**CFBT Showcase Seminar 2021 Day 1 Martin Rutter introduction, automated transcript 13-Jul-2021**

I'm going to be talking about the people, projects, PPI and the plans. I've noticed they all begin with P. And we'll start with the people.

So as Rob has explained we've got quite a large grouping of researchers in circadian biology here in Manchester. It's said to be the largest group within Europe and we have a diversity really of research fields and this allows us to have a range of funding applications and from multiple sources as well which is again quite a strength Rob's already mentioned that we have a good track record of developing young researchers in Manchester. I think David Ray, particularly deserves a lot of credit for the work in sort of helping to develop this area. And so, thanks, thanks again, David for that. We had an external review about three years ago. Now that really highlighted, the fact that we involve a lot of practicing clinicians, we've got excess hospitals on our doorstep and this is a feature that isn't really part of many similar centres around the world, so we've got strength there as well.

Just an overview really of the sorts of research areas where we're starting to work and have worked already, in the translational area and the sort of themes that come through our cardiometabolic, mental health particularly as that relates to light interventions that have been led by Rob and Tim. We've got a whole series of projects that are broadly under the theme of inflammation and several other people are going to be talking today in those areas. And then we've got transplantation, anaesthesia, surgery are also relevant to our clinical interest as well. And we have fabulous support from mathematicians, bioinformaticians and other people that help to make all this possible. So there's a few people mentioned there. So, thank you very much indeed for all those people who support this body of work. Rob's mentioned that we have this quite impressive track record of gaining, fellowships, independent funding for several researchers. And these are just a few of those individuals, Julie, Hannah and Gareth have recently been awarded individual fellowships and we're very proud of that.

As I said, Manchester has a strong track record of this.

When we're talking about people that are involved, it's also I think quite important to highlight the collaborations that we have internationally and I'm really speaking here from my own perspective, which is around UK Biobank projects, which I think is a good example of collaborations. But of course, lots of other PI's working in the centre, will have their own links and their own international collaborations. Back in 2014, we put together an application for UK biobank with us looking at the causal links between sleep and chronotype and cardiometabolic and chronic inflammatory outcomes. For those that are not familiar with UK Biobank. It's a fabulous resource involving about half a million people with rich data on phenotype and genotype and now outcomes going out to about 15 years. So this has provided us with a great opportunity for collaboration internationally and I would like to acknowledge the fabulous collaborations that we've had, particularly in the USA and Germany, and other countries, and of course, collaborators around UK, there's too many people really to mention in person, but Richa Saxena and Jackie Lane have certainly been very important for our genetics work.

So just in UK Biobanks where we've had collaborations across the UK and as I said also internationally which have really added hugely to the quality and the productivity of our unit.

So that's all I wanted to say on people as I said this is quite a high level sort of talk. About the projects, I'm just going to mention a few and this is again quite an overview. I mentioned a lot of P words, I apologize for now using the c word but COVID-19 has had devastating effects across our communities and has affected our research in many ways. I'm pleased actually, that we've been able to contribute research outputs in this area that are relevant to our interests. This is a paper that we've done recently with collaborators in Boston, looking at sleep behaviour burden and its links to COVID-19 mortality and hospitalization, I just thought I'd share this slide with you which is just giving an overview of results. This was a study involving 46,000 UK Biobank participants who are tested for COVID. There's about 8,000 of those tested positive and the top panel is just showing the risk of mortality in relation to sleep exposure, which was a school related to sleep duration, sleepiness, insomnia, a range of sleep phenotypes, but people with more, with a higher score, have a greater burden of sleep on health, if you like. And you can see as the as the score goes up. The risk of mortality is significantly higher. That's a 30-day mortality having tested positive for COVID. And, of course, this could relate to immune function, through circadian disruption and possibly to thrombosis, which may also be influenced by these things, but certainly showing the relevance of other particular interests in the COVID pandemic.

Next another project that has come mainly from Manchester has been looking at the relationship between shift work and COVID-19 positivity. This study showed that shift workers were more than two fold higher risk of being positive for COVID in patients, tested in hospital and this was particularly the case for a regular night shift workers, permanent night shift workers perhaps a little less. So the day workers, and health care workers and essential workers also appeared to be a slightly higher risk of being positive for COVID-19. And of course, this is a lot more in this paper and I've not really done it justice by presenting this minimal amount of data. But obviously, this could be again because of immune function related to circadian disruption caused by shift work. The next section, I'd like to cover is just really an overview and I think it has to be said that probably the major strength in Manchester is its basic science research. And the translational research is you know, we have some very nice outputs already but it is something that is evolving and is developing. And as I mentioned, there's a few themes that I'd like to emphasise and a lot of these sections of work, build out of really important basic science discoveries. And I think we're very keen to be the first to test out these discoveries that have been found in animal models or cellular models in people. And that's our aspiration over the next few years. But for example, in the cardiometabolic field we've shown that circadian clocks set the daily rhythms in SA nodes and AV nodes and these impose a time of day dependence on the susceptibility to arrhythmias. In the light interventions area we've designed new metrics for light measurement and these are allowing optimal lighting design in hospitals, care homes and other workplaces. And we also identified opportunities for using light as a therapeutic in psychiatric disorders. So just a few examples there of some of the work that we're doing.

We have the strongest team in the pulmonary area, Anna will be talking later on and will go into some detail about some of the work that she's doing in asthma. For example, we've shown the time of day affects the eosinophill biomarkers and exhaled biomarkers in people with asthma. In the pulmonary fibrosis area, we've shown that the circadian clock protein REVERB-(alpha) inhibits the development of the condition.

And in pneumonia, we shown that the clock Gene, Bmal1 inhibits macrophage motility, and phagocytosis, and influences the defence against pneumonia. So, again, we're working to develop these ideas and studies are ongoing. It's probably not fair of me to sort of go into too many details about the clinical studies that are planned at the moment. But I'd just like to emphasise that we're working in these areas.

And finally, in osteoarthritis, we discovered the role of the intrinsic circadian clock in articular cartilage. And again, would like to build on some of the discoveries, the very important discoveries in basic science that are coming out of the, the researchers working in this area. So again, if you're interested in these areas in more detail, then I'd encourage you to contact me and I'll put you in touch with the relevant PIs.

Finally, just to mention transplantation, we've shown that lung transplants perfuse between 4 a.m. and 8 a.m. of a higher instance of primary grasp dysfunction and we've shown some relevant data in Mouse models as well. So these findings are starting to have implications as far as clinical work is concerned clinicians are more closely monitoring outcomes following transplant in those organs at these particularly high risk times.

The area that I've been most involved in myself, is the UK biobank research. As I mentioned, we put an application in about seven years ago, and we've been very fortunate to be leading many of the discoveries identifying novel genetic loci for chronotype, for sleep, duration, insomnia, and other sleep phenotypes. And also identifying the biological links to some of these findings, and there's very many clinical insights that we've gained from these works as well. And again I'd just like to acknowledge the great work of the collaborators that we've had. I'm particularly interested in the mendelian randomisation work that has followed on from these genome-wide association studies. We've shown again with collaborators, that short sleep is causally linked, to myocardial infarction risk, that morning preference is causally linked to a lower risk of breast cancer.

And more recently that insomnia is causally linked to higher HbA1c. That's a manuscript that's under review at the moment. So understanding mechanisms of disease through genetics is very important. Clearly from a therapeutic, from a translational point of view because by understanding causal mechanisms, we can start to identify relevant therapies that can ultimately benefit patients. So I'm very excited about the work that we've done so far. And the work that's being planned too.

Just a couple of words about PPI. So involving patients is really key, I think we're all interested to see that the work that is done here has relevance for the general public and for patients. And as far as the translational work is concerned, I think PPI is at the heart of our current and our future plans, Annie Keane I'd just like to mention in person because she's been so supportive and she's involved in the NHR, so apologies for the typo.

The biomedical research centre, we've had some funding specifically to support PPI work at the centre. And we've got lots of examples recently of patients being involved to help us define and refine research questions to be involved in the co-design of research and to contribute to grant applications. So I think it's worth emphasising that too.

And our plans for the future. There are opportunities to work in Manchester through either PPI's that are mentioned here and if you or others might be interested then please contact us, as Rob's highlighted a couple of contacts in his presentation, and we're also excited about the opportunities that we have now to develop our infrastructure. We have been limited to some extent by our facilities in Manchester in terms of the types of clinical studies that we can do. But we do have real opportunity now to develop new facilities that will extend the range of studies that we can do in the circadian and sleep space. That's very exciting for the future too. So in summary I just like to just highlight that we have a critical mass of circadian researchers. I think primarily in basic science, but increasingly in translational area, we have an outstanding track record in developing young researchers and especially now, those with clinical backgrounds and I'd like to just emphasise the new opportunities that we're having for translational research here in Manchester. So, I like to finish there. Thank you very much, indeed, for listening and I'll hand you back to Robert at this stage or perhaps it's Julie, I'm not sure.

Thank you.