The Diabetes Reference Panel [DRP] & Diabetes Online Review Group [DORG]

NEWSLETTER

Nr. 4 - Autumn-Winter 2018

Welcome to the fourth edition of our Newsletter.

The Reference Panel [DRP] and the Online Group [DORG] met on the 12th of June 2018 for the 3rd BRC-sponsored meeting, with researchers and clinicians to hear more about the research taking place in Oxford and get a glimpse of the scientific world behind the closed door of a lab.

This newsletter aims to recap the main points of the talks, connecting our scientists and managers with patients and providing an important communication channel between them. At the end you will also find some active calls for participation to trials and other opportunities to get involved in research.

Dr. Marco Pontecorvi

TAMPA-NAFLD: A new treatment for fat in the liver in patients with diabetes *[Prof. Jeremy Tomlinson]*

Prof. J. Tomlinson

Non-alcoholic fatty liver disease (NAFLD) is one of the largest health burdens facing the NHS today. It is characterised by the storing of excess fat in the liver, which can progress to inflammation, scarring and can lead to cirrhosis in the same way as consuming too much alcohol. By 2020, NAFLD will become the leading indication for liver transplantation worldwide. NAFLD is tightly associated with obesity and type 2 diabetes (T2DM), both of which speed the progression of the disease increasing inflammation and scarring, but the processes that drive this advancing liver disease are not known. Currently, there are no drugs available to treat the condition and the mainstay of clinical management is to optimize lifestyle and reduce weight. A specific molecule called AMPK that regulates energy levels within cells and organs does not function properly in patients NAFLD and in laboratory-based experiments increasing the activity of AMPK appears to improve NAFLD.

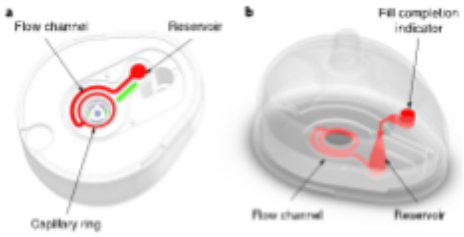
We have now wrote a grant application to test whether targeting AMPK can really help patients with NAFLD – the study that we propose will aim to recruit 80 patients with NAFLD, 40 with, and 40 without T2DM. We will use state-of-the-art detailed investigations to characterize the amount of fat in the liver and determine the precise metabolic pathways that contribute to this. These investigations will include the measurement of fats and sugars from blood samples and quantifying the amount of fat in the liver using a magnetic resonance imaging (MRI) scanner. In combination, these tests provide a comprehensive assessment of the mechanisms that drive the development and progression of NAFLD. The techniques that we will employ will allow us to look specifically at the synthesis and utilization of fat within the liver and in fat tissue. We will then enrol these patients into a dedicated clinical study to see if taking a medication that increases the activity of AMPK (PXL770), improves their NAFLD. PXL770 has been used in clinical studies previously; it is safe and well tolerated, but its impact on NAFLD in humans has not been examined. All of the scans and investigations that were performed at the initial assessment will be repeated after 12 weeks of treatment. Half of the patients will receive the active medication (PXL770) and half will receive an inactive placebo that looks identical. Neither the investigators, nor the patients will know which arm of the study they are in (active drug or placebo) until the study has been completed.

How can we improve the ability to perform research in children with diabetes? A painless transdermal blood collection technique *[Dr. Rachel Besser]*

Dr. Rachel Besser introducing the new device to our panel.

Rachel presented her vision for developing a Paediatric Diabetes Research Programme within Oxford, building on the strengths of the Unit; Paediatric Diabetes Research is active in Oxford but most studies originate externally. Rachel has a vision for creating and developing in-house research studies in the future. The first study will be to develop a new method of painless blood collection, using a device that collects blood through the skin on the upper arm. The device will test whether whole blood can be collected from young children with diabetes as well as older children and adults, using the device.

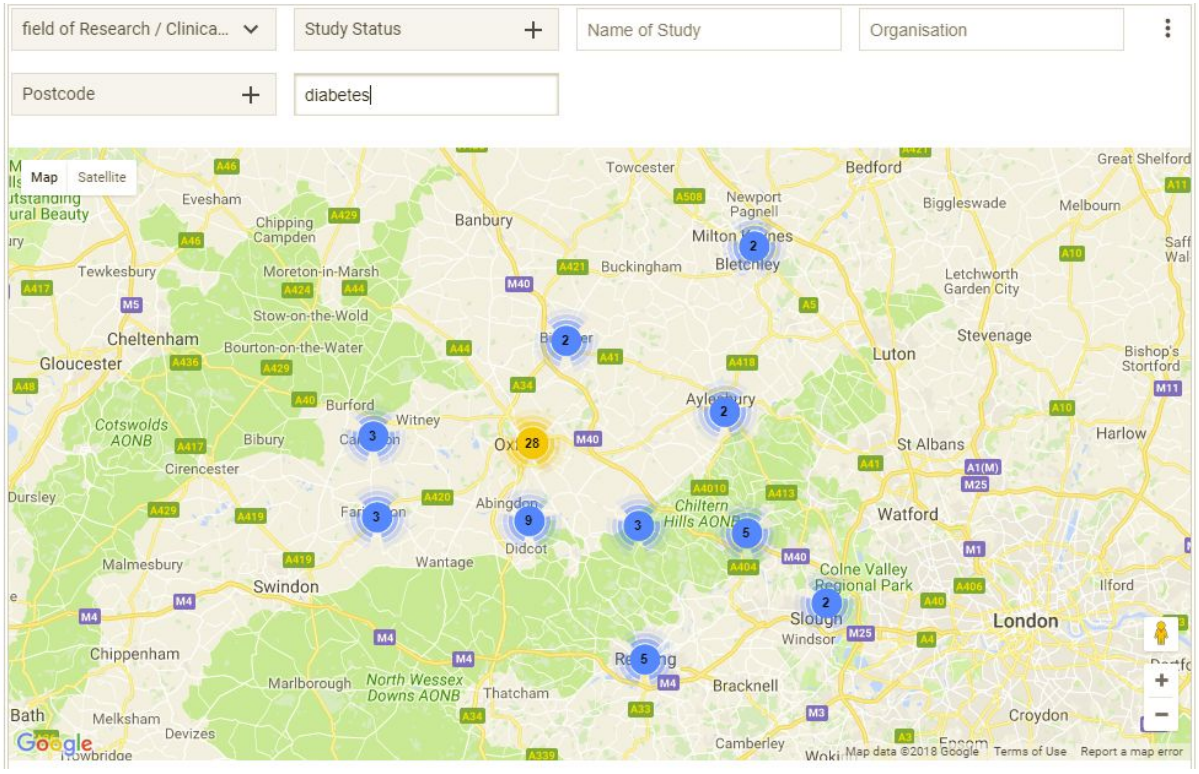
The patient information sheets and concept of the study were discussed at the PPI meeting with a positive response. Rachel plans to finalise the protocol and information sheets and hopes to go to ethics and then start the study in early 2019. She would be happy to present the results at a 2019 PPI meeting.



The TAP device.

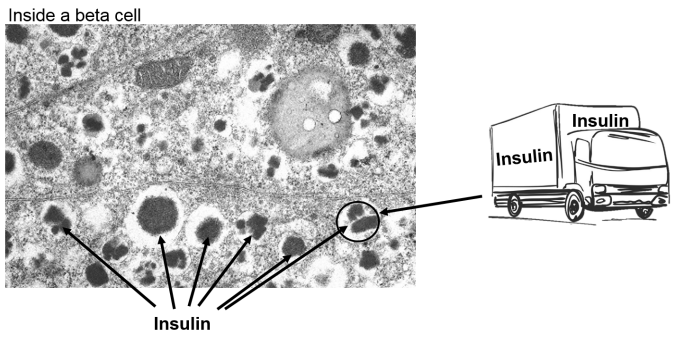
Diabetes...on Google Map! *[Dr. Chris Hille]*

The Thames Valley & South Midlands Local Clinical Research Network is developing a Google map based platform for highlighting the available clinical research studies in the region. The map could be searched by keyword, research area/clinical condition, postcode, organisation and will provide hyperlinks through to study information. The project is at the development stage and would benefit from patient and public input to improve the functionality, language and general format. Eventually this will be publically available but in the development stage we are looking for reviewers to assess the site. **Please click HERE to indicate if you would like to be a beta-tester for this new service as soon as it becomes available**. https://goo.gl/forms/FncSiCx6jjgnY7zm2



If interested please contact Dr. Christopher Hille at Christopher.Hille@ouh.nhs.uk

Traffic jams and T2D *[Dr. Benoit Hastoy]*



Insulin is the only hormone that reduces the sugar level in blood (glycaemia). This hormone is secreted by only one cell type in the body called the beta cells. After a meal, these cells sense the increased glycaemia and secrete the correct amount of insulin in order to maintain the glycaemia in a normal range. However, in type 2 diabetes (T2D) the beta cells are unable to deliver insulin in the correct amount. Consequently, the glycaemia remains high and this has multiple negative consequences on heart and kidney functions. When we look inside the beta

cells with a microscope, we see that insulin (black structures) is packaged in bags called vesicles (Figure 1). If we make an analogy, these vesicles are like delivery lorries. They deliver insulin (their cargo) outside the cells, in the blood stream. To reach their destination, the vesicles as lorries, follow a road called the trafficking pathway. Once arrived at destination, they need to properly dock to the platform and fully unload their content (insulin). In normal beta cells, the traffic is dense, highly regulated like a rush hour in a busy city, but the vesicles manage to reach destination and deliver insulin. In T2D the regulation of the traffic progressively disappears. Consequently, the traffic is fully blocked and insulin cannot be efficiently delivered (Figure 2).

Normal

T2D

My project aims to identify how the regulation disappears in T2D and what are the causes of this. There is not only one reason for this. These regulations are very complex and involves many factors that are not fully known. One way to pinpoint the causal defect is to use human genetics. Recent analyses have shown that some genes are dysregulated in T2D patients and I predicted from clinical associated traits that they may influence (directly or indirectly) the traffic of vesicles. I am going then to reproduce artificially these gene dysregulations in beta cells. I will use several types of microscopy and other high-resolution tools to track the traffic of vesicles (lorries) in beta cells and understand what goes wrong. I may then identify a new layer of regulation that disappear in T2D. In turns, this can become a potential target for a medication to restore normal traffic and proper insulin delivery.

What does it mean for the patients? In a long term, we could identify people carrying these gene dysregulations at earlier stage and slow down T2D diabetes development more efficiently.

Autoantibodies in Type 1 Diabetes: A Window into the Immune Response

[Dr. Kerry McLaughlin]

Dr. K. McLaughlin

Dr McLaughlin, a scientist at OCDEM, explained how, in type 1 diabetes, there are antibodies circulating in the blood against molecules found in insulin-producing cells of the pancreas. These antibodies are representative of the damaging autoimmune response that kills insulin-producing cells, and they offer an opportunity to visualise that immune response very early in the disease process, often long before there are any symptoms of diabetes. Dr McLaughlin recently identified a new molecule targeted by antibodies called tetraspanin-7 and has been working on developing a blood test to measure these antibodies in people with diabetes or who might be at risk of developing diabetes in the future. With the support of the BRC, she has now evaluated this blood test in the Islet Standardization Program, an international effort to improve the quality and consistency of antibody testing in type 1 diabetes. Following successful participation in the Program, testing of large numbers of blood samples to understand the usefulness of antibodies to tetraspanin-7 as a biomarker in type 1 diabetes can now go ahead.

How communication can support patient involvement

[Dr. Roy Probert

Roy Probert, Senior Communications Manager for the NIHR Oxford BRC explained his role and what it encompassed – including media relations, social media engagement, e-newsletters publications and the BRC website. He has a colleague whose responsibility is events, marketing and public engagement and they work very closely together. Roy introduced the BRC website, explaining there was a patient involvement section, where the BRC's PPI strategy could be found. There was also a link to the PAIR website. The Diabetes & Metabolism Theme area is fairly well populated with information about the various sub-themes, but a PPI page has been created specifically for diabetes patients. It is proposed that the DRP/DORG newsletter is posted here, along with the short videos from the diabetes research pilot day. Roy encouraged participants to consider what they would like to see on this page.

Final remarks *[Prof. K. Owen]*

Thanks to Marco for organising such an interesting meeting, which was very well attended. We heard about planned research and had some project feedback from two of the young researchers benefiting from pump-priming research funding from the BRC. We also discussed communication of both ideas (the BRC website) and improving the way in which volunteers can find out about research that they may be able to participate in (The Google map project). This nicely illustrates several of the points in the research cycle where patient or lay involvement is important.

There have been a few requests for input to projects - links to be found in this newsletter or sent out separately by Marco. Thanks to all those who have time to comment.

It's already the autumn and our next meeting will be held in 2019! We had a reflection recently on the outputs of the Diabetes theme researchers over the last 12 months and together we have had many achievements in research published, funding for new projects and involvement in local and national research strategy. Onwards and upwards for 2019!

FROM PATIENTS' EYES *[Dr. M. Pontecorvi]*

All patients in the group are welcome to submit a short comment they may want to share about their experience in the group, the meeting, other involvements they may have across the numerous and different PPI bodies and organizations.

If interested, please contact Marco Pontecorvi (marco.pontecorvi@ocdem.ox.ac.uk), thanks.

Feedback Request *[Dr. M. Pontecorvi]*

If you have any feedback on the meeting (if you attended), this newsletter or the NIHR/BRC website, please do feel free to contact me at marco.pontecorvi@ocdem.ox.ac.uk and discuss any suggestion you may have. Also, if you wish to participate to the next edition of the Newsletter you are very welcome to contact me as well. Thanks!

More News

SAVE THE DATES! Calendar and dates for 2018-2019 meetings

Tuesday 29th of January 2019 - Meeting #5

Tuesday 18th of June 2019 Meeting #6

All Panel meetings are still planned to run from **1:00pm to about 3:30pm**, and the results of our online survey, conducted during the last few months, seems to indicate that this time remains the most popular choice for the majority of our patients.

We are still open to evaluate different needs and we aim to propose again a similar poll in a few months time. However, for the next couple of dates we will keep our norm

Our survey HERE (***https://goo.gl/forms/KFxbZbsS0NThNcYX2***) will remain open for now and monitored regularly.

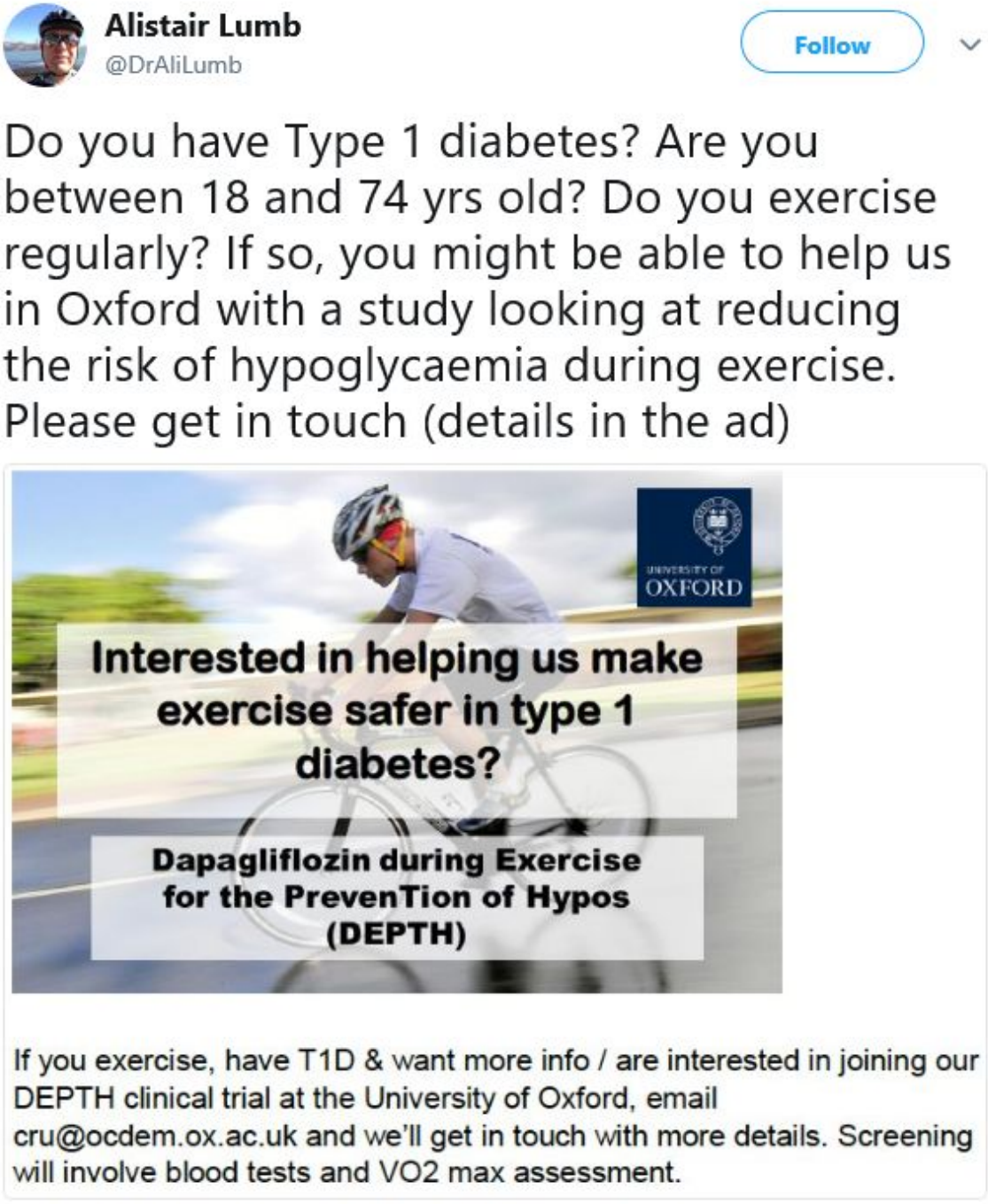
You will be kept informed on any development on the matter.

Further you will find information about the following trials:

DEPTH Clinical Trial

TICSI Trial (JT/Nantia)

TriMaster Trial



For more information please contact cru@ocdem.ox.ac.uk

TICSI TRIAL

Tackling Iatrogenic Cushing's Syndrome through 11β-HSD1 Inhibition (TICSI)
Poster v1.03_23022018
IRAS ID no. reference: 212634
Chief Investigator: Prof J Tomlinson

UNIVERSITY OF OXFORD

UNIVERSITY OF OXFORD

NHS
National Institute for Health Research

Want to know your body fat percentage? Join our study into limiting the impact of steroids.

We are running a clinical study to trial a new medication to block the unwanted side effects of steroid medication.

If you are a healthy man aged between 18-60 and interested in taking part - please contact:

Dr Nadia Othonos
Oxford Centre for Diabetes, Endocrinology and Metabolism,
Churchill Hospital,
Headington.
01865 857359
Nantia.Othonos@ocdem.ox.ac.uk

Prof Jeremy Tomlinson
Oxford Centre for Diabetes, Endocrinology and Metabolism,
Churchill Hospital,
Headington.
01865 857359
Jeremy.tomlinson@ocdem.ox.ac.uk

We will reimburse any travel costs and offer compensation for your time and inconvenience

For more information please contact Nantia.Othonos@ocdem.ox.ac.uk or Jeremy.tomlinson@ocdem.ox.ac.uk

TriMaster

A research study to help improve treatment of type 2 diabetes, by learning how individuals respond to different blood sugar-lowering drugs

Would you be willing to try three regularly prescribed diabetes medicines over a year, to see which one works best for you and to help us improve diabetes care for others?

- **Before you decide whether to take part, it is important to understand why the research is being done and what it will involve.**
- **Please take the time to read the following information carefully.**
- **You are free to decide if you want to take part in this research study.**
- **You can decide to stop taking part in the study at any time without giving a reason.**
- **Please ask us if anything is not clear or if you would like more information.**

Important things you need to know

The study will involve taking three standard diabetes drugs alongside your current medication: sitagliptin, canagliflozin and pioglitazone. They will be prescribed randomly, one drug at a time, for 16 weeks. There will be an appointment before starting each drug. Participation in this study will involve six visits over a year (2 x 30 minute visits, 3 x 60 minute visits and 1 x 3 hour visit) The 30 and 60 minute visits may be able to be conducted at your home if you are unable to attend the hospital. We will ask you to provide blood samples to ensure you are safe and eligible to participate in the study. All the drugs will be made to look identical, so that you and the study team will not know which drug you are taking. A dedicated team will be available to help if you suffer any side-effects and your doctor needs to find out what you are taking.

If you would like to find out more information about the OPTION-DM TRIAL, please contact Viv Thornton-Jones Vivien.thornton-jones@ouh.nhs.uk or Nicky McRobert nicky.mcrobert@ouh.nhs.uk OR telephone 01865 857511