KILIMANJARO CHRISTIAN MEDICAL UNIVERSITY COLLEGE
(A Constituent College of Tumaini University Makumira)

TITLE OF THE STUDY: The Effect of Diet on Immune and Vaccine Responses in People Living with Obesity in Transitioning Communities

COMPOSITION OF THE RESEARCH TEAM

The proposed study will be led by the following team of researchers from KCMUCo: Dr. Godfrey Temba, MSc Biomedical Sciences, PhD (PI), Prof. Reginald Kavishe, MSc Biochemistry, PhD (co-investigator), Dr. Eka-Patricia Kisali, MD, MSc Immunology, PhD student (study coordinator), and Dr. Mary Mosha, MPH, MSc Nutrition for Global Health, PhD (nutritionist). The team of researchers at KCMUCo will collaborate with the following external partners to realize the proposed study: Dr. Quirijn de Mast, MD, PhD (external PI), Prof. Mihai Netea, MD, PhD, Prof. Leo Joosten, MD, PhD, and Prof. Musa Mhlanga, PhD, from Radboudumc, The Netherlands; Dr. Martin Larsen, PhD, and Dr. Delphine Sauce, PhD, from Cimi-Paris; Dr. Tal Pacht, PhD, from LIMES Institute in Bonn; and Prof. Shai Shen-Orr, PhD, from CytoReason in Israel.

WHAT IS THE PURPOSE OF THIS STUDY

The purpose of this study is to understand how overweight and obesity impair the function of the immune system, including the response to vaccination, and whether dietary intervention with a plant-based high fiber diet also rich in polyphenols as well as fermented foods may improve immune function and the vaccine response in overweight and obese individuals. The prevalence of overweight and obesity is rapidly increasing globally. Obesity is associated with immune dysfunction leading to an increased risk of severe infectious diseases and decreased response to vaccination. Our previous studies in the Kilimanjaro region have shown that diet has a pronounced effect on the function of the immune system in healthy individuals. The traditional high plant-based fiber and polyphenol diet and a locally consumed fermented banana brew were anti-inflammatory. However, it is still unclear to what extent dietary variation directly or indirectly influences the host immune defense in individuals who live with obesity and whether certain dietary interventions may enhance immune responses and improve vaccine efficacy. The current study aims to fill these gaps by establishing the cause-and-effect relationship between specific nutritional factors and immune responses to common viral and bacterial infections, as well as the response to vaccines, in people living with obesity.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

The study will enroll a total of 150 participants aged 35 to 60 years. One hundred (n=100) participants with a BMI >27 Kg/M^2(Obese) and the remaining fifty (n=50) will be age and sex-matched controls with a BMI between 18.5–24.9 Kg/M^2 (normal weight controls).

WHAT IS INVOLVED IN THE STUDY?

Participation in this study is entirely voluntary. If you refuse to participate or withdraw from the study, it will not affect any present or future relationships you may have with your medical care team. If you voluntarily agree to be in this study, you will be asked to sign and date this consent form.

After fulfilling the inclusion criteria you will be asked questions to assess your readiness to enrol in the study and if eligible you will be enrolled into the study after providing written informed consent,. Initial assessment will include screening for malaria, HIV, hypertension, and blood glucose levels. In premenopausal women, a pregnancy test will be performed. Your weight and height measurements will also be taken. Based on these anthropometric measurements 100 participants aged 35 to 60 years with a BMI >27 Kg/M2 (Obese) at screening will be recruited, as well as 50 age and gender-matched participants with a BMI between 18.5-24.9 Kg/M2 at screening (normal weight controls). You will not incur any cost for the screening tests. You will be provided with a food log sheet to record your food and beverage intake the week before starting the intervention (a 24-hour dietary recall on three non-consecutive days, that is two weekdays and one day in the weekend/public holiday). You will also be required to describe whether the food was prepared from unprocessed or processed products (e.g., unprocessed maize flour 'Dona' vs. processed maize flour 'Sembe"). These food logs will be assessed by the nutritionist to determine your average consumption. The next step will be filling out two questionnaires one collecting information on the general lifestyle including health status and the other one collecting information on frequency intake of different food items (food frequency questionnaire, FFQ) to describe the dietary habits.

At the start of the intervention, the first consecutive ninety of the 100 overweight volunteers will be randomly assigned to one of three arms: i) plant-based high fiber and polyphenol diet (n=30); ii) daily consumption of fermented banana beverage (n=30); iii) remain on their regular diet (obese controls; n=30). Participants in the 'high plant-based fiber and polyphenol diet' arm will be invited for breakfast and lunch every day at a restaurant on the hospital premises during which they will receive a meal. In addition, they will receive a family-size food package for dinner on weekdays as well as a package for all three meals on Saturday (breakfast, lunch and dinner). Participants in the 'fermented banana brew' arm will receive 1 litre of fermented banana beverage ('mbege') every evening after work (Monday to Friday) from the same facility. The dietary intervention will last for six weeks.

The flow of activities during the study is detailed in figure 1 below. Individuals who agreed to participate in the study will be invited for an initial screening visit (visit 1), and those who match the inclusion criteria will be enrolled. Blood (37.5ml) and handed a container for a stool sample (about 2 g) samples will be taken on visit 2 for immune assays and a suite of omics technologies (baseline sampling, 100 overweight participants, and 50 lean participants). Blood (37.5ml) and stool (about 2 g) samples will be taken from 90 participants in the intervention arms at week 4 (visit 3). (post-interventional sampling). Participants will

receive a conjugated pneumococcal vaccine (Prevenar13) and tetanus toxoid vaccine at week 4 and continue with their diets for another 2 weeks to examine the impact of the dietary intervention on vaccination responses. The effect of diet on the immune system and the vaccine response will be evaluated four weeks following vaccination (visit 4), blood (37.5 ml) and stool (about 2 g) samples will also be collected to investigate how long the health benefits of the plant-based diet and fermented banana beverage on immune function and vaccine responses can last. The measurements for the different samples will be conducted in part at the Kilimanjaro clinical research institute (KCRI) and the rest conducted in laboratories outside the country in institutions collaborating on this project. These laboratories will handle the samples following strict protocols and confidentiality measures. The collected blood samples will be used for measuring immune responses to different micro-organisms including different bacteria, viruses and fungi of clinical relevance. They will also be used to assess vaccine responses, changes in plasma proteins and other changes to immune cells following the diet intervention. The stool samples will be used to assess the changes in the microbiome which plays a crucial role in immune regulation and gut health.

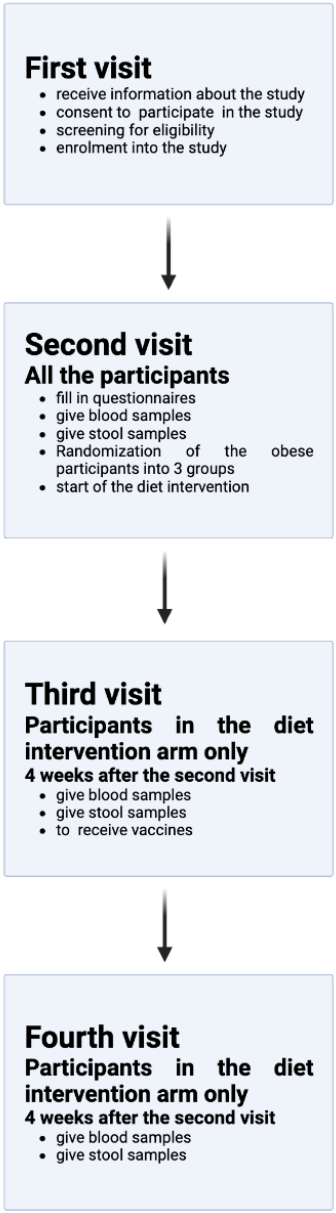

Figure 1: Flow chart showing the events scheduled at each visit during the 2 months of the study duration.

CONFIDENTIALITY OF THE INFORMATION

Data will be handled confidentially. Each participant will receive a study identification number. The key to the code will be safeguarded by the principal investigator. Only collaborator Temba, the data monitoring unit at KCMUCo, and partner de Mast will have access to non-anonymized data, whereas all other partners will only have access to the anonymized donor ID. The case report forms (CRF) and signed informed consent forms will be archived for a maximum of 15 years. All data obtained in TransInf will be handled confidentially.

FUTURE USE OF MATERIAL

Stored material, including samples and associated data, may be used for additional research questions in the future, provided that the new research is approved by the relevant ethical committees and complies with all applicable legal requirements. The samples will be stored for a maximum period of 10 years.

THE RISK AND BENEFITS OF PARTICIPATING IN THIS STUDY

Risks associated with the intervention are negligible. The alcohol percentage of the fermented banana beverage is low averaging between 1 and 3 percent, and is unlikely to induce liver damage. Prior to your recruitment to the study we will assess your alcohol consumption as well as screen you for any liver diseases by measuring a liver enzyme in your blood so as to establish that you are healthy and able to consume the beverage safely.

The pneumococcal (Prevenar 13) and tetanus toxoid vaccines are among the most commonly administered vaccines worldwide with an excellent safety profile. Some minor adverse effects may occur after receiving a vaccine, including redness, swelling, pain, or tenderness where the shot is given, fever, loss of appetite, feeling tired, headache, muscle aches, joint pain, and chills. These symptoms usually last for a few days, however, if they persist or increase in severity then the participant should report to the nearest health facility and also inform the research team.

Participants will be reimbursed transportation costs for the four visits to be made to the study site(figure 1). During other days, since the study participants will be coming into work, there will be no reimbursement of transport costs. The advantages of participation will be receving free screening for diseases including common infections like HIV and non communicable diseases like diabetes mellitus and hypertension. Participants will also receive nutritional health information and nutritional health advice. Additionally, participants will receive vaccinations for key public health diseases i.e pneumococcal and tetanus toxoid vaccines.

RIGHTS TO WITHDRAW FROM THE STUDY

You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study

at any time. If you withdraw from the study, no new data about you will be collected for study purposes. Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care in the future. If you do decide to withdraw, we ask that you contact the research team.

WHAT ABOUT COMPENSATION?

Participants will be financially supported to come to the study site during the four sampling periods.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, or if you have complaints, concerns, or suggestions about the research, contact Dr. Godfrey Temba (PI) at the Kilimanjaro Christian Medical University College Tel. +255 753584878 or Dr. Eka-Patricia Kisali (study coordinator) at the Kilimanjaro Christian Medical University College Tel. +255 687500303.

Either if you need to report or obtain more information related to ethical misconduct in this study please contact the ethics office via phone number 0272753909, or email: kcmc.rec@kcmuco.ac.tz

CONSENT FORM

I have read the information for this study and my questions have been fully answered by a member of the research team

I agree to participate in the study.

Name …… Signature…….. Date……..

I have read and explained the study information to this person and have answered all question raised

Name …… Signature…….. Date……..