Message from Professor Ian Bruce, Chief Investigator

Wishing you a very happy New Year! MASTERPLANS is now at its 18 month point and has two and a half years remaining. Our research is well under way and we have received more positive feedback from the MRC Stratified Medicine Monitoring Group.

The project has welcomed several new staff. This newsletter contains articles from Su Wang (Kings College London), Alyssa Gilmore (Imperial College London), Carmen Gibbard and Sean Gavan (both University of Manchester). Jane Dunnage has provided an update on what is happening in our very active PPI group, which she chairs.

The PLANS observational study will start recruiting patients soon. PLANS aims to identify biomarkers and and patient data items that, singly or in combination, predict patient response to two drugs (mycophenolate mofetil and rituximab). We are planning to recruit in 20+ hospital Trusts and will be setting them up as quickly as possible in the coming months. The speed at which we can recruit patients will be critical to the success of MASTERPLANS in achieving research that ultimately can make a real difference to lupus patients’ lives.

Results of MRC Strategic Medicine Monitoring Group, 18th November 2016

Every six months, MASTERPLANS sends a report to our funding body, the Medical Research Council (MRC) and normally we give a presentation to the MRC’s Strategic Medicine Monitoring Group. This time, we only had to submit a report as the Group was satisfied with our progress at the previous meeting. We have now received informal feedback from the MRC Programme Manager as follows:

As you know, we asked you to submit a written report only for the meeting in November. As this was a paper review only, there is no formal feedback. I can tell you though that the Group welcomed your report and did not voice any concerns regarding MASTERPLANS progress.

The next monitoring meeting will be on 19th May. The report will be due in mid- to late April and we will report project finances up to the end of March.

Consortium meeting Friday 21st October 2016

We held a full day Consortium meeting at the Friends House in London on 21st October. This was a joint meeting of the MASTERPLANS Consortium Management Board, Project Steering Group, Analysis Group and PPI group. The morning was dedicated to progress reports and each of our new staff gave a talk about their work. The projector failed partway through, and Sean Gavan gave his talk without slides while the technician worked on the projector in the background!
The lunchtime Consortium Management Board meeting reviewed progress and looked closely at the project’s risks and issues. In the afternoon, Professor Tony Whetton (University of Manchester) gave a talk on the Stoller Biomarker Discovery Centre, of which he is Director, and what the Centre could do for MASTERPLANS. Professor Yanick Crow, also from Manchester, gave a talk on interferon biomarkers. We then split into three groups (Analysis Group, biomarkers, interferon) to do some cross-partner planning in these areas.

Jane Dunnage (Chair, MASTERPLANS Patient and Public Involvement (PPI) group)

The MASTERPLANS PPI group has its own area of the MASTERPLANS website (http://www.lupusmasterplans.org/PPI.html) and we are working hard on an update. We have had a good response to the request for PPI members to write about why research is important to them, and we have created an infographic that gives details of the PPI group demographics. These will be live on the website soon. We are also creating a glossary of scientific terms in lupus research, written in lay persons’ language, to assist patients’ understanding and participation in the research.

We have been busy spreading the word about MASTERPLANS and our full page article about MASTERPLANS was published in LUPUS UK’s News and Views autumn magazine. Yvonne Norton gave a presentation at the 10th European Lupus Meeting in October 2016, and I was a panel member at the World Precision Medicine Congress (May 2016) and the Precision Medicine Forum (July 2016), as well as attending a number of patient open days.

One of the PPI group has joined the MASTERPLANS Analysis Group, which will use statistical and other techniques to spot the relationship between different biomarkers and disease outcomes (both clinical and patient-reported outcomes). Other PPI group members continue to contribute to the senior MASTERPLANS committees, including the overall Consortium Management Board and the monthly Project Steering Group.

We held a PPI group meeting embedded in October’s Consortium meeting. Dr David Morris from King’s College London gave a great talk on the genetics of lupus, and we worked together on materials for the website.

Analysis of existing data- and sample sets (work streams 1 & 5)

We now have access to data from the BILAG Biologics Register and SLICC, and from the commercial ALMS (Vifor/Aurinia) and LUNAR / EXPLORER (Roche) trials. The arrival of other data is expected early in 2017. UCB has provided samples from the EMBODY trial and has kindly provided support for DNA extraction from those samples prior to their analysis at King’s College London. The cross-partner data Analysis Group was constituted as quite a small group of statistics and machine learning experts from the MRC Biostatistics Unit (Cambridge), King’s College London and the University of Manchester. Following the addition of clinical outcomes specialists and patient representation to the group, it now has 16 members and meets every 6 – 8 weeks. The group is primarily working on the BILAG Biologics Register data at the moment, pending loading of other datasets into the tranSMART data warehouse in the desired format for analysis.
PLANS prospective study (work streams 2-4)

Part of the MASTERPLANS work is to run a clinical study (PLANS), collecting patient data and biological samples from patients with kidney or skin manifestations of lupus, who have been prescribed MMF or Rituximab as part of their standard care. We will collect samples from several hospital Trusts who are already contributing to the BILAG-BR lupus registry. Samples will include skin and renal biopsies; skin samples using tape; urine and blood.

After achieving Research Ethics Committee approval in July, it took quite a long time for the Health Research Authority (HRA) to consider our application. We now have HRA approval and are working hard to set up our first sites at Manchester Royal Infirmary, University College Hospital and Leeds Chapel Allerton Hospital, and we hope to recruit our first patients in late January / early February. We are concerned about the delay and a good rate of recruitment in the early months will be crucial.

Sample processing arrangements have been challenging, with many different sample types being routed to different partners at different temperatures. Most samples will go direct from hospital clinics to sample processing hubs at University College London and the Universities of Leeds and Birmingham. The skin samples will go direct to Leeds and the kidney samples direct to Imperial College London. We constituted a Sample Processing Technical Operations Group (SPTOG), with representation from the hubs and the University of Manchester, where many samples will be stored pending shipping for analysis. The group is currently finalising Standard Operating Procedures regarding samples.

Dr Su Wang (King’s College London)

Genetic statistics (work strands 1 & 5)

I joined Tim Vyse’s lab at King’s College London at the beginning of October 2016 as a postdoctoral statistician. My PhD topic mainly focuses on variable selection problems in high dimensional time series data as well as developing useful algorithms for big data problems, which are particularly useful in understanding genetic data. The overall goal of my work for MASTERPLANS is to apply my knowledge and experience in statistical analysis to discover novel relationships between genetics and adverse drug reactions in SLE.

Through the study of genetic effects, we hope to gain a better understanding of patients’ response to therapy. I have recently been working on statistical analysis of SLE phenotype data in order to find a plausible set of SNPs involved in the disease process, and also improving statistical methodology (Bayesian) for variable selection.

Carmen Gibbard (University of Manchester)

Study coordinator, PLANS prospective study (work strands 2 - 4)

I started as PLANS Study Coordinator in October 2016. I work directly with Gillian Armitt (MASTERPLANS Project Manager) and we share an office. I assist with everything involved in the day to day running of the PLANS study. So far I have been involved in the final stages of study set up; requesting permissions for questionnaires, and finalising pathways for sample collection and sample distribution. I have also written three fictional scenarios to gain insight into how a clinician, nurse and patient would experience PLANS. These will soon be live on our website to help give people a feel of what’s involved in the study, from different perspectives. They are
also helping with planning site initiation visits. I am looking forward to MASTERPLANS opening recruitment. I will then be getting out and about to the various sites, meeting staff to help get the sites up and running.

Dr Alyssa Gilmore (Imperial College London)

Tissue and circulating biomarkers in patients with lupus nephritis (work strand 3)

I’m a postdoctoral researcher, working on MASTERPLANS in Imperial College London since September 2016. One of the major difficulties in SLE therapy, which I hope to tackle, is the lack of reliable markers that predict treatment response and monitor treatment effectiveness in patients with Lupus Nephritis (kidney inflammation).

My initial goal will be to identify distinct signatures between different classes of Lupus Nephritis. Through the use of surplus tissue from patient biopsy samples, I will extract RNA and conduct targeted analysis on the collection of RNA sequences (the transcriptome) to determine which genes are turned on or off in the kidney tissue, and to what extent they are activated or repressed. This “targeted gene expression profiling” will be conducted using cutting edge technology, allowing us to look at the expression profile of 800 genes. To date, I have designed the initial panel of 800 transcripts, which has been sent off for manufacture, and we hope to obtain our first round of profiling data early in 2017.

The overall goal will be to use this information to design a panel of markers to investigate patient response to treatment. In using surplus biopsy tissue, we have the unique opportunity to retrospectively look at marker expression in patients that responded well, or did not respond to treatment, over the past 10 years. We hope that this approach can be used clinically as a step towards personalised medicine, assigning the most effective treatment to patients at time of diagnosis based on transcript expression profiling.

Dr Sean Gavan (University of Manchester)

Health economics (work stream 6)

I am responsible (along with Professor Katherine Payne) for the health economics analysis component of MASTERPLANS. In order to introduce a stratified approach to treatment in routine practice, decision makers within the NHS require evidence of its relative cost-effectiveness. The evidence that we generate will aim to assess the relative impact of a biomarker-based treatment algorithm on health outcomes and costs to the health care system.

To generate evidence for informing decisions, we will construct a decision analytic model which simulates the cost and health outcomes of patients with lupus over the duration of treatment with MMF and rituximab. By performing this analysis at an early stage of developing a stratified approach to treatment, we will be able to estimate (1) the likely key drivers of relative cost-effectiveness, and (2) the value of conducting further primary research to reduce uncertainties in the evidence base.