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Investigating the microorganisms found in the mouths of healthy people

Submission date 17/12/2018	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 20/12/2018	**Overall study status** Completed	
Last Edited 05/10/2022	**Condition category** Oral Health	

Plain English summary of protocol

Background and study aims
Human microbial communities are highly complex ecosystems, but the microbial composition of distinct sites of the oral cavity (mouth) is not clear. On the other hand, dysbiosis (microbial imbalance) has been associated with different diseases, including autoimmune disorders, diabetes, obesity, colon cancer and even psychiatric conditions. Studies are needed to define the human microbiota in healthy people, before studying any potential association of the microbiome with specific diseases. The aim of this study is to create a site-specific map of the oral microbiome in order to define which microorganisms colonize each surface of the oral cavity using non-invasive sampling procedures. Furthermore, a technique analyzing the whole microbiota (by mouth rinse) will be compared to the results obtained with individual sampling at the different sites, to find out whether it is equally sensitive and precise, as it might be used routinely in the diagnosis of dysbiosis.

Who can participate?
Healthy volunteers, both genders, aged 18-75

What does the study involve?
Participants are sampled by a non-invasive method (swabs, periodontal curettes, mouth rinse) in order to collect representative samples of the oral microbial population, to be analysed in detail.

What are the possible benefits and risks of participating?
Benefits include the characterization of the microbial population of the oral cavity, and the possible identification of potential pathogens. There are no risks associated to participating to the study as all the samplings will be performed in a non-invasive way during routine teeth control.

Where is the study run from?
University of Ferrara (Italy)

When is the study starting and how long is it expected to run for?
September 2018 to December 2019

Who is funding the study?
University of Ferrara (Italy)

Who is the main contact?
1. Prof. Elisabetta Caselli
2. Prof. Maurizio Franchi
3. Prof. Sante Mazzacane

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
02

Study information

Scientific Title
MOMap: a mapping protocol for human oral microbiome

Acronym
MOMap

Study objectives
The aim of this study is to create a site-specific map of the oral microbiome in order to define which microorganisms colonize each surface of the oral cavity using non-invasive sampling procedure.
The purpose of the current study is also to evaluate whether specimens collected by the protocol used in a prospective cancer cohort (PLCO screening procedure), could be used for oral

microbiota research by comparing specimens with seven other site-specific oral sample types from the same subjects.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval by Ethics Committee has been requested (central EC of Emilia Romagna region, Italy) and is expected within December 2018 - pending

Study design
Observational monocentre cross-sectional study

Primary study design
Observational

Secondary study design
Epidemiological study

Study setting(s)
Community

Study type(s)
Screening

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Oral microbiome

Interventions
This is an observational study. Fifty healthy adult subjects with no systemic or oral disease will be recruited.
The study design was chosen according to the current standards for observational clinical trials.
a. A Single-Arm, Single-Visit observational study will be established
b. A total of 60 subjects will be recruited to participate in the study. It is expected all subjects will complete the study in total
c. The data will be stratified according to age, gender, sample site, plaque index and BoP scoring
d. Admission into the study will be via rolling admission (estimated recruitment time: 6 months)
e. Each subject must be in good general health
f. Each subject must be in good oral health
g. Each subject will follow the following treatment protocol:

Visit 1 - SCREENING and ENROLLMENT: consent secured; screening and entry into study; baseline data collection, including full periodontal charting (full-mouth PD, BOP, O'Leary PCR); identification of sampling sites; sampling collection.

j. All clinical assessment data will be recorded via hard copy CRFs. CRFs will be submitted to the microbiological testing site for entry into the statistical database. At the conclusion of the study,

such statistical database will be submitted to the statistician for the preparation of the statistical analysis and the final study report.

2. PROCEDURE

Screening and Selection of Subjects
Subjects will report to the clinical facility and be screened by the dental examiner to identify those subjects who meet the inclusion/exclusion characteristics. The findings of screening procedure will be recorded on the CRF. Subjects who meet the inclusion/exclusion characteristics and sign an Informed Consent Form will be entered into the study.

General Health Screening
At the time of screening visit, subjects will be excluded if they have:
• Heart diseases or blood pressure alterations that need a medication
• Chronic obstructive pulmonary disease and asthma
• Any renal, hepatic, gastrointestinal diseases that requires a medication
• Presence of any STDs or sieropositivity to HBV, HCV, HIV
• Presence of any neoplastic lesion or cancer or paraneoplastic syndrome
• Current radiotherapy or chemotherapy
• Pregnant or lactating women

Oral Cavity Screening
a. At the time of the screening visit, subjects will be excluded if they have:
• Chronic dry mouth, as assessed through questioning of the subject by an experienced clinician
• Untreated cavitated carious lesions or oral abscesses
• Tumors or significant pathology of the soft or hard tissues of the oral cavity
• Evidence of precancerous or cancerous lesions
• Evidence of candidiasis
• Clinically meaningful halitosis as determined by organoleptic assessment by an experienced clinician
• More than 8 missing teeth, with missing teeth accounted for by third molar extractions, teeth extracted for orthodontic purposes, teeth extracted because of trauma, or teeth that are congenitally missing
• Periodontal pockets > 4 mm
• Presence of orthodontic appliances

b. Screening procedures require a standard dental chair with good lighting and an examination kit containing at least one long-handled mouth mirror, dental explorer, and calibrated CP15 periodontal probe (Hu-Friedy Italy s.r.l., Milano, IT)

A. Obtain a careful dental and oral history including recent history of oral infections, inflammation, pustules, canker sores, benign or malignant masses. Record length of time since last oral prophylaxis or periodontal treatment
B. Perform a complete soft tissue examination: gingivae, oral mucous membranes, tongue, pharynx, palatine tonsils. Record findings on the oral screening examination form.
C. Note number of teeth. Subjects should have at least 24 teeth with missing teeth accounted for by 3rd molar extractions and/or teeth extracted for orthodontic reasons and/or for trauma and/or teeth that are congenitally missing.
D. Note number of untreated cavitated carious teeth and restored teeth. Only obvious carious lesions are anticipated to be detected by this examination.
E. Periodontal examination should include 6 surfaces on all teeth: (1) mesiofacial; (2) midfacial; (3) distofacial; (4) mesiolingual; (5) midlingual; (6) distolingual.

Periodontal measures will include full mouth evaluation of pocket probing depth – PPD, Clinical Attachment Level – CAL, Plaque index – PL and Bleeding on probing – BOP.

Collection of Clinical Specimens - Site mapping procedure
The sample list is similar to the one described in the Human Microbiome Project (Manual of Procedures for Human Microbiome Project, Core Microbiome Sampling, Protocol A, HMP Protocol # 07-001, Version Number: 12.0, 29 Jul 2010).
The study is designed for the properly defined oral cavity microbiome evaluation. The specimens will be collected from soft tissues and hard tissues located in the area that includes the lips, the lining inside the cheeks and lips, the front two thirds of the tongue, the upper and lower gums, the floor of the mouth under the tongue, the bony roof of the mouth, and the small area behind the wisdom teeth.

Collection Methods
Aseptic technique will be used for collection of all specimens.
Sequence of collection: 1. Saliva; 2. Soft tissue sites; 3. Hard tissue sites
After each specimen is collected, the tube will be placed in a Ziploc bag in ice, and taken to the Microbiology section within 4 hours.

Intervention Type
Other

Primary outcome measure
Characterization of the microbial communities colonizing the different anatomical sites of the oral cavity. Methods include two types of molecular analyses: 1) NGS, 2) quantitative real time PCR microarray. Measured at a single timepoint, as the study does not include a follow-up phase of enrolled subjects.

Secondary outcome measures
The optimal methodology for characterization of the oral microbiome, to define a gold standard method for microbiome analysis. Methods used include comparison of the different types of sampling (microbial collection by swabs, by periodontal curettes, or by saliva collection) and of molecular analyses (NGS, or quantitative real time PCR microarray). Measured at a single timepoint, as the study does not include a follow-up phase of enrolled subjects.

Overall study start date
01/09/2018

Completion date
31/12/2019

Eligibility

Key inclusion criteria
Participants of the study will be enrolled among healthy subjects at the Dentistry Section of the University of Ferrara. Eligible subjects will have the following characteristics:
1. Age 18-75 years
2. Both genders
3. Good general health conditions
4. Absence of oral pathologies
5. Willing to cooperate to guarantee participation to all planned experimental procedures, and

for the whole duration of the study
6. Ability to understand and give informed consent

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
75 Years

Sex
Both

Target number of participants
50

Total final enrolment
20

Key exclusion criteria
1. Pregnancy and breastfeeding
2. Systemic diseases, including diabetes, viral infections by HIV, HCV, genetic disorders, respiratory diseases (chronic bronchopneumopathy, asthma)
3. Chemotherapy or radiotherapy
4. Presence of orthodontic devices
5. Presence of tumors or severe pathologies of soft tissues and oral cavity
6. Presence of tooth decay lesions, conservative or prosthetic devices potentially impeding the correct sampling procedures
7. Systemic therapy with antimicrobials/antibiotics in the previous 3 months and during all the study
8. Dental prophylaxis in the previous 3 months
9. Consumption of drugs potentially interfering with periodontal conditions and/or with recovery after periodontal treatment in the previous 3 months (i.e. corticosteroids, calcium antagonists, systemi antibiotics, etc)

Date of first enrolment
01/01/2019

Date of final enrolment
30/06/2019

Locations

Countries of recruitment
Italy

Study participating centre
School of Dentistry of the University of Ferrara
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Sponsor information

Organisation
CIAS - University of Ferrara

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Sponsor type
University/education

ROR
https://ror.org/041zkgm14

Funder(s)

Funder type
University/education

Funder Name
Università degli Studi di Ferrara

Alternative Name(s)
University of Ferrara, UNIFE

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location

Italy

Results and Publications

Publication and dissemination plan
The trialists plan to publish the results of the study as soon as they have all the patients and data collected and elaborated.

Intention to publish date
31/07/2020

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		18/05/2022	05/10/2022	Yes	No