Guy's and St Thomas' NHS
NHS Foundation Trust

KING'S College LONDON

Oral Microbiome & Mucosal Immunity in COVID-19 disease (MIMSA)

PATIENT INFORMATION SHEET

This is a study to understand how the body's immune system responds to SARS-Coronavirus-2 at the sites of infection. It will provide information on natural protection against the infection in different ethnic groups and may help in the design of effective vaccines against COVID-19.

We invite you to take part in a research study. Before you decide, it is important that you understand why the research is being done and what it will involve for you, personally. Please read the following carefully and discuss with anyone you wish. **When you feel ready we will go through this sheet with you and answer your questions.** Reading this should take about 15 minutes.

Part 1 of this Patient Information Sheet tells you the purpose of this study and what will happen if you take part.

Part 2 gives you more detailed information about the conduct of the study.

Please ask us if there is anything that is not clear. Take time to decide whether or not you wish to take part.

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PART 1

- **What is the purpose of the study?**

COVID-19 is a serious infection of the respiratory system and other mucosal tissues of the body. Mucosal tissues are linings of areas that are inside your body, but exposed to the environment – such as the nose, mouth, lungs and gut.

Mucosal tissues are protected by your general immune system, but also have their own special immune mechanisms. An infection in your lungs or gut can result in localised immunity in your mouth or nose and vice versa. A healthy mouth has special microbes which probably help to protect against COVID-19: an unhealthy mouth, (for example with inflamed gums), may also be one of the ways COVID-19 gets into the body. Some ethnic groups with COVID-19 become much sicker than others, and it is not clear why.

This study:

- investigates how mucosal immunity responds to COVID-19 and whether gum disease or particular mouth microbes have an influence.
- **Saliva and blood** will be taken from volunteers who have had, and not had, COVID-19. In some cases, repeat samples will be collected so that we can study the immunity over time.
- The results will provide valuable information about natural immunity to COVID-19 and how this is boosted with vaccines.
- Also, comparison of responses in South Asian and non-Asian (White British) participants may reveal why there are different outcomes to the same infection.

- **Why have I been invited to take part?**

We are looking to recruit up to 800 patients. You have been invited because you belong to one or more of the following groups:

1. <u>You have never had COVID-19 and are therefore 'a control'.</u> Such patients are important to help confirm that our tests are specific for COVID-19 and not other infections.

2. You have recently had a positive test for COVID-19, even though you have not had any symptoms, or had only mild symptoms. In this group, immune responses and oral microbes will be compared with those who have had moderate or severe symptoms with COVID.
3. You are currently an inpatient and have been diagnosed with COVID-19. Patients in this group will have had symptoms from COVID.
4. You are attending Guys & St Thomas Hospital as an outpatient having had COVID previously.
5. You have recovered from COVID-19 having attended Guys & St Thomas Hospital or your GP practice or volunteered to be a participant in this study.
6. You have recently been vaccinated against COVID-19. Patients in this group allow us to look at detailed responses to vaccination.

- **Do I have to take part?**

No. This is entirely up to you. We will go through this information sheet with you. **If you wish to go ahead, you will be given this information sheet to keep and asked to sign a consent form, a copy of which will also be given to you.**

You are free to withdraw at any time and do not have to give a reason. Your decisions will not affect the standard of care you receive.

- **What would taking part involve?**

1. Consent

If you have indicated interest, a member of the research team will give you a copy of this participant information leaflet and the informed consent form on the ward or at your outpatient appointment. We will arrange either to meet you on the wards, or at your next routine hospital appointment, or for volunteer participants, in the Oral Medicine Department or Oral Clinical Research Unit (OCRU) at Guys Hospital.

We will explain the study in more detail, answer any questions and, if you are willing to participate, invite you to sign the "informed consent form". Please do not sign until you have discussed the form with a member of the research team. If you are 18 years old and over, only you can give consent: your next of kin or other relative cannot do this on your behalf.

2. Mouth examination, saliva and blood samples

For this research we need samples of saliva and blood and a mouth examination to check your oral health status, and you will be asked to complete a short questionnaire about your dental health. This should take no longer than 20 minutes and will not interrupt or delay any clinic appointment. Care will be provided as normal by your hospital care team.

The blood sample: Three or four small tubes of blood for the study (each ~2-3 teaspoons) will be taken in the usual way from your arm. If blood is being taken for other reasons during your clinic visit, we will take our tubes at the same time so will not need to have a separate drawing of blood. One tube is to check for normal blood values and your GP may be notified of any abnormal results.

The saliva sample: You will be asked to provide a small sample of saliva by chewing on a piece of wax or gum and dribbling into a chilled plastic tube. We aim to collect 4-5ml, which will take 5-8 minutes.

The oral health questionnaire

We will ask you a short series of questions about your oral/dental health. This will take about 3 minutes.

Oral Health Examination

A Clinical Research Dentist (daljit.jagdev@kcl.ac.uk) will examine your mouth and record any gum disease or other inflammation or pathology. This will take less than 10 minutes. To record your relevant medical and COVID-19 history, we will ask you a few questions to supplement your medical notes.

Sampling site: for inpatients we will visit you on the wards; for outpatients, we will visit you in your clinic and for controls, those without symptoms, and for any follow up appointments you may be seen at the Oral Medicine Dept., Floor 22 in Guys Tower or the OCRU on floor 26.

Repeat samples

For those willing to give repeat samples (at 2, 4 and 12 weeks), we will co-ordinate with your next routine visit to Outpatients or make an appointment at the OCRU or Oral Medicine Dept. We will not need to repeat the oral health questionnaire or oral examination.

- **Expenses and payments**

We are not offering payment for participation in this study. However, we will reimburse travelling expenses for any baseline and follow-up visits where these do not coincide with routine hospital appointments.

- **What do I have to do?**

The only thing that you have to do is to avoid eating or drinking anything but water for 30 minutes before providing the saliva sample.

- **What are the alternatives?**

If you do not wish to take part, you will continue to receive your usual standard of care from the clinical team at the hospital.

- **What are the possible disadvantages and risks of taking part?**

The only risks from the research study are those associated with routine blood sampling. Staff are trained and experienced in minimising discomfort.

Where possible research samples will be taken at the same time you attend Hospital for your follow-up appointments. This minimises risks of COVID-19 transmission from an additional visit.

All staff will follow Hospital policy on COVID-19, which includes wearing PPE, maintaining good hygiene of the clinic areas and social distancing. When you are on site, you will be expected to follow current government guidance with regard to wearing a face mask and social distancing.

- **What are the possible benefits of taking part?**

Apart from being informed about your oral health, or any abnormal blood results, there is no direct clinical benefit to you. However, the valuable information we get from the study will improve understanding of immunity to COVID-19 and should help to improve the design of vaccines against the virus that causes COVID-19. The research may also identify factors related to susceptibility to COVID-19.

- **What if there is a problem?**

Any problems or complaints about the way you have been dealt with or any possible harm you might suffer will be addressed. Detailed information on this is given in part 2

- **Will my taking part in the study be kept confidential?**

We will follow ethical and legal practice and all information about you will be handled in confidence. Your sample will be pseudo-anonymised before transfer to the research laboratory at the ***Centre for Host Microbiome Interactions, Faculty***

of Dentistry, Oral & Craniofacial Sciences, Floor 18, Guys Tower, London SE1 9RT for analysis. The details are included in Part 2.

This completes Part 1. *If the information in Part 1 has interested you and you are considering participation, please read the additional information in part 2 before making any decision.*

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PART 2

Oral Microbiome & Mucosal Immunity in COVID-19 disease (MIMSA)

- **What will happen if I don't want to carry on with this study?**

You can withdraw from the study at any time, without giving a reason. There will be no impact on the usual care that you receive from your hospital team.

If you decide you don't want to carry on with this study, we will keep all of the samples and data that we have already collected from you, unless you specifically tell us not to. We will not collect any more samples or data from you for this study.

- **What if there is a problem?**

Complaints or concerns:

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions [Principal Investigator Professor Mark Ide at Tel: 0207 188 5391 or by email: mark.ide@kcl.ac.uk or the Chief Investigator, Professor Stephen Challacombe at Tel: 020 7188 4399 or by email: stephen.challacombe@kcl.ac.uk] If you remain unhappy and wish to complain formally, you can do this through the Guy's and St Thomas' Patients Advice and Liaison Service (PALS) on 020 7188 8801, pals@gstt.nhs.uk. The PALS teams are based in the main entrance on the ground floor at St Thomas' Hospital and on the ground floor at Guy's Hospital in the Tower Wing.

In the event that something does go wrong and you are harmed during the research you may have grounds for legal action for compensation against Guy's and St Thomas' NHS Foundation Trust and/or King's College London but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

- **Will my taking part in the study be kept confidential?**

Yes; your samples and medical history will be coded before transfer to the research laboratories at the ***Centre for Host Microbiome Interactions, Faculty of Dentistry, Oral & Craniofacial Sciences, Guys Tower, London SE1 9RT***. Your medical history sheet will contain your hospital number (but not your name) as well as your study number so that we can access your blood and pathology results and add them to your study data sheets.
All information which is collected about you during the course of the research will be kept strictly confidential, and any information about you which leaves the university/hospital/surgery will have your name and address removed so that you cannot be recognized. Once you enter the study you will be identified only by a unique code number and information about the code will be kept in a secure location and access limited to research study personnel. Coded samples may be sent to commercial Labs or academic institutions in or outside the UK. Your coded samples and your coded personal data will be stored at GSTT, archived for 3 years from the end of the study and then destroyed.

The de-identified data derived from your samples will be stored and is likely to be part of research results which are published and presented at research meetings. None of the data will be identifiable or traceable to you, and with your permission may be used for further research.

It is not necessary to inform your GP of your participation in this study but you are welcome to do so. However, we will ask you for permission to notify your GP of any abnormal blood results.

- **How will we use information about you?**

We will need to use information from you and your medical records for this research project. This information will include your name, contact details, date of birth, ethnicity and NHS number. To answer our research question, we will need to collect data from your medical records relating to COVID-19 and any other relevant health conditions. People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

- **What are your choices about how your information is used?**

You can stop being part of the study at any time, without giving a reason, but we will keep the information about you that we already have.

We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data that we hold about you.

If you agree to take part, you will have the option to take part in future research regarding the immune system and microbiome using your information and microbial DNA data saved from this study.

- **Where can you find out more about how your information is used?**

You can find out more about how we use your information:

  - at www.hra.nhs.uk/information-about-patients/
  - our leaflet available from: www.guysandstthomas.nhs.uk/research/patients/use-of-data.aspx (For GSTT) and www.kcl.ac.uk/research/support/research-ethics/kings-college-london-statement-on-use-of-personal-data-in-research (for KCL)
  - by asking one of the research team (contact details included below)
  - by contacting the Data Protection Officer: Nick Murphy-O'Kane DPO@gstt.nhs.uk;

- **What will happen to any samples I give?**

Apart from those samples sent to the haematology laboratories for routine clinical monitoring, the samples of blood and saliva you have provided for the study will go to the research laboratory ***at the Centre for Host Microbiome Interactions, Faculty of Dentistry, Oral & Craniofacial Sciences, Guys Tower,*** to be coded, with a study number to link to your medical history and the data that we collect. This means that it will not be possible for anybody who is not part of the Research Team to identify you. After processing and testing, any excess sample will be stored in a secure freezer labelled only with your study number. Only members of the study team will have access to the samples.
The samples will be processed and analysed in the ***Centre for Host Microbiome Interactions, Faculty of Dentistry, Oral & Craniofacial Sciences, at Guys Tower*** except for microbial DNA extracted from your saliva samples which will be sequenced by a specialised commercial provider.

The samples of blood and saliva that you give will be kept for up to 10 years and then destroyed but we may decide to carry out future ethically-approved research during this time using these samples, with your consent.

- **Will any genetic tests be done?**

Microbial DNA sequencing will be performed on your samples, but no genetic testing related to human DNA will be done.

- **What will happen to the results of the research study?**

The broad scientific results will be presented at an early stage to the scientific and medical community at research meetings and conferences. The results will be made publicly available by publishing in peer-reviewed scientific journals. The study participants will be able to see summaries on https://www.kcl.ac.uk/research/mimsa

- **Who is organising and funding the research?**

The research is being co-sponsored by King's College London and Guys and St Thomas' Hospital. It is being funded through a grant from the Medical Research Council to the Chief Investigator. Additional funding may be sought from public sources and other research grant funding bodies (including commercial organisations) to allow larger numbers of samples to be tested.

The Chief Investigator is employed by King's College London and receives no payments for conducting this study and has no conflicts of interests.

- **Who has reviewed the study?**

All research involving NHS patients is reviewed by an independent group called a Research Ethics Committee (REC), to protect your interests. This study has been reviewed and given favourable opinion by the Oxford Research Ethics Committee.

COVID-19

We are taking extra steps to ensure both staff and patients are kept safe at all times and to prevent any further spread.

We assure you that we are taking every step possible to ensure your visit is as safe as possible: as part of this you will be asked to follow Hospital policy on social distancing and PPE whilst you are on hospital premises. Staff will be adhering to strict cleanliness guidelines and, in some cases, this may mean full PPE.

Please attend the appointment on your own if possible. Do not bring any children or relatives. Exceptions to this are official Carers.

Please do not attend if you:

1) Have been informed that you are in a vulnerable group and should not attend hospital (unless specifically instructed by your doctor that particular tests are needed)

2) Have a household member, or are yourself, currently experiencing any COVID-19 symptoms. Then you must stay at home. Please let us know so we can reschedule your appointment.

If you feel your appointment is no longer needed, please let us know.

What if there is a problem?

If you have a concern about any aspect of this study, you can speak to the researchers who will do their best to answer your questions: [daljit.jagdev@kcl.ac.uk, Professor Mark Ide at Tel: 0207 188 5391or by email: mark.ide@kcl.ac.uk] If you remain unhappy and wish to complain formally, you can do this through the Guy's and St Thomas' Patients Advice and Liaison Service (PALS) on 020 7188 8801, pals@gstt.nhs.uk. The PALS teams are based in the main entrance on the ground floor at St Thomas' Hospital and on the ground floor at Guy's Hospital in the Tower Wing.

In the event that something does go wrong and you are harmed during the research you may have grounds for legal action for compensation against Guy's and St Thomas' NHS Foundation Trust and/or King's College London but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you (if appropriate).

You will be given a copy of this information sheet and a copy of the signed consent form to keep. Thank you for considering taking part in this study.