Behind the scenes: DIRECT project Data Analysts

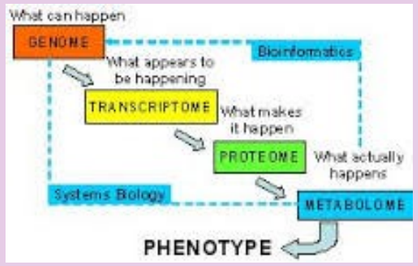
Dr Caroline Brorsson and Dr Ana Viñuela are both post-doctoral researchers in the DIRECT project whose roles are to analyse the data from some of the studies. We caught up with them to get their perspectives about their work on the project.

Caroline is based at the Technical University of Denmark near Copenhagen but works closely with research colleagues within DIRECT all across Europe. She works with large sets of data to try to identify biomarkers that predict diabetes progression. Specifically, linking data together, e.g. clinical data, MRI scans, blood test results, molecular data, and analysing it to answer the question of why some patients' diabetes progresses faster than others and what factors affect this process. She says "Analyzing the wealth of data that has been collected within the DIRECT project is a huge task, and no single analyst can be an expert on all the different data types. Luckily, this is a collaborative effort among many analysts".

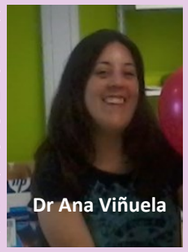
One of Caroline's regular tasks is to coordinate telephone conferences for DIRECT analysts, where they discuss practical issues related to the data and analyses, and present and compare results from the research. "One of the challenges we face when working with the data is to ensure the quality of the different data types, so that errors and mistakes don't affect the results or the conclusions that we draw". Another challenge, which Caroline finds interesting, is that there is no single method or analysis that fits all the research questions or data types. Therefore, it is necessary for the analysts to work with many different methods and compare the results.


Dr Caroline Brorsson

Caroline presented some of her DIRECT research at the annual meeting of the European Association for the Study of Diabetes in Lisbon, Portugal in September 2017.



Similarly, Ana's work at University of Geneva, Switzerland, investigates the data generated from the DIRECT studies to better understand the changes influencing development of diabetes. In particular, Ana's work looks at identifying regions of the human genome that increase the risk of developing diabetes. "We already know a lot of the important regions, and having one particular DNA sequence in those regions increases your chances of developing diabetes, but a lot of different things influence the process (exercise, diet, medication) and we need a lot of different kinds of clinical data to learn how molecules work together" Ana explains. This is such a rich data set that there is a lot of research to be done over the coming 5-10 years. This work may lead to new research and other research groups working in collaboration with the DIRECT teams to learn about other aspects of how the human genome and its molecules work.


Dr Ana Viñuela

Much of Ana's work involves analysing data on a computer. "I have to write my own computer programs and use mathematical models that find useful relationships within the data that explain why some people develop diabetes faster than others. I am not alone in this, and often I exchange programing code and ideas with other researchers in DIRECT".

Ana's passion for her work stems from her personal experience with people she knows with diabetes – "I often find myself thinking of the participants in the study. I do not know who they are, as we give them a code to protect their privacy... It is very impressive and inspiring to see the same people coming back for follow up visits. Their commitment to the study is an example to us and the work we do with the information they [participants] have provided. If they can spend so many hours travelling to a hospital, filling questionnaires and donating samples, I should be working hard to make their efforts as useful as possible for everybody."

Ana has presented her work in DIRECT at international scientific conferences in New York, Vancouver and Cambridge (UK).


Researchers presenting DIRECT results at the 2017 annual meeting of DIRECT in Mainz, Germany

Receive updates or talk to us directly:

'The Direct Project'

@DIRECTdiabetes

http://www.direct-diabetes.org/

Did you know?

Volunteers who have agreed to take part in any of the DIRECT studies have helped us accumulate a collection of data and samples from people with Diabetes or at risk of developing the disease. Not only does this help with current investigations but it provides a hugely valuable resource for future, as yet un-defined, studies enabling further research into the causes of diabetes and how treatment can be improved.

Thank you once again for your time and help!

DIRECT Project newsletter. Issue 3 WINTER 2017 www.direct-diabetes.org

DIRECT

DIABETES RESEARCH ON PATIENT STRATIFICATION


Participants at the 2017 annual meeting of DIRECT in Mainz, Germany

The results are in for the patient engagement survey!

Over a 15-month period, participants of the DIRECT studies were invited to complete a survey asking about your views and experiences of participating in medical research and opinions about sharing your de-identified data after the project has ended. There is an increasing need to share study data more widely, because it helps to optimise the use of the data and samples obtained in genetic research. However, this must be done ethically and responsibly. Therefore, it was important for the DIRECT project to elicit your views about what is important to you about sharing your study data with other research groups.

Between September 2015 and May 2017, we received **855** completed anonymous surveys from DIRECT participants in Denmark, Sweden, The Netherlands, and The UK. So, a **BIG THANK YOU** to those who participated! DIRECT researchers at the University of Oxford have now analysed the results, which are summarised here.

Experiences of taking part, participation in future medical research: The survey asked participants to rate their agreement about their experience of taking part in the DIRECT studies. Since taking part in DIRECT, 44% of participants said they understand more about diabetes, 73% enjoyed taking part, 53% said they wanted to change their lifestyle (e.g. diet, exercise, alcohol, smoking), and 56% understand more about medical research. Next, when asked about participating in future medical research, overall 65% of participants said they would participate again in future research, 32% said maybe, and 3% said no they would not.

Support for sharing data and views about types of researchers who may be able to use data: Overall, 97% of participants are supportive of sharing their de-identified study data with researchers outside of DIRECT after the end of the project. A high proportion of survey participants in all countries were happy to share their de-identified data with European or global universities (78% and 76% respectively); in addition, 58% were happy to share their data with commercial organisations.

What is important to participants if data is shared with other researchers?: Participants rated how important are factors such as 'Researchers cannot identify me'; 'the database is highly secure'; 'withdraw at any time'; 'an expert committee must approve every application before researchers have access to data'; and 'members of the DIRECT project can monitor how data is being used by other research teams'. The factor rated with the highest importance was that when sharing data with other research teams, the database should be highly secure - 80%. Members of the DIRECT project can monitor how data is used by other research teams was rated important by 69% of participants.

The next steps are to complete analysing the survey and publish the results in a peer-reviewed journal. The Oxford team would like to thank all those who participated in the engagement survey and to all the research teams who helped disseminate it. We aim for these results to help us to plan how the data will be managed in the future after the end of the DIRECT project.

RESEARCH ROUND-UP

The DIRECT research programme is split up into a number of different studies (called work packages) all of which have been making good progress – here are some updates.

Why do some people develop type 2 diabetes?

A major part of the DIRECT research programme is designed to look at how and why type 2 diabetes develops differently in different people. For some who are diagnosed with type 2 diabetes, their disease does not alter much over time and can be controlled quite well (by watching what they eat, increasing their exercise and, if required, by taking just one type of medication). However, for other people, their condition gets worse more quickly and they may need to take several different drugs to combat the disease. Similarly, people who may not currently be diagnosed as having diabetes but who are considered to be at high risk (i.e. their blood sugar level is higher than normal, but not high enough to be classed as having type 2 diabetes – so called 'pre-diabetes') may not always go on to develop the disease. There is much more that researchers need to discover about why the condition of some people deteriorates - while in others it does not. The purpose of our research is help find ways to identify those individuals whose disease will remain stable and may only require limited support, and those in whom the condition is likely to worsen - and to find out which treatment is most appropriate for them.

As part of our investigations, over 800 volunteers diagnosed with diabetes were recruited at 6 different study centres across Europe (Amsterdam, Copenhagen, Dundee, Exeter, Lund and Newcastle). Individuals attended their local centre on up to 6 different occasions over a 36 month period and had various assessments and samples taken. (In parallel, another group of nearly 2000 people at high risk of diabetes are also being followed over a 48 month period). Now that the 36 month study period has ended, the data from the first group is being analysed and their samples tested to see if we can find out if there are any indicators that highlight those who show disease progression from those whose disease remained stable. A wide variety of possible indicators are being checked, e.g. a person's genetic make-up and the proteins and metabolites in their blood, the amount of exercise they take, their diet and how their body fat is distributed.

A major difficulty in such research is that blood test results and other measurements vary naturally among individuals - and also within the same individual - from week to week. As a consequence we need to clarify true differences or changes from what is normal variation. This task requires sophisticated statistical processes and highly skilled data analysts - some of whom we hear from elsewhere in this newsletter.

Researchers believe that by understanding more about type 2 diabetes during its early stages, they will be in a better position to tell how it is likely to progress for different people and so enable doctors to offer them the most appropriate treatment.

Interested in finding out more about diabetes research?

The results of DIRECT studies and other diabetes research are presented at scientific meetings such as those held by the European Association for the Study of Diabetes (EASD), In international Diabetes Federation (IDF) and the American Diabetes Association (ADA) as well as being published in scientific journals.

It is possible to search for relevant publications on line although many are written in scientific language. Websites for those with a more general interest are available such as ***Diabetes.co.uk***, which provide a wide variety of helpful information on the condition, its treatment and advice on living with the disease. If you have not done so, why not have a browse?

Louise Cabrelli and Heather Loftus from the DIRECT team at Dundee were among those attending the EASD 2017 scientific meeting in Lisbon, Portugal.

Do your genes influence how well you respond to anti-diabetic drugs?

As highlighted in the previous newsletter, one of the investigations within the DIRECT research programme aims to discover why treatment with a type of drug known as a 'GLP-1 Receptor Agonists' (GLP-1RA) provides benefit for some people with type 2 diabetes - whereas other people do not respond so well. This type of drug, which is taken by injection, is generally prescribed when patients need extra help to improve their blood sugar levels. GLP-1 Receptor Agonist drugs work by improving the body's response to GLP-1 (a naturally occurring biochemical involved in the control of blood sugar levels) and come in several different forms including Exenatide (Byetta, Bydureon), Liraglutide (Victoza, Saxenda) and Lixisenatide (Lyxumia).

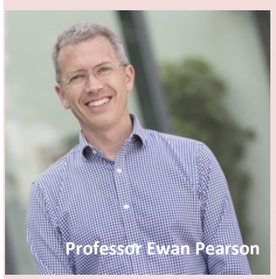
People who had just started taking one of these drugs, or who had been taking it for a few months, participated in this study. Participants made one or more visits over a few months to their local research centre where various blood samples for an assortment of tests were collected from them. The blood samples were taken both before and during a period when they were treated with the drug while also having a 'meal' (in the form of a high energy drink) in order to see how their blood glucose levels changed. Analysis of the samples and the data collected from the study is still ongoing but analysts have shown that the genetic make-up of an individual appears to have an impact on how well they respond to the drug i.e. how well the drug helps them maintain their blood glucose within normal limits.

People with an alteration (or 'mutation') in the gene that codes for the receptor for GLP-1 did not respond so well, and those with 3 or more alterations in this gene responded least well. It remains to be seen whether this observation holds true more widely, but it suggests that in the future doctors may need to check a patient's genetic make-up before deciding the best treatment for that individual.

DIRECT researchers honoured

The 2017 European Association for the Study of Diabetes (EASD) Minkowski Prize, a major European prize for research in diabetes has been awarded to **Professor Ewan Pearson** who is the Academic Lead for the DIRECT study and Chair of Diabetic Medicine at the University of Dundee. The prize recognises research contributing to the advancement of knowledge concerning diabetes. Professor Pearson, delivered the Minkowski Lecture at the 53rd EASD Annual Meeting in Lisbon and said "I am honoured to receive the Minkowski Prize and to join the list of names who have received this award over the past fifty years." The prize is named after Oskar Minkowski who, with others, discovered the role of the pancreas in diabetes, which ultimately led in turn to the discovery of insulin.

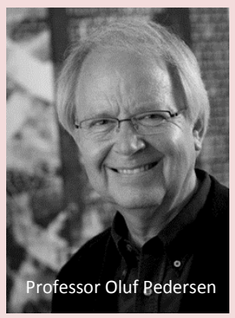
Professor Pearson's research focuses on the role 'precision medicine' can play in treating diabetes. "People are all different, and this is no different when we consider people with diabetes, yet the current approaches to management of diabetes tend to treat everyone the same," he said. "The field of precision medicine aims to recognise these differences." Over the last decade, Professor Pearson's research has established that an individual's genetic profile can have a dramatic impact on patient response. "There is increasing evidence that genetic and other molecular and clinical characteristics will impact on treatment outcomes for diabetes. The exciting challenge now is how we incorporate this information into clinical care and establish that this improves patient outcomes."



Professor Ewan Pearson

Above: Professor Pearson receives Minkowski Prize, Lisbon 2017

Similarly, at the same meeting another key diabetes investigator within the DIRECT consortium, **Professor Oluf Pedersen** from the University of Copenhagen, was made an Honorary Member of the EASD in recognition for his contribution to diabetes research. Prof Pedersen is a past recipient of the Claude Bernard medal, which is the EASD's highest award in recognition of an individual's innovative leadership and lifetime achievements in the study of diabetes. Prof Pedersen's current focus within DIRECT is examining the role of the microbiome (a vast ecosystem of micro-organisms such as bacteria, yeasts, fungi, viruses and protozoans that live in our digestive tract, many of which are vital in breaking down food and toxins, making vitamins and training our immune systems). In recent years scientists have increasingly recognised the importance of the microbiome and its role in maintaining a healthy body. DIRECT will be among the first studies to examine the possible role of the microbiome in diabetes.



Professor Oluf Pedersen