

Microbial markers of oral carcinogenesis in Fanconi Anemia and cancer patients

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Introduction

- Infection as a risk of cancer
- Data begin as observational: people with cancer also harbor a given bacterial species
- Example: *Helicobacter pylori*
- Gastritis can lead to gastric cancer
- Infection with *H. pylori* correlates with incidence of gastritis: bacteria might be associated with initiation of gastric cancer
- 1994: WHO International Agency for Research on Cancer classified *H. pylori* as a definite cause of cancer



Introduction

- Other possible **associations**:

Bacteria	Cancer
<i>Chlamydia trachomatis</i>	Cervical
<i>Chlamydophila (Chlamydia) pneumoniae</i>	Lymphoma; lung
<i>Streptococcus bovis</i>	Colonic carcinoma
<i>Salmonella typhi</i>	Gallbladder

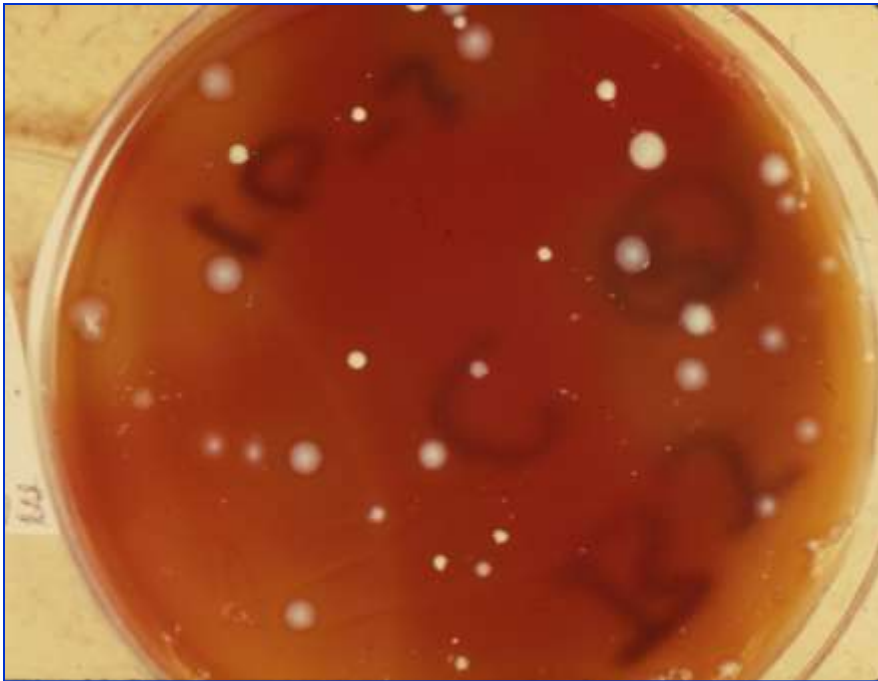
- **ASSOCIATION DOES NOT MEAN CAUSATION...**



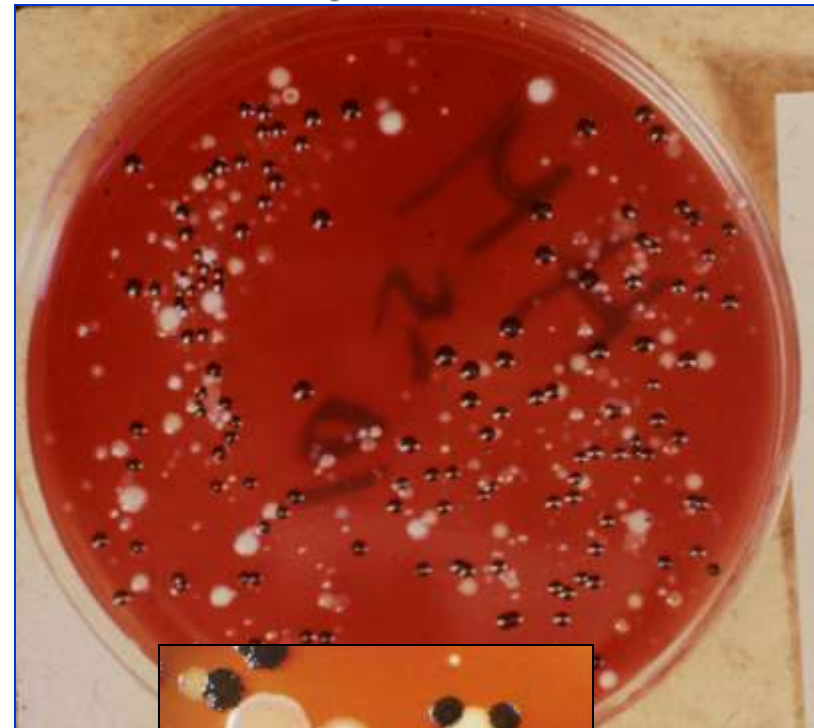
Introduction

- The oral cavity harbors many types of bacteria

Health



Chronic periodontitis



Oral Bacteria and Head and Neck Cancer

- Elevated levels of common oral bacteria have been found in esophageal cancer lesions and their lymph nodes
- *Streptococci, Prevotella, Veillonella, Porphyromonas, Capnocytophaga*

Salivary Bacteria and Oral Cancer

Oral Squamous Cell Carcinoma (SCC)

	OSCC - free	OSCC	OSCC - free matched	OSCC
N	229	45	45	45
Mean age (\pm SEM)	42.1 (\pm 1.04)	57.6 (\pm 2.3)	53.7 (\pm 2.1)	54.5 (\pm 2.3)
Minimum age	18	18	19	18
Maximum age	81	92	81	85
Males	107 (47%)	32 (71%)	32	32
Smokers	46 (20%)	18 (40%)	18	18

- OSCC patients had elevated salivary levels of certain oral bacteria, specifically *Capnocytophaga gingivalis*, *Prevotella melaninogenica*, and *Streptococcus mitis*
- Potential non-invasive diagnostic tool

How bacteria may cause cancer?

1) Activation of procarcinogenic chemicals

- Ethanol (alcohol) → Acetaldehyde
- Acetaldehyde can cause DNA damage
- *Streptococci* and *Neisseria* can convert ethanol into acetaldehyde

How bacteria may cause cancer?

2) Infection and Inflammation

- Local (chronic) inflammation can participate in the induction and expansion of malignant cells
 - *H. pylori* & gastric cancer
 - *P. acnes* & prostate cancer
 - *C. pneumoniae* & lung cancer
 - *S. bovis* & colonic carcinoma
- Many oral bacteria can stimulate inflammatory response

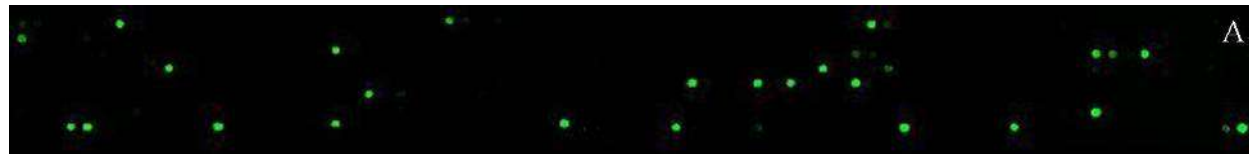
Rationale

- Previous studies focused on up to 40 species of bacteria
- The oral cavity can harbor > 700 bacterial species
- They might also be associated with oral cancer
- Different bacteria are present in different oral locations
- Tongue (lateral) is #1 location of oral cancer

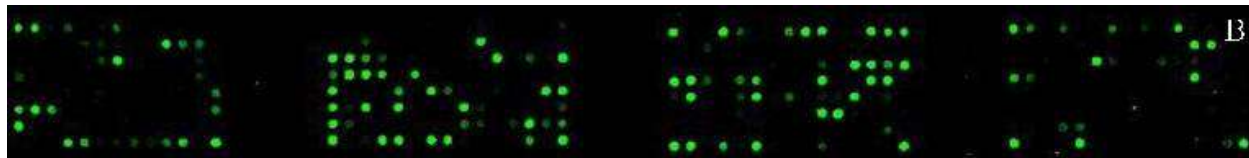
Human Oral Microbial Identification Microarray (HOMIM)



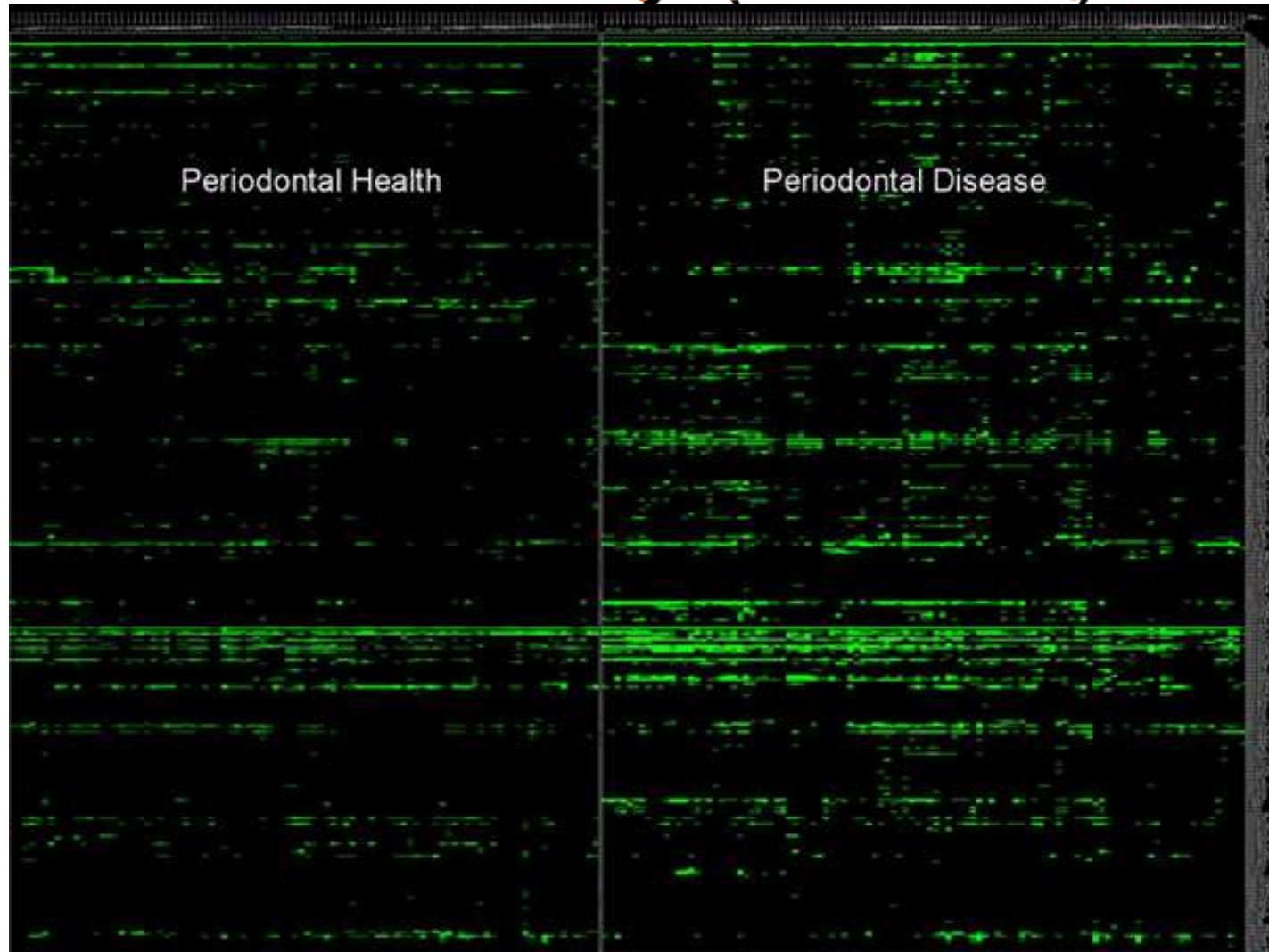
Healthy



Disease



Human Oral Microbial Identification Microarray (HOMIM)



Purpose

- To characterize the oral microbial profiles of FA patients, their non-FA sibling/parent (and non-FA oral SCC patients)

	n	Saliva	Tongue Lateral	OSCC lesion	Healthy contralateral to OSCC	Microarrays
FA	42	X	X			84
Non-FA relative	42	X	X			84
OSCC	42	X	X	X	X	168

- Personnel involved:** Bruce Paster, Dr. Phil Stashenko (Forsyth), Eva Guinan and Marshall Posner (DFCI), Meredith August (MGH), Carmen Bonfim (Federal University of Parana, Brazil), Eleni Gagari (University of Athens School of Medicine, Greece).



Sampling

- Approximately 30 min. visit
- Informed consent and medical questionnaire
- To the extent possible, participants will be asked to refrain from drinking, eating and brushing in the 2 hours prior to sampling
- Stimulated saliva samples will be collected (about 2 teaspoons) by spitting into a plastic tube after chewing on a paraffin stick
- Samples of the material covering the surfaces of the sides of the tongue (i.e., biofilm) will be collected using a sterile soft brush and swabbing the tongue

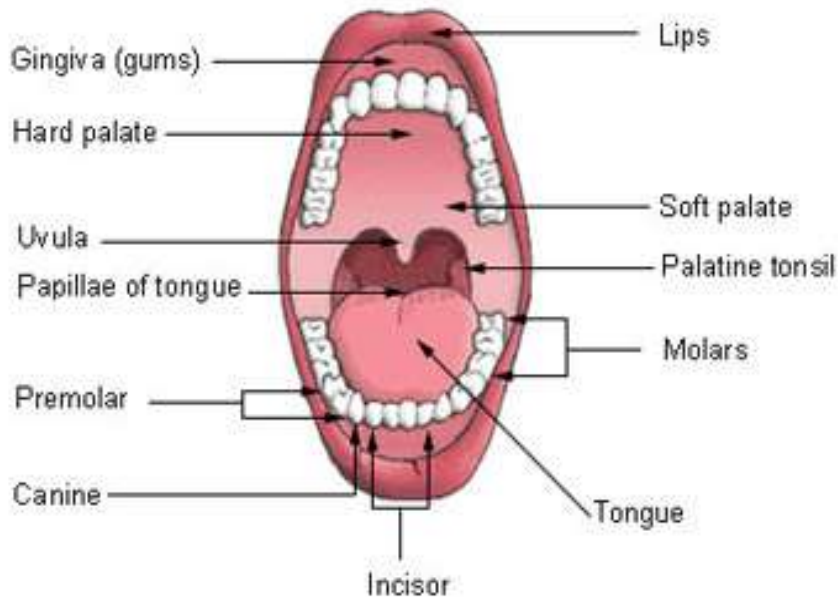


Sampling: Saliva

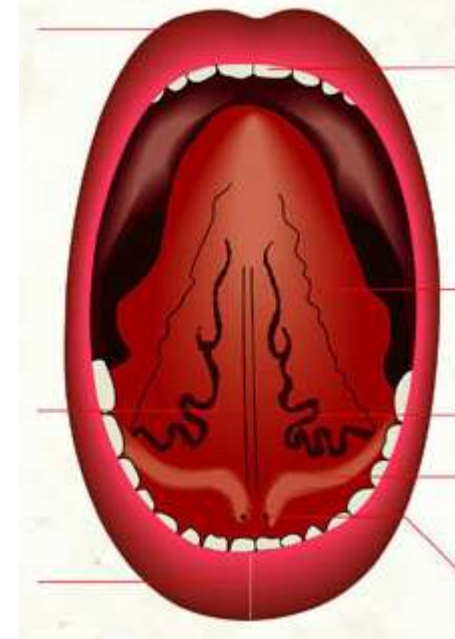


Sampling: Tongue

Mouth (Oral Cavity)



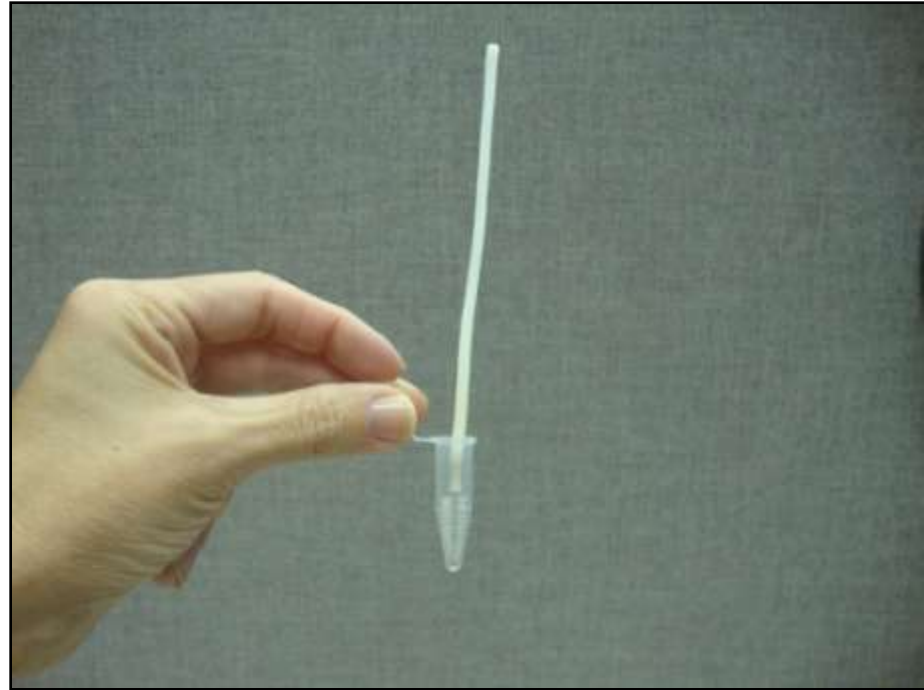
TONGUE (lower surface)



<http://training.seer.cancer.gov/images/anatomy/digestive/mouth.jpg>

<http://kimberlyunderwood.files.wordpress.com/2009/02/tongue2.jpg>

Sampling: Tongue



Anticipated Results and Future Studies

- Types of bacteria present in FA patients will be different from those present in non-FA
- Selected bacterial species present only in FA patients will merit further study:
 1. Can they induce infection/inflammation?
 2. Can they make carcinogenic compounds?
 3. Are they similar to those present in non-FA OSCC patients?
- This study would be a first step in the development early diagnostic test for patients who are at greatest risk of developing head and neck SCC

Example: Multiple Salivary Biomarkers for Pancreatic Cancer Detection

- Search for compounds in saliva of 30 pancreatic cancer (PC), 30 chronic pancreatitis (CP) and 30 healthy matched-control (H) saliva samples
- The levels of six microbial biomarkers, eleven mRNA biomarkers and eight metabolites were significantly different between PC, CP and H
- Microbial biomarkers (*Prevotella nigrescens*, *Neisseria elongata*) contributed to provide a sensitive and specific means of distinguishing PC from H, as well as PC from CP
- Combination of multiple (4) salivary biomarkers could detect pancreatic cancer with great clinical discrimination
- First report demonstrating the value of salivary biomarkers for the detection of pancreatic cancer.

Questions?

