

Ep. 1 Inflammation Nation

Grainne O'Leary

Welcome to Season Two of inflammation nation. My name is Grainne O'Leary. Inflammation nation is a podcast from Arthritis Ireland, aimed at increasing awareness and understanding of arthritis and related conditions. It's my great pleasure to be joined today by Professor Frank Berry. Professor Frank Berry is a professor of cellular therapy at the University of Galway, and a principal investigator at the Regenerative Medicine Institute Remedy. Here he directs a large group of researchers who focus on the development of new repair strategies in stem cell therapy, and gene therapy in orthopaedics. He's contributed to the fields of tissue engineering and regenerative medicine by developing innovative and successful cellular therapies for tissue repair, joint injury and arthritic disease. You're very welcome, Frank, and thank you for joining us today.

Frank Barry

Thank you very much. It's great to be here.

Grainne O'Leary

I'm going to start by asking you about, I suppose, taking you back to maybe your childhood or your schooling, and what was it that sparked that first interest in science that maybe led you to pursuing a career in this area?

Frank Barry

To be honest, I always had a strong interest in science, and especially life sciences and biology. And probably the beginning of that, for me was when I was a kid, and you know, wildlife and bird watching and an interest in animals was what sparked that, that pursuit, which I then went on to continue and made a career out of it.

Grainne O'Leary

So you started off? Did you start off with doing a science degree?

Frank Barry

Yeah, I did a science degree. I got a degree in biochemistry. And then I went on to do a masters and a PhD also in biochemistry. And so that was where it all started. Then, after my PhD, I went to the Kennedy Institute of rheumatology, in the UK to do a postdoctoral fellowship. And that introduced me to the field of osteoarthritis research, cartilage repair, cartilage biology, joint diseases, and inflammatory arthritis. And so I stepped into that field, then, and I pretty much stayed in the same area ever since. Along the way, when cell therapy began to become a topic of some interest, I became involved when I was working in the US, and then, you know, the question came up, can we think about cellular therapies as a potential treatment for arthritic diseases? So that took me down that path, which I'm still pursuing today.

Grainne O'Leary

Okay, so we're going to come back to that whole definition of the fields of cellular therapy that you've just mentioned, which is your speciality. So can you tell us a little bit about what that is? What does it involve?

Frank Barry

So cell therapy is a sort of a new principle of treating patients that involves delivering living cells to the patient, either by infusion into the bloodstream or locally to a specific tissue or organ. The idea is that delivered cells can elicit a repair response, or they can lead to the formation of repair tissue, so that we can think about a number of potential disease treatments, by the use of these cell preparations. Sometimes their stem cells, sometimes their adult cells from adult tissues, but the whole idea is to regenerate and restore tissues rather than trying to replace them.

Grainne O'Leary

So in that case, are you sort of putting healthy cells into, you know, a joint for perhaps its damaged

Frank Barry

So the idea that you're putting healthy cells into damaged tissue, and the healthy cells can come from the patient himself or herself, or they can come from another person or donor. And the healthy cells, the idea is that they will repair the damaged tissue, and it could be a joint for example, it could be the heart, it could be damaged muscle, and so on. But the idea is that the delivered cells in the cell therapy application, those cells, repair the damaged tissue and lead to recovery of the patient.

Grainne O'Leary

Okay, of course, this has been applied in the area of osteoarthritis, and that's obviously of keen interest, I'm sure to many listeners, because, you know, osteoarthritis is very prevalent. You know, it's a form of arthritis that's traditionally been difficult to treat. Is that one of the main motivations for your work?

Frank Barry

Yeah, absolutely. So, you know, we understand that osteoarthritis is a very prevalent condition. It's probably the most common type of arthritis and it has a huge impact on patients and on their families. It causes a great deal of pain and loss of mobility. It has a significant economic impact, the health care costs associated with treatment of these patients is very significant. And it's as significant as you know, cardiovascular disease and cancer in terms of its impact on society and on patients. But yet despite all, despite the prevalence of the condition, there is not one treatment, which is disease modifying as opposed to symptom modifying, there isn't one treatment that reverses the destruction that happens in the osteoarthritic joint. There isn't any drug, any medication, no therapeutic, that can be delivered to stop the degeneration of joint tissues and osteoarthritis. And to me, that was a very striking observation that there's this disease, which is so prevalent, but yet there are so few therapeutic options. And then, when I became aware of the idea of cell therapy, I thought, you know, we have to try this because the potential if you've got a tissue, which is undergoing degeneration, and these cells are supposed to be regenerating, then why not put the cells into those osteoarthritic joints, to see if they'll stimulate a repair response. So that was the motivation for starting this. And, you know, we're still testing it.

Grainne O'Leary

And just to come back to a point you made there about, you know, that they've had no therapies developed to sort of act as a disease modifying agent and of course, huge transformation happened in the whole area of inflammatory arthritis treatment, such as rheumatoid arthritis for the last few decades. And you know, certainly in the people we interact with in Arthritis Ireland we hear the stories, we know, it's had a huge impact on how people on their quality of life, etc. Why do you think that transformation has never happened in the area of osteoarthritis?

Frank Barry

Yeah, it's a very good question. So you're absolutely right, of course, in the area of rheumatoid arthritis and inflammatory conditions, the treatments have been absolutely transformative, you know, dramatic changes in the quality of life of the patients who have received these, these medications. I think the reason why we haven't seen nearly as much progress in osteoarthritis is because it's actually a much more complex disease. It's a multimodal multi symptomatic condition, where a large number of different factors contribute to the development of the disease. And there's genetics, there's lifestyle, there's previous injury in the joint. There's aspects of mobility and use of the joints all contributing to the development of the disease. So the causation of osteoarthritis is much more complex, I think, and therefore, the treatments are also much more complex.

Grainne O'Leary

Okay, so let's move on a little bit now to actually talking a little bit about the current research that you're involved in. So can you tell us I know, so far, you've gone through phase one and phase two. So can you tell us a little bit about that. And what's happened in those stages?

Frank Barry

I guess it all started with, when we started testing, cellular therapies for the treatment of osteoarthritis, we did some studies in animals, where the animals had arthritic joints, and we were able to deliver the cells into these and there was really quite a dramatic repair response, quite impressive, positive response. And so that led us on to seeking approval to do a human study. And we did a phase what so called phase one study, small sort of first preliminary study. We finished that in 2015, there was 18 patients enrolled, this happened in France. And the majority of the patients that received the cell treatment in that early trial, had quite a dramatic positive response to their pain, that there was a significant reduction in their pain, their mobility improved after they received the injection of the cells directly into the knee joint. By the way, all of the patients that we're talking about have osteoarthritis of the knee. That's the focus. That's the joint we're focusing on. So the results of that phase one study were really quite promising, even though it was too small to be statistically significant. The real purpose of the phase one study is to make sure that it's safe and that there are no adverse events. Because of the results, we got in the phase one study, then we applied for approval in Europe to do a phase two study. And we've just literally finished that now. And we're waiting to see the results of that.

Grainne O'Leary

And did that involve a greater number of patients in that phase two.

Frank Barry

It involved a larger number of patients, the target was 150 patients in total, would be enrolled in the trial in the phase two trial, because of COVID, things got interrupted in a fairly serious way. So we ended up treating just 100 patients and that's all now done. And so we're literally doing the analysis of the results at this point.

Grainne O'Leary

And you mentioned there about some of the benefits the patients experienced such as reduced pain, were there any other benefits even from from the from the first couple of phases.

Frank Barry

In the early phase trial, within 24 hours of receiving the cell treatment, most of the patients showed really quite a dramatic improvement in their pain scores. There's these standardised pain scoring systems, most of the patients showed a dramatic improvement in pain outcomes. And this was sustained for a year, at least a year following the treatment. So it wasn't just a, you know, a placebo effect, we think because it was sustained. Within a week of receiving the cell treatment, most of the patients again, had improved knee function. And again, this was sustained for the year that they were followed up. We didn't do any imaging of the joints, there's no X rays or MRIs of the joints in that phase one study. So we weren't able to see if there was actual repair of the tissue. But at least in terms of the functional scoring, the results were quite good. In the phase two trial, there's very elaborate imaging of the joints before and after the cell treatments. So when the results are disclosed, we will know if there was a regenerative or structural change associated with the treatment.

Grainne O'Leary

And when do you when do you expect to, or will it be publicly known the results of that phase, phase two.

Frank Barry

All will be published. The results are literally being unblinded right now you know that this when the study is active, it's fully blinded. So the physicians and the patients don't know which group they belonged to. But in October, the six month time point was reached after the last patient was treated. And so that's when the results are opened, analysed, they're reviewed and all put together. And so in the near future, in a matter of weeks, I think we'll know the results of that, that's a six months time point. And then of course, the patients will be monitored up to two years after they receive the treatment. So we'll know both the short term and the long term outcome of the treatment.

Grainne O'Leary

Okay, so certainly very exciting point in the study.

Frank Barry

Very exciting, but also along the way, just very recently, in fact, it turns out that a similar study was carried out in Australia. And that was just published in the last few weeks. And that also reported quite a positive outcome. So based on another study, it's a completely

separate, unrelated study done somewhere else, where there's a positive outcome, I think we can be very optimistic that we will also see a positive outcome.

Grainne O'Leary

Certainly very positive news. And then in terms of there's a third phase, so can you tell us a bit about what's going to happen and what timeframe.

Frank Barry

So the way these clinical trials work is that you have to start off on a small scale, that's the phase one study, then you do something that's a bit bigger, a phase two, and if the results of the phase two study are good, we go ahead and do a phase three study, which is much, much bigger, involving hundreds and hundreds of patients. And it's likely that the phase three trial will happen in the US. And I'm spending a lot of time in the US this year, trying to make arrangements for that phase three study to begin, and we've made quite a bit of progress. So the plan is that the phase three study will involve 400 to 600 patients, maybe even more than that, instead of them receiving their own cells, they'll receive cells from a donor. So instead of being an autologous, that is cells coming from the patient themselves, it'd be an allogeneic study where the cells come from the unmatched donor, that just makes it logistically much easier. And it also makes it much cheaper to carry it out.

Grainne O'Leary

And was the basis on which the first two phases were done, were they from donor, I suppose donors other than the patient.

Frank Barry

No the first two phases where the patient's own cells. So what happened in those two studies, the phase one and the phase two study was the patients came in, they underwent a small liposuction, like an abdominal liposuction and a small amount of fat tissue was taken from the abdomen, usually about 20 grammes quite a small amount. And then that fat tissue is sent to a processing, a cell processing facility, and the cells are extracted and grown in culture. And then when the cells are already, they go back to the hospital, and they're injected into the patient's knee joints. So in those two studies, the phase one and the phase two, the patients were receiving their own cells. But in the phase three, the plan is that the patients won't receive their own cells, they'll receive donor cells. The reason for doing that is that, as I said, it's much logistically much easier and it's also much cheaper to prepare those cells from the donor rather than from the patient himself or herself.

Grainne O'Leary

So is the phase three also about, you know, moving this study forward in terms of it being you know, a realistic treatment possibility.

Frank Barry

Absolutely. The hope is that when the phase three study is completed, we will then get approval to essentially launch the cell therapy product and make it available both in the US and in Europe. That's the intention, that's what we hope. And that's the motivation for doing all of this is that eventually there will be this treatment available for, you know, large numbers of patients. And even though we focus only on the knee, of course, we also have our eye on

on other joints, you know, the hip, the ankle, and so on. We've just focused our attention so far on the knee.

Grainne O'Leary

And why was that actually?

Frank Barry

It's easier to deliver the cells into the knee joint than into other joints. And so that's really the only reason.

Grainne O'Leary

I suppose it is one of the main joints, affected by osteoarthritis, that and the hip.

Frank Barry

Yeah, that's exactly right. But there's no reason to think that it wouldn't also work in other joints. We just haven't been able to test that so far.

Grainne O'Leary

So certainly sounds really exciting. And certainly welcomed news for many listeners who are living with osteoarthritis. What sort of steps are involved after and what kind of timeframes are involved in terms of, you know, I suppose the endpoint being a patient receiving this treatment?

Frank Barry

So we'd have to do the phase three study, that's, that's the way it works, we have to do a study in a large group of patients that's highly controlled, very sort of scientifically designed and very well controlled, and very well carried out. We have to do that trial, before we can go to the regulator either in Europe or the US and say, 'do you think these results are good enough, and that the treatment is safe enough that we can now essentially make it available to the population in full, the patient population in full'. So the data would then be reviewed by a panel of experts who will look at it in sort of forensic detail. And they'll look at every part of the results and every part of the conduct of the study. And if they're convinced, and the threshold for this is really quite high, but if they're convinced that there is a positive benefit, there is no adverse consequences, there's no risk to the patients, then we can get a market approval to launch the product, and make it widely available. So that's the burden, the burden of proof then rests with us to show that it works, that it's safe, and that it represents a reasonable benefit to the patients. We also have the challenge of how to then make the product in such a way that it's economically viable.

Grainne O'Leary

Yes, I was gonna ask you about that.

Frank Barry

So I mean, a lot of these technologies, cell therapy and gene therapy we hear a lot about nowadays, they tend to be incredibly expensive. And for a condition such as osteoarthritis, which is so common, I think it only makes sense, if the cost of the final product, the cost of the treatment is low enough for it to be widely available. So we have the challenge, then of

optimising the manufacturing technology to make it highly efficient, cost effective. So that the final, the final treatment is, you know, within a reasonable price range, that it can be either supported by insurance companies, or that individuals can pay for it themselves. So we're talking about quite a small, quite a low cost for this to work, there's no point having a treatment available that works, but it's inaccessible because of cost.

Grainne O'Leary

And maybe you don't know the answer to this at this point in time. But is the therapy something that a patient would need on an ongoing basis? Or is it envisaged that it would be a one off treatment?

Frank Barry

That's a very good question. So far, all the work we've done has been on a single treatment only, there's no particular reason for that, except that's what we focused on. I would expect that patients would receive several repeat treatments throughout their lifetime. So if a person has, for example, early osteoarthritis, they might cell therapy injection, then a few years later the match receive it again, and they might continue receiving it, you know, at intervals throughout their life.

Grainne O'Leary

And we're not talking about a homogenous group either there's different stages of disease and that. And therefore reducing the need for further joint replacement surgery when people are living longer now and they have to go in for revisions.

Frank Barry

Of course, but the whole objective here is that number one, the patients will feel better, that they won't have so much pain and they won't have so much disability. And number two is that they won't need that joint replacement surgery. You know, for many more years that they'll be able to live with functioning joints for much longer than would otherwise be the case. So the need for the knee replacement or the hip replacement surgery is put off by years that's the ambition here. Yeah, the risks associated with revision and so on. So if we can do it in such a way that patients are much older when they receive that joint plate then I think will have succeeded.

Grainne O'Leary

So I suppose, Frank, if I can finish by asking you this question, you know, what is your hope for people living with osteoarthritis in relation to your research?

Frank Barry

So I think before I retire and sort of hang up my hat and give up this, this business that I've been in for a very long time, what would give me the most satisfaction personally and professionally would be that there was a treatment, which was going to be given to patients that made them feel better that I contributed in some way towards the development of, that to me would be an achievement that I'd be very proud of. So what I do hope is that at the end of all of this, we'll have something that works for those patients and something which is effectively, you know, life altering for him for many people. That's, that's what I hope.

Grainne O'Leary

And on that positive note, I'll bid you farewell and thank you so much for joining us Professor Frank Barry.

Frank Barry

Thank you very much.

Grainne O'Leary

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