

Weston Park Cancer Charity Podcast

Episode 5 – Breast Cancer – Professor Ingunn Holen

Ruby Osborn: Hello and welcome to the Weston Park Cancer Charity Podcast. sharing stories about our work, what we do and the people we support. From funding life-saving research to providing practical help and emotional support, it's our job to care in every sense for our patients and their families. I'm Ruby, and in our second breast cancer awareness month interview, I'm talking to another of our research grant holders working on breast cancer and how it spreads to the bone.

Ingunn Holen: My name is Ingunn Holen and I'm Professor of Bone Oncology in the Medical School, so I work at the University of Sheffield. We're working on how cancer spreads throughout the body, and I think most people are aware that that's a really dangerous situation. So when a tumour gets detected early on, before it spreads anywhere else, the chances of survival are often very very good, but when it starts to spread to other sites, now then it becomes a much more serious problem, much more difficult to treat, and in some times, impossible to treat successfully. So there's lots of things we can do to prolong patients' lives once the cancer has spread but ideally we'd like to prevent that happening in the first place, and that's really at the heart of our research, how we can understand the cancer spread so that we can stop it.

Research in the team is focused around breast cancer spread and it spreads very often to the skeleton, if it does spread, and that is a problem that causes patients a lot of pain and other complications, very unpleasant. The other big problem with breast cancer is that it can remain dormant for many years, so when you have your first treatment, the surgery and the chemotherapy and the radiotherapy and it's all looking good, and then maybe five years later or even ten years later the cancer returns. And we know that that's caused by some cancer cells managing to remain dormant and just avoid being detected by our immune system and avoid being killed off by the treatment that we give, because they just remain dormant, they don't do very much, they just sit there. And so we want to understand how these dormant cells survive for all those years, for starters. And in many patients they never wake up and cause a problem, but in some patients they do, and we don't understand which patients that is going to be.

Ruby: Obviously you're still trying to find a lot of the finer details but broadly, what differs between a dormant cell and an active cell? What are they doing or not doing?

Ingunn: So the dormant cell doesn't do very much at all. I think most people know that cancer cells are dangerous because they grow and then they divide very quickly, and then they cause a lump and then the lump grows bigger and bigger and it causes lots of problems as they just kind of takeover the neighbourhood. Whereas these dormant cells don't do any of that. And that means that the drugs that are very good at killing cells that are very active and that divide very often and that grow very fast, which is most of our cancer treatments are aimed at

eliminating those cells, they aren't effective against cells that actually don't grow and divide at all, they just kind of sit there and say, well, you can try and stop me from growing but that doesn't matter to me because I'm not growing anyway.

If we could understand how they survive by just sitting there, because they are alive so they must use some mechanism to survive for five years, then we can move on to disrupt those processes and say, okay, you need this mechanism to survive, but we can interfere with that, and now you can't survive anymore. And that's one of the things that we're studying in the lab, where we make what's called model systems of these dormant cells, cause we can't really study this in patients but we can do it in our various cell models in the lab. And then we create dormant cells, and then we try every which way to kill them.

We also study these dormant cells that we have in the lab and try and find out what is it they make that differs from the molecules that growing cells use. Is that the key? And we also look at how these dormant cells interact with normal cells to see if it's something to do with their surroundings and how they adapt to that, that makes them so able to just stick around for years and do nothing much. And ultimately we need to understand what it is that triggers them to wake up and grow again so that we can prevent that from happening.

Ruby: So what could this research mean for patients in the future?

Ingunn: If we could prevent cancer recurrence, and I'm talking about breast cancer here that we know this is a problem, then that is pretty much the Holy Grail in terms of preventing patients dying from breast cancer. Because we are very good at treating the, what's called the primary disease, which is in the breast. For the majority of breast cancer patients they will not die from breast cancer, they will die from something else. But around 20%, unfortunately, will get this recurrent disease which is much harder to treat. And so if we can prevent recurrence because we can eliminate these dormant cells or prevent them from growing again, then that would bring that ultimate aim of nobody dying from breast cancer just a little bit closer.

Ruby: Why is it important that we keep doing research?

Ingunn: Research is important because it underpins absolutely everything we do. If you go to your doctor and there's something suspicious and you have some sort of test, and then you maybe go to the hospital and you have some kind of imaging done, some kind of screening test done, or indeed you enter the treatment pathway, all those different things are based on research. Somewhere, somebody did the research to make those tests, to develop those imaging systems, and of course drugs don't just appear, there's a huge amount of research behind every single effective drug that we have. So yeah, research is important to keep that flow of new developments coming so that we can do even better for the patients in the future than what we are doing today. And so we will get new drugs, we'll get new combinations, we'll get better kinds of treatments, we'll get earlier detection, and all of that together is going to improve survival.

Ruby: What led you to your career and what motivates you to keep doing research?

Ingunn: I think I'm a problem solver by nature really. I see a problem, I quite like to have a go at fixing it, and if it's a big problem –

Ruby: Classic scientist.

Ingunn: – or it's more challenging even, yeah, it doesn't put me off, let's say, if it's a really big and complicated problem, and it kind of appeals to my logical mind I guess. So, I like a challenge, I'm interested in the biology, and I'm also interested in people. So when I had the opportunity to do a PhD at a cancer hospital I went for it and I really enjoyed it and I have been in cancer research ever since, because the challenge is still there. I can see also that research makes a difference. In breast cancer, within my lifetime, so since about the 1970s, we've just improved outcome all the time, and we've gone from a point where around 60% of patients died from their breast cancer to now 20% or less than that. Things are happening and I think that's been really encouraging for all of us researchers to see that we're not banging our heads against the wall, the research that we do does make a difference to patient outcome. There's still work to do but we have the talent here in Sheffield to tackle it, we can make progress together.

Ruby: What does make Sheffield such a good place to do research?

Ingunn: There are many good things about Sheffield and research. We have an excellent university, and we have a medical school – not all universities have medical schools but we have a very good one. And we are very highly ranked in the UK when it comes to both clinical and preclinical health research. So we have this environment for clinicians and scientists are working very closely together and where they're expected to do research and they want to do research, and it helps us recruit really excellent people to Sheffield. Of course we have Weston Park Hospital, that's essential, a specialist cancer hospital on our doorstep. It means we have patients who are interested and able to participate in research through clinical trials. And the charity is important because the funding that you provide allows us to link these pieces together: the scientists, the clinicians, all the different healthcare professionals that are involved in patient care, and the patients themselves and their relatives, so that we are all kind of a bit in it together.

We've had support from Weston Park Cancer Charity for a long time to do a number of different things and we're incredibly grateful for this. We've had some excellent research output from this work, investigating how cancer cells interact with normal cells in the skeleton and how drugs that actually work on the bone, on the skeleton itself, how they then also change the ability of tumour cells to grow. And through our research we've shown a number of things in how these tumour cells and bone cells interact in order to grow and we've also worked on particular drugs that been shown to reduce the ability of cancer cells to grow so quickly in bone. Another thing that we've done with the help of these grants is to create a number of really good research tools that both we and other researchers

can use to investigate these problems and that's really benefited not just our own work but researchers probably all over the world, and then they can use those models and study the problems that they're working on, and so we all contribute to that big jigsaw of solving how cancer cells spread to bone.

We also benefit from being able to train the next generation of researchers and that's super important. It means that we can recruit the best medical students and get them really interested in research and have the ability to actually do research for a year by joining our team. We've had a number of clinicians who have done PhDs in the lab team and then gone back to Weston Park Hospital and they're now consultants and treating patients, doing clinical trials, and we still work together these many years later. We've also had technical support and that is kind of the unsung and somewhat forgotten heroes of cancer research, I feel. The technicians who do all those little jobs of training students, looking after our samples, developing our new technologies, they really are so valuable to us.

So Weston Park Cancer Charity funding has really helped us put Sheffield on the map and be a leading force when it comes to this type of research into tumours and bone in particular. It's really been great to be able to build this research environment that just continues to grow and produce excellent science for the future. And I think that's a really important message for people who think about supporting Weston Park Cancer Charity who do fantastic work in facilitating that research community for the improvement of patient outcome, because cancer research is teamwork. Nobody makes these big steps alone.

Ruby: Thank you for listening to this episode of the Weston Park Cancer Charity podcast. I was speaking to Professor Ingunn Holen, Professor of Bone Oncology at the University of Sheffield.

Dean Andrews: Cancer changes everything, but so can we.