CUSTOMER PROFILE

Cancer transcriptomics and radiobiology

Changes in the transcriptome reflect tumor biology and predict response to therapy

Darren Roberts is a postdoctoral research associate within the Division of Cancer Sciences at The University of Manchester. Dr. Roberts studied genetics at the University of York and then moved to Leicester where he was employed as a research technician on a transplant team in the department of surgery at the University of Leicester. An interest in how and why cells die led to an MSc in molecular genetics and a PhD in mechanisms of cell death at the MRC Toxicology Unit in Leicester. Following postdoctoral work at the University of Alberta in Edmonton, Canada, he joined The University of Manchester in 2004 to investigate the role of hypoxia on chemotherapy resistance in colorectal cancer. From there, Dr. Roberts worked on the identification of biomarkers for a range of cancers, such as the genetic characterization of pseudomyxoma peritonei, and interactions between cancer and comorbidities such as obesity and colorectal cancer. Since 2015, he has worked on the development of gene signatures to detect hypoxia in prostate and bladder cancer in order to personalize treatment for patients undergoing radiotherapy. More recently, Dr. Roberts has been working on preparation of these signatures for use in routine clinical practice.

Darren Roberts, PhD
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"… we're investigating how changes in the transcriptome reflect the biology of the tumor …"

Thermo Fisher Scientific: Please introduce yourself and your research.

Darren Roberts: Certainly. I'm part of the translational radiobiology group based at The University of Manchester. Specifically, I'm in the Division of Cancer Sciences, and we're focusing on improving cancer outcomes for a variety of different patients, including those undergoing chemotherapy and radiotherapy treatments.

As part of translational radiobiology, we're interested in the effects [of radiotherapy] or changes within the actual tumor itself, and how they interact with radiotherapy. There are a lot of changes that are triggered by the microenvironment of the tumor, such as hypoxia, which results in large transcriptomic changes. So we're investigating how changes in the transcriptome reflect the biology of the tumor and predict how it will respond to therapy.

Thermo Fisher: Tell us what you set out to achieve with your latest project.

Darren Roberts: In our most recent project, we developed a prostate signature, and this was to predict a modified form of radiotherapy. We were interested in using a technology that would give us maximum amounts of data on the old degraded samples. So, in this project, we investigated RNA-Seq using Illumina™ platforms, and we also compared it against our current gold standard, which is the Applied Biosystems™ TaqMan® low-density array platform. We needed a third technology to actually compare them against this, and Applied Biosystems™ Clariom™ S Assays were the closest we could find to the old Affymetrix™ array systems.

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Thermo Fisher: When planning your research, how do you select the technologies you use?

Darren Roberts: We're quite agnostic for which technologies we use. We take the approach of using the correct technology for the correct sample. We have looked at array-based technologies, we've used next-generation sequencing (NGS), we've used targeted NGS, we've used qPCR, and we've even used Invitrogen™ QuantiGene™ assays.

As we move through a project, we have different focuses. In our discovery phase and initial verification phases, we'll be looking for a technology that can handle high numbers of samples. Because our focus is on radiobiology, quite often we will be looking at hundreds, if not thousands, of samples, and we want it to be able to deal with old formalin-fixed, paraffin-embedded (FFPE) material. The DNA and RNA tend to be quite degraded and difficult to be extracted, so at that stage we need a technology that deals with that type of material.

We generally use Clariom S assays in our discovery phase and early-stage verification because the technology is excellent with degraded RNA, which is something that is easy to obtain from old FFPE tissues. In the later stages of our projects, we move to technologies such as qPCR. We have a phase 3 clinical trial ongoing using the TaqMan low-density array, for example, in different tumor types.

Because we're focused on cancer itself, our main source for samples is FFPE samples, which are quite difficult to use. In addition, we use fresh-frozen tissue and cell lines to verify our results.

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Thermo Fisher: How does the research stage affect the technology selection?

Darren Roberts: Because of the samples that we deal with, there are generally certain technologies that work better for discovery and others that work better for development and analytical validation of the changes in the transcriptome that we're interested in.

And because of the way our projects develop—since we're focused on getting our data into routine clinical practice—different technologies at different stages are subjects. In the discovery phases, we want to have as much information as we possibly can, but as we progress through the project, we're interested in developing a test that is clinically useful, so that, along with which samples are available at that time, puts a different focus on which technology we use.

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Thermo Fisher: What made Clariom microarrays the ideal match for that phase of your study?

Darren Roberts: The Clariom S Assays actually performed far better than we were expecting, particularly because of the RNA-Seq results that we received. We had looked at the RNA-Seq data and found that, basically, there was very poor-quality data there. We were also looking at the qPCR data and found that there were several genes dropping out. So, we were quite relieved seeing the Clariom S Assay data, that we had high-quality gene expression data. And that has provided us with a database of a transcriptome of the samples. That was particularly important in this study because we were dealing with prostate samples, so we were dealing with really tiny pieces of tissue—usually on the order of about 10 mm x 1 mm—and we were taking a full micron section of that.

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Thermo Fisher: How does Thermo Fisher fit into your research workflow?

Darren Roberts: Having Thermo Fisher offer a range of technologies for our gene expression studies is certainly an advantage. They currently outperform most other suppliers.

Thermo Fisher: What would your advice be to others planning a similar study?

Darren Roberts: What we consider now is the sample itself rather than the technology. I think we've learned quite quickly that there is always a technology that is suitable for a particular sample. So, as we move forward, we'll look at the sample and the constraints we have on using that sample in order to decide which technology to use.

Personally, if I were going to this kind of study again, I would be looking at array-based technologies for early discovery with old samples. From there, I would move on to targeted NGS or qPCR, whichever one is most appropriate for the clinical setting to progress this into patient benefit.

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