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Cornea Update

Sheraz Daya

Ex-vivo stem cell allograft transplantation could be the source of forward leaps in clinical practice in the future

Gary Finnegan
in Leeds

TECHNOLOGICAL advances and techniques borrowed from bio-engineering have sparked innovations in corneal surgery, but many recent advances are essentially a recycling of existing theories with the benefit of better science, according to Sheraz Daya MD, East Grinstead, UK.

He notes that progress in areas such as limbal transplants are changing the prognosis of patients with stem cell deficiencies but he believes it would be a mistake to view this as entirely new.

Delivering the annual Choyce Medal Lecture at the UKISCRS Annual Meeting in Leeds, Dr Daya said corneal surgeons had described stem cells in action in the 1960s, even though it would be decades before scientists unraveled the underlying mechanisms.

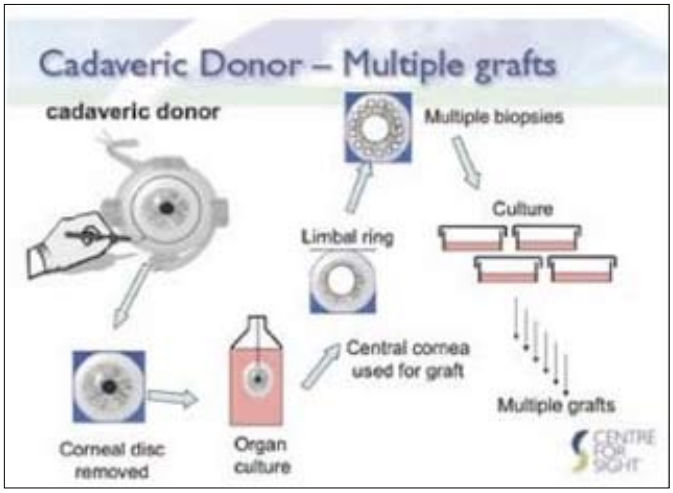
"We've been pushing the boundaries with our work on stem cells but this is not a recent discovery. Conjunctival limbal autograft and allografts were discussed in the proceedings of the Royal Cornea Congress in 1964," said Dr Daya, who has himself mined our surgical textbooks for inspiration.

"In fact, a lot of the things that we think are new are actually ideas that are reborn because we've got better technology and better understanding. They didn't understand the concept of limbal stem cells in those days but they knew that if they transplanted the limbus, those eyes did better," he added.

In a wide-ranging talk tracking innovations in corneal surgery, Dr Daya described how stem cell-deficient cornea patients were treated, and revealed a potentially groundbreaking observation that could have major implications for medical science.

He commented that ex-vivo stem cell allograft transplantation has sparked considerable excitement over the past decade and could be the source of future forward leaps in clinical practice. The team at East Grinstead has been working with the limbal ring of cadaver cornea and, after digesting the tissues with trypsiin and culturing the cells, they can transplant stem cell sheets into the eye.

He said preparing the cells can take two or three weeks but from the time he began applying it 10 years ago, the results have been intriguing. Dr Daya told how one of his



patients had unusually grown around 20 layers of cells on his central cornea five months after the thin sheet of tissue had been transplanted. The team then performed DNA fingerprinting to see whether the cells present were those of the host or the donor.

"Much to our surprise, there was no donor DNA. So what was going on? Well, we believe we've stimulated a mechanism that brings stem cells into that area to heal that eye. And it seems to continue for some time afterwards," said Dr Daya, acknowledging that the group including the Blond McIndoe Research Centre and the Corneoplastic Unit is now working to prove their hypothesis.

In any case, the fact that no donor cells are present

means that immunosuppression can be discontinued after nine months and that it is feasible to prepare cadaver corneas for transplantation rather than relying on autografts - a major boost for patients with stem cell deficiencies in both eyes.

"Something we did triggered a host response. If we can find out what that is we might not even need stem cells. The ultimate goal is to be able to trigger this response using a cocktail of chemicals and cytokines," he said. This, he added, could be applied to other disciplines including, for example, liver and pancreas regeneration.

"Triggering tissue regeneration would mean you need not worry about donor shortages," he told Eurotimes in an interview after the lecture. This could also do away with the delicate and labour-intensive process of culturing and transplanting cells, but is still some way off.

In the meantime, Dr Daya and colleagues at East Grinstead are now examining ways of transporting the thin sheets of stem cells they prepare for transplantation. The trouble is these cells last just two hours in the operating theatre so the hospital has tasked a PhD student with figuring out how to preserve them for transplantation. Freezing is one option and alternative carriers is another. Eventually, the team would like to prepare larger volumes of stem cells at the UK hospital and ship to centres around the world.

"This type of work is currently quite expensive. The key is to make it cheaper by using automated and high volume generation techniques. The expensive elements of this technique are laboratories and people. If you have scientists spending time culturing cells when they could be doing other things, it increases the costs," he said.

In the Choyce Lecture, Dr Daya paid tribute to the ophthalmic industry. The technological advances that have made surgeons; lives easier - and patient outcomes better - in recent years have arisen in part thanks to developments by industry. Dr Daya, who trained in the US before taking up a consultant post at East Grinstead,

Sheraz Daya (right) receives medal award from Diana Choyce (wife of Peter Choyce) pictured with Tayo Akingbehin, president of UKISCRS

works closely with a number of companies and told the UKISCRS Annual Meeting that risk-taking by innovative firms has been vital to progress in his field.

"There's no way you could do these things without the industry. They take an awful lot of risk on what sometimes seem like whimsical ideas. They've given us the tools of our trade and this is often overlooked," he said. Dr Daya said attracting research grants is not always easy for smaller hospitals without university links but that the lab at East Grinstead had been central to his pioneering stem cell work to date.

"You can't do this alone. As a leader you can initiate things but you depend a lot on people around you to ask the right questions and to challenge answers. You also need a great deal of help to do all the donkey work. It's often said that people who succeed and have good ideas invariably have a large competent team around them and I'm the first to acknowledge that," he said.