was room for improvement in the harvesting process.

Spring 2016
You need to know your cells before you can grow them. It had already become clear that betas are not the easiest of cells. They were not impressed either by the restriction enzymes that can usually separate cells from their microcarriers pretty easily. Even after taking a bath for an hour in a mixture with the enzyme, by no means all the cells had let go. Do they have to soak a bit longer? If truth be told, we had better not, for long soaks also destroy cells.

Autumn 2016
On to the next step: culturing the cells in the bioreactor. It can hold an equivalent of a hundred flat culture flasks of cells simultaneously. Two hundred million cells, if they are lucky. That would be enough beta cells for tens of patients with type 1 diabetes. That is to say, if they manage to change stripped betas back into insulin producing cells. That work is currently in progress.

Winter 2017
The first rich harvest was a fact! It was a breakthrough. Stripped beta cells could be transformed into insulin producing cells. To turn one into the other, the stripped beta cells had to be transferred to a so-called enrichment process. A more or less harmless protein mixture, containing for sixty per cent beta cells, was flushed away with the medium. The remaining microcarriers were washed clean of extraneous material and stripped beta cells were left behind. The microcarriers were then washed in a mixture with restriction enzymes that could cut the beta cells open: the cells could now divide properly. Viva the enrichment process!
Transplanting islets in an artificial pancreas

A fifty eurocent coin

In the lab of bioengineer Aart van Apeldoorn, researcher Don Hertsig is pouring some type of elastic biomaterial in a tiny, especially designed mould. After a while, the material has hardened enough to be removed from the mould, and ready for the controlled puncturing of tiny holes in the material. The result is an elastic, thin layer of biomaterial that is not much larger than a fifty eurocent coin.

This wafer thin “coin” is meant to be a carrier for islets of Langerhans during transplantation. “Pressing or pouring the biomaterial creates a kind of micro egg container with tiny cups”, Van Apeldoorn explains. “You can collect one islet in each cup. The holes make it easy for blood vessels to grow in to give islets access to oxygen and nutritional substances. When we cover up the graft with yet another layer of material, the islets have their own protective environment.”

In the meanwhile, the new location for the transplantation material has been successfully tested in small lab animals. The next step is to test the material in pigs.
Eleven artificial pancreases

Immunologist Paul de Vos is researching the effectiveness of an artificial pancreas in rats and mice. “First, the empty graft is placed underneath the skin of a mouse or rat”, he explains. “The material is foreign to their body, so a rejection reaction is initiated. Once this reaction is done and over with and the graft contains sufficient blood vessels the islets are administered intravenously. If we do it sooner, all the islets will die immediately.”

The first results of the artificial pancreas are very promising. In the large picture, the back of a rat has been cut open in order to assess the blood circulation in the graft. The circulation is fine; the islets are surviving and producing a normal amount of insulin. In the small picture, the isolated islets are visible under a microscope.

Eleven lab animals have been supplied with an artificial pancreas, and some animals have been doing well for four months already. In the next few years, the graft will be gradually scaled up from small lab animals via bigger lab animals to humans.
Since several years, patients with severe forms of type 1 diabetes are eligible for an islets of Langerhans transplantation. These islets are extracted from a donor pancreas and injected into the patient’s liver. The transplantation in itself is successful, but since the islets have to be infused into the liver, many of them are lost during transplantation and in the following period. Bioengineer Aart van Apeldoorn and immunologist Paul de Vos are trying to find a better transplantation location with the help of biomaterials.

“Islet transplantation is a good alternative option but more than fifty per cent of the islets die.”

The fact that the islets are transplanted into the liver is mainly for practical reasons. De Vos explains: “Doctors do not want to touch the pancreas, as the organ also produces digestive juices. If these start leaking, the problems are incalculable. Islet transplantation is a good alternative option but more than fifty per cent of the islets die after the transplantation. We want to prevent this loss by transplanting these very delicate islets into an artificial environment that mimics the pancreas.”

This artificial environment must meet certain criteria. “The material may not be degradable and should be easily removable from the body”, Van Apeldoorn explains. “Furthermore, the material may not be toxic to cells and the islets may not attach to it, for this could make the islets change shape and lose their function.”

Creating an artificial pancreas using islets should at least be as efficient as the current method. Otherwise, it is useless to continue. If and whether a method is adequate enough, however, is not an open-and-shut case. De Vos: “We receive islets from deceased donors, so we have to take care. They are not lying on a shelf waiting for us to be used whenever we feel like it. That is also the reason why we want to monitor as much as possible.”

In some type 1 diabetes patients, the glucose level in the blood is so poorly controllable despite insulin treatment that a transplantation of a new pancreas is their only option. This transplantation is a difficult procedure with a great risk of damage to the organ. Researchers Henri Leuvenink and Marjolein Leemkuil at the University Medical Center Groningen are working on a solution so as to improve the condition of donor pancreases.

Patients with type 1 diabetes usually manage to keep their glucose level under reasonable control by injecting insulin when needed. For some patients, however, it proves to be very difficult: their blood sugar varies enormously and they often already suffer the consequences at an early age. A continuously high blood sugar level may lead to kidney failure, for instance, or damage to the retinas or nerves; an excessively low glucose level may make you lose consciousness or even induce a coma.

These patients are better off with a pancreas transplant. Leemkuil: “This is a far-reaching operation with a high risk of complications. Some of the patients are not physically fit enough to undergo such a major operation. Sometimes a patient has to stay in the hospital for months. The results after a successful transplantation are good, by the way; many patients are without insulin after the operation.”

In the Netherlands, around thirty pancreases are transplanted each year. Such an operation demands extensive preparation and great precision. A pancreas has a soft structure and is far less solid than a kidney or a liver – which means that it is easily A human pancreas is prepared for connection to the pump.
damaged. Such damage has major consequences: only two per cent of a pancreas is made up of islets of Langerhans (containing insulin producing cells); the greater part is comprised of cells that produce digestive enzymes. If these enzymes start to leak into the recipient’s abdomen, they might also digest their own organs. Furthermore, despite the doctors’ carefulness, complications are anything but rare.

Leuvenink and Leemkuil want to lower the risk of damage to the donor pancreas as much as possible, so that the number of suitable donor organs increases. “Damage to organs occurs in different stages of the donation procedure”, Leuvenink explains. Even at the moment of the donor’s death there is the risk of damage. Next, the organ is cooled in the operating room, taken from the body, and transported on ice in a polystyrene box to the hospital of the receiving patient where it is connected to the recipient’s blood vessels. This is the moment when, finally, warm blood flows through the organ again. There must be a different way, the Groningen researchers believed.

An alternative for the polystyrene box is the so-called machine perfusion, a method that has been copied from the heart-lung machine. If you can connect the organ that is to be transplanted to this type of machine as soon as you have taken it out of the donor’s body, you limit the chances of damage. “When an organ cools down, its metabolism falls to approximately ten per cent. So the organ still needs oxygen and nutrients. The pump allows you to continually flush the organ with the specific fluid of choice and, moreover, it helps keep it at the desired temperature. An oxygenator provides the oxygen. You could even administer medication or repair the organ”, Leuvenink says.

If you connect the organ to a pump straightaway, you can also perform tests on it before you transplant it. Leuvenink: “If you buy a used car, of course you want to make sure that the motor runs properly. But when you receive a donor organ in a polystyrene box, you are completely in the dark. ‘Test driving’ the organ first is, therefore, very relevant. If it is a pancreas, the first thing you want to find out is: does it produce insulin?”

The first tests with pig pancreases were successful. Leemkuil also tested the pump’s effects on the tissue of rejected human donor pancreases and compared these with the tissue of pancreases that were stored in the conventional way. The pump system did not harm the tissue, and the vitality of the pancreases was greater: they contained more ATP, the carriers of energy in cells. Today, the pump’s effects on the quality of isolated Langerhans islets are being studied – in a collaborative partnership with the Leiden University Medical Center.

“Sometimes a patient has to stay in the hospital for months.”

Similar pumps are already being used for kidneys, livers and lungs. Machine perfusion for the pancreas, on the other hand, is still uncharted territory. Within DCTI, Leemkuil worked on a prototype for the pump, using the existing devices for kidneys as a basis. “We have found that the kidney pump as such is not suitable for a pancreas and that we will have to make quite some adjustments, but we wanted to find out first whether this type of installation would be useful for this organ in the first place. If it looked safe, we could develop a pump specifically for the pancreas.”

“Sometimes a patient has to stay in the hospital for months.”

Once the pancreas pump is finally there, it might also be used in order to optimize conditions for islet isolation and improve islet transplantation. The expectations are that the islets in a donor pancreas that is connected to the pump will stay in a better condition. This would be an added bonus, since separated islets do not function as well as an entire pancreas. That is the reason why a transplantation now still requires the islets of two or three donors. Leuvenink: “We want to try and use the pump to improve the condition of the pancreas and thereby the quality of the islets, so that in the future one single pancreas will do.”
After a transplantation, the Langerhans islets do not give their best performance yet. Why are these transplantations performed anyway?

"Because the treatment is often effective. The first islet transplantation took place in the 1980s. This procedure has been performed worldwide 2,000 to 3,000 times so far. The treatment improves difficult glucose control in the patient, albeit that there are side effects, such as infections or a higher risk of certain types of skin cancer. At the moment, we want to improve the treatment through the use of carrier materials."

As for those carrier materials, can you simply try them on humans?

"No, we cannot. They will have to be tried in a research setting, with the consent of the hospital’s Medical Ethics Board. We have tested the carrier materials in small lab animals within the DCTI project. We will now have to prove their effectiveness and safety in larger lab animals, such as pigs. If, and only if, those tests are successful, the treatment may first be applied in patients."

What would, or could, this first application involve?

"We could transplant most of the islets in their carrier material into the liver in the usual way, apart from a small amount of islets that we could implant in another part of the body, for instance underneath the skin. In this way, the first patients will receive the regular treatment, while we can also see how the islets in their carrier materials behave in the human body."

Due to the shortage in donors, there is talk of a treatment with stem cells. Would that involve the same procedure?

"Each carrier material has already been approved by the authorities for use in humans. That is also one of the reasons why we chose these materials at the start of our research. If you add stem cells, you will enter a completely different area."

What is the big difference?

"We now isolate the donor’s pancreatic islets and try to keep them alive until they are transplanted a few days later. We do nothing special to the cells themselves. Stem cells, on the other hand, will first have to multiply so that you end up with a nice amount. You will then have to let them grow to maturity with the help of growth factors. It takes longer to culture stem cells than donor cells, and during their cultivating they may undergo all kinds of changes, including genetic ones."

What consequences does this have for tests on humans?

"It means that you will first have to soundly test the cell product. You will, for instance, have to prove that your culturing procedure does not leave you with cancer cells. It will take some time before the treatment with stem cells will be available."

If we ever get there, for cancer cells make it all sound pretty risky.

"There are not enough donors to treat everyone with type 1 diabetes, so if we want to do more than treat symptoms with insulin injections alone and come up with a definite solution, we will have to find it in other cell sources. There is no other way. It is important, though, that patients will always have to give their consent if they are to participate in research. They will have to be very well informed about the potential risks beforehand and the safety of the cell products will have to be tested extremely thoroughly first."

What is the current state of affairs?

"One in six hospital beds in England are now occupied by a patient with diabetes who is suffering from complications from treatment, so a true solution would be more than welcome. However, as with all medical research, it is not a matter of weeks or months, but years and years. Patients with type 1 diabetes will have to be patient before they can grasp this last straw."
DCTI is a research initiative to improve beta-cell replacement therapy and to make this therapy accessible to patients with failing beta cells. These patients have developed diabetes because beta cells in the islets of Langerhans no longer produce insulin. The main research goals are to increase the availability of high quality islets for transplantation, identify factors for long-term islet function and survival, and to exploit alternative transplantation sites with the use of biomaterials.

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