

# Managing Dental Caries with Modern Sciences

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# The molecular revolution in medicine

- 1950- DNA double helix
- 1960- Molecular biology tools
- 1970- Gene regulation
- 1980- Genetic engineering
- 1990- Genomics and gene therapy
- 2000- Human genome project
- 2010- Individualized medicine...

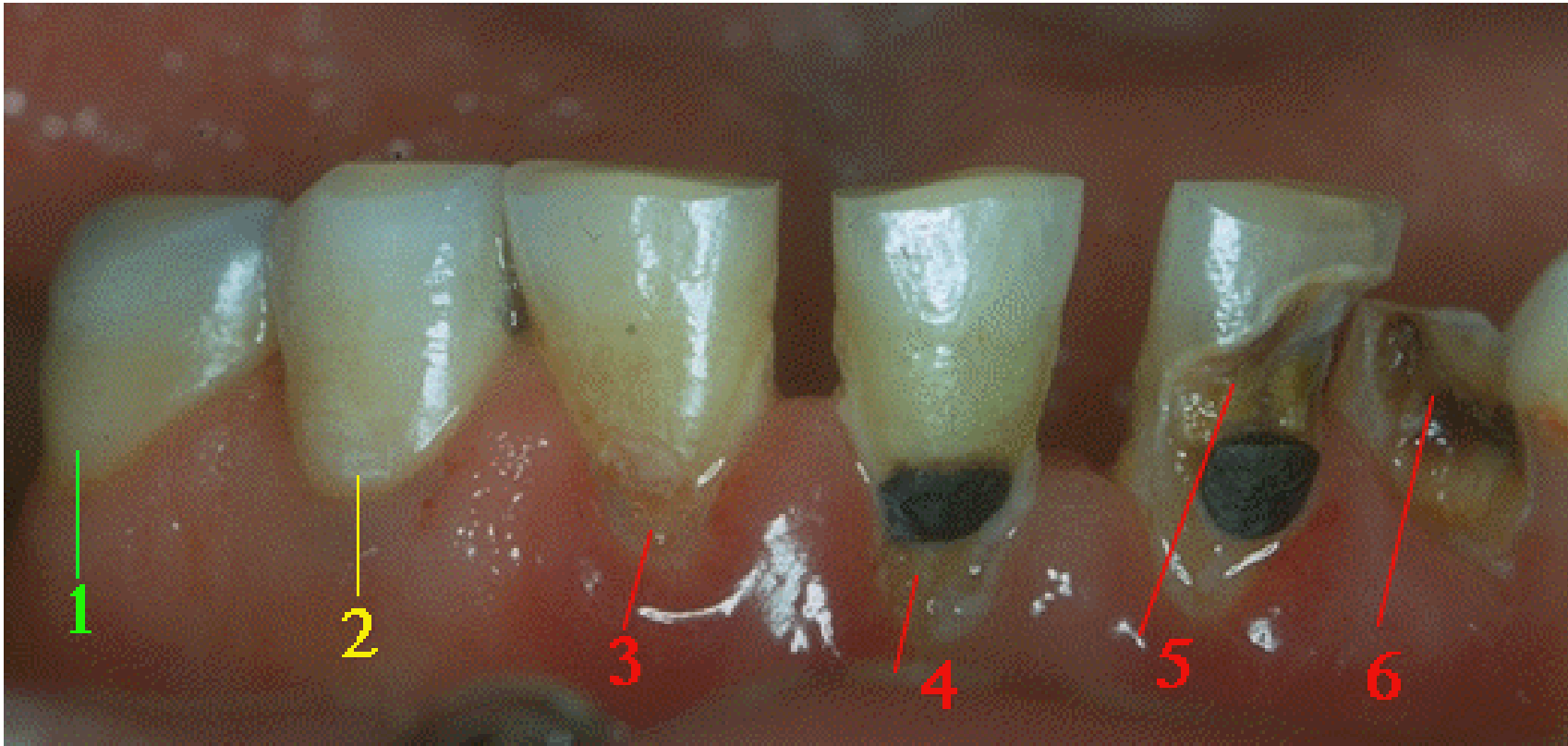
# The impact of molecular medicine on dentistry

From surgical to medical approach

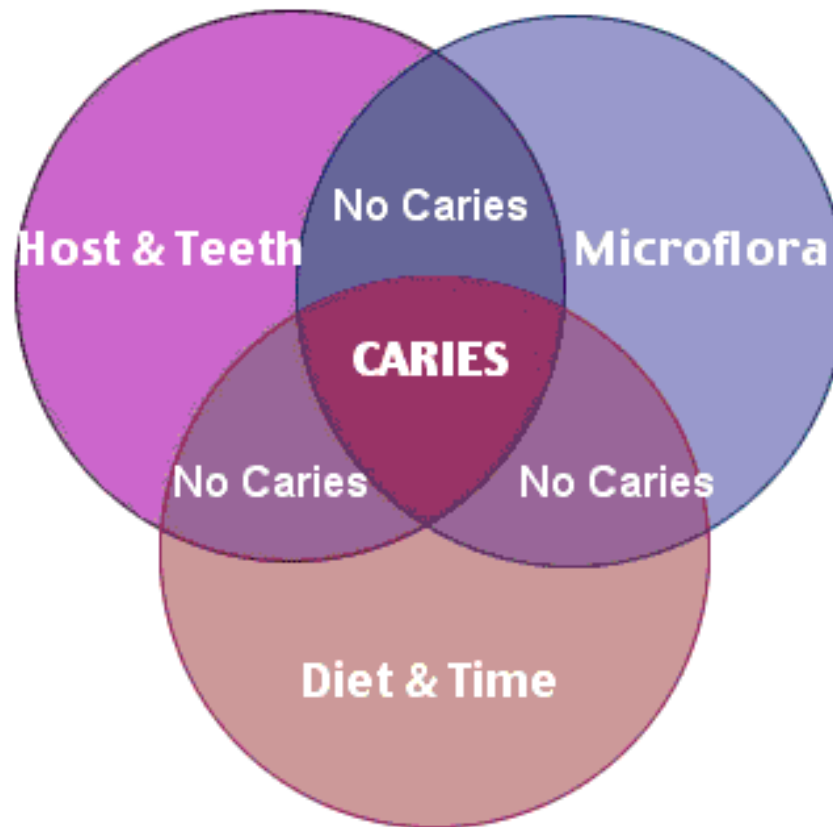
From treatment to prevention

From professional care to self-care

# Dental Caries



**Dental Caries is the localized destruction of the hard tissues of the tooth**



Does each factor contribute equally?

# **Bacteria are the ultimate guilty party!**

Genetic defect in tooth (new born mice)

Poor immune system (mice with no B/T cells)

Poor saliva flow (mice with salivary glands removed)

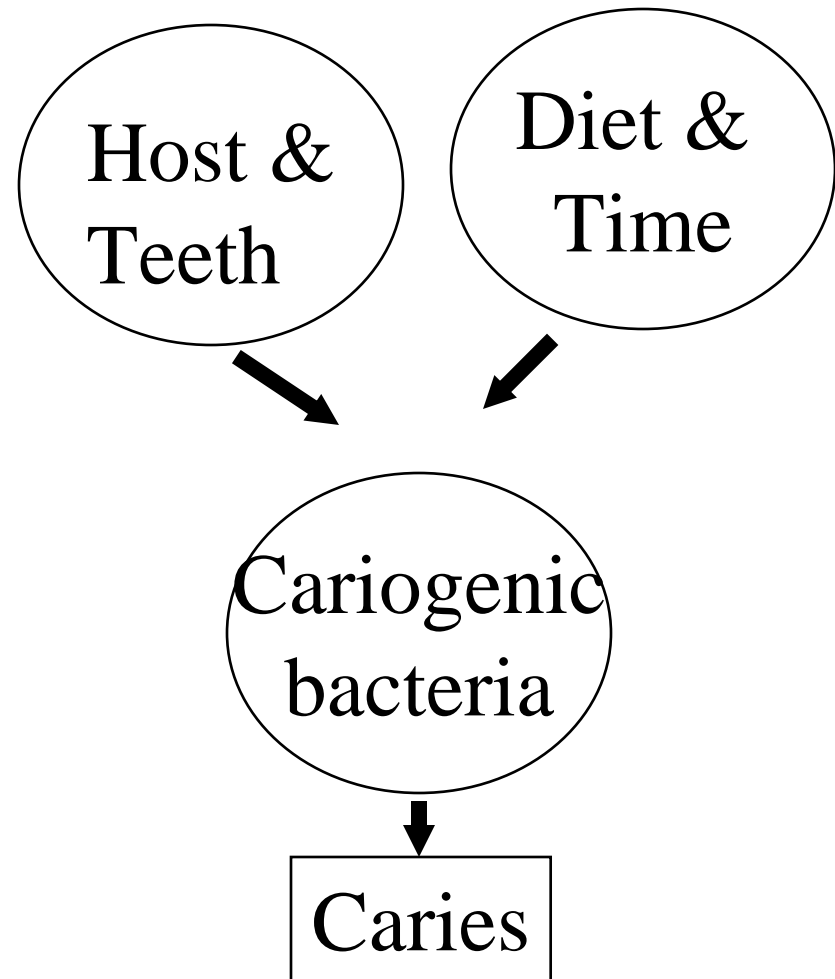
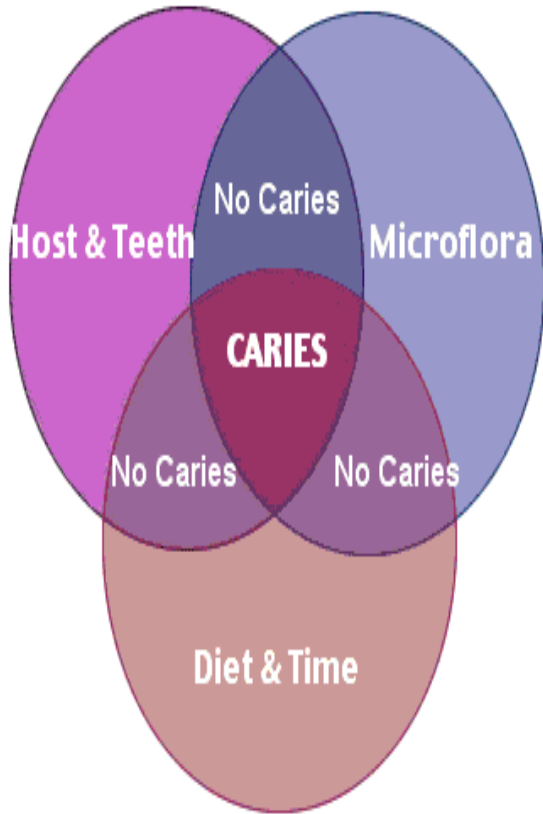
Diet (mice eating sugars as major food source)

Poor oral hygiene (mice in dirty, but sterilized cages)

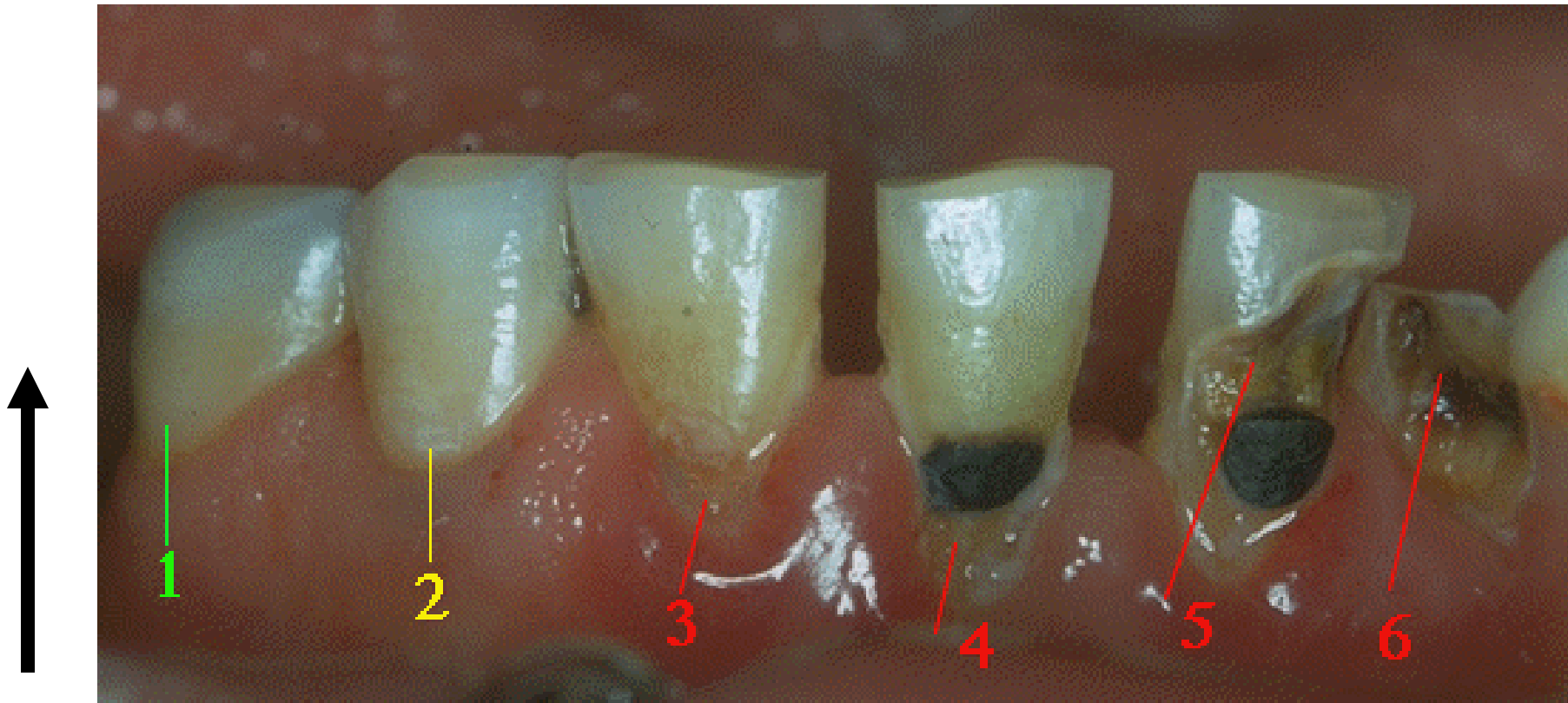
No bacteria inoculation, no cavity

Bacteria inoculation, full of cavity

**All other cariogenic factors work through bacteria!**

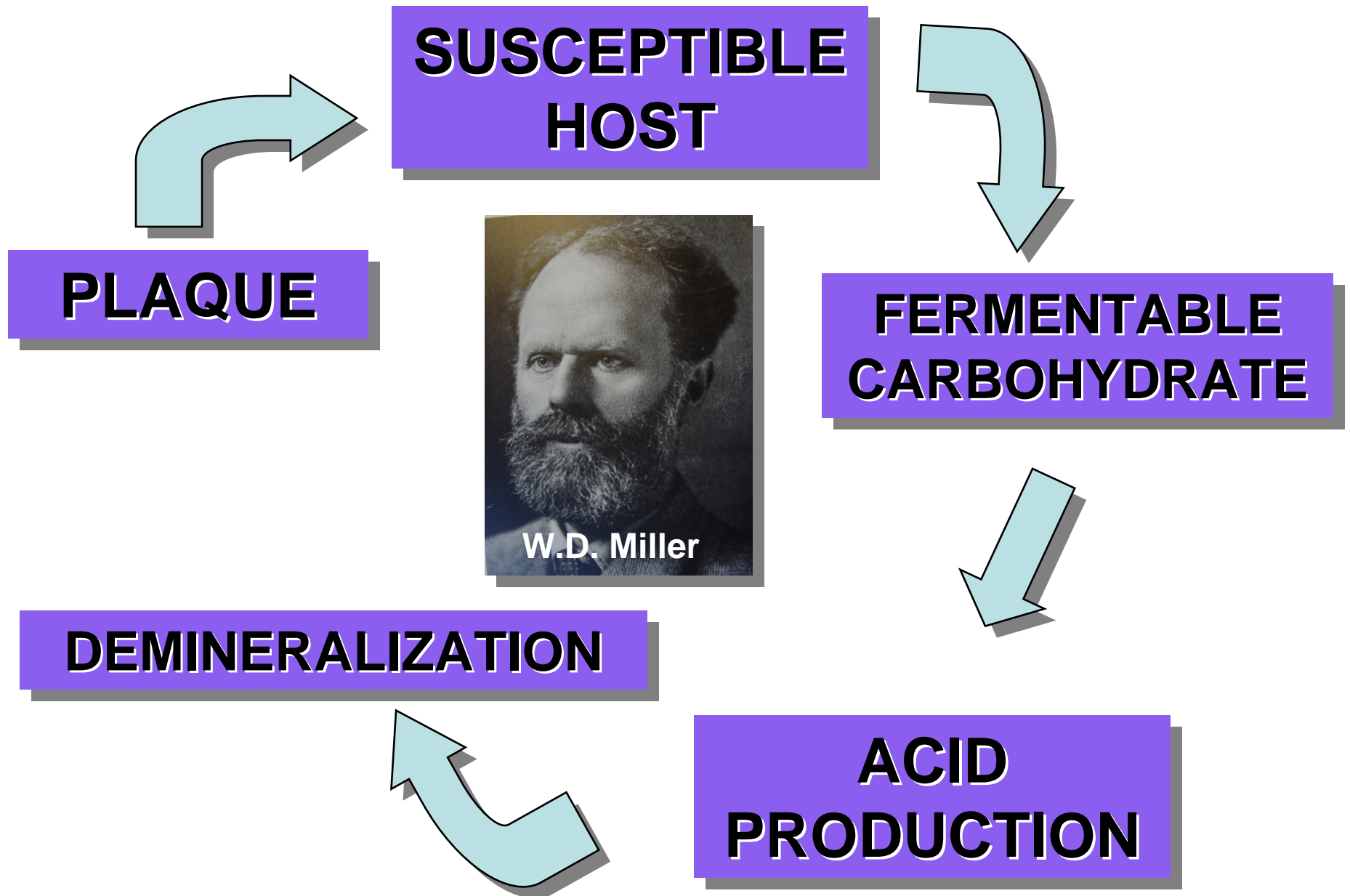


# A medical approach to dentistry



**Dental Caries is the localized destruction of the hard tissues of the tooth**

# The Miller light: a biological view of tooth decay



# Dental Caries

Carbohydrates (Sucrose)



Specific set of cariogenic bacteria (*S. mutans*)



Glucans/Levans

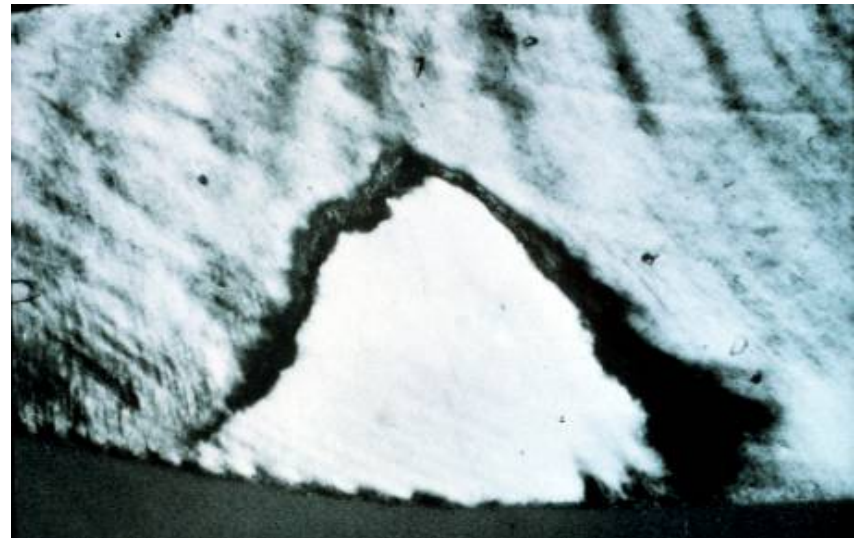


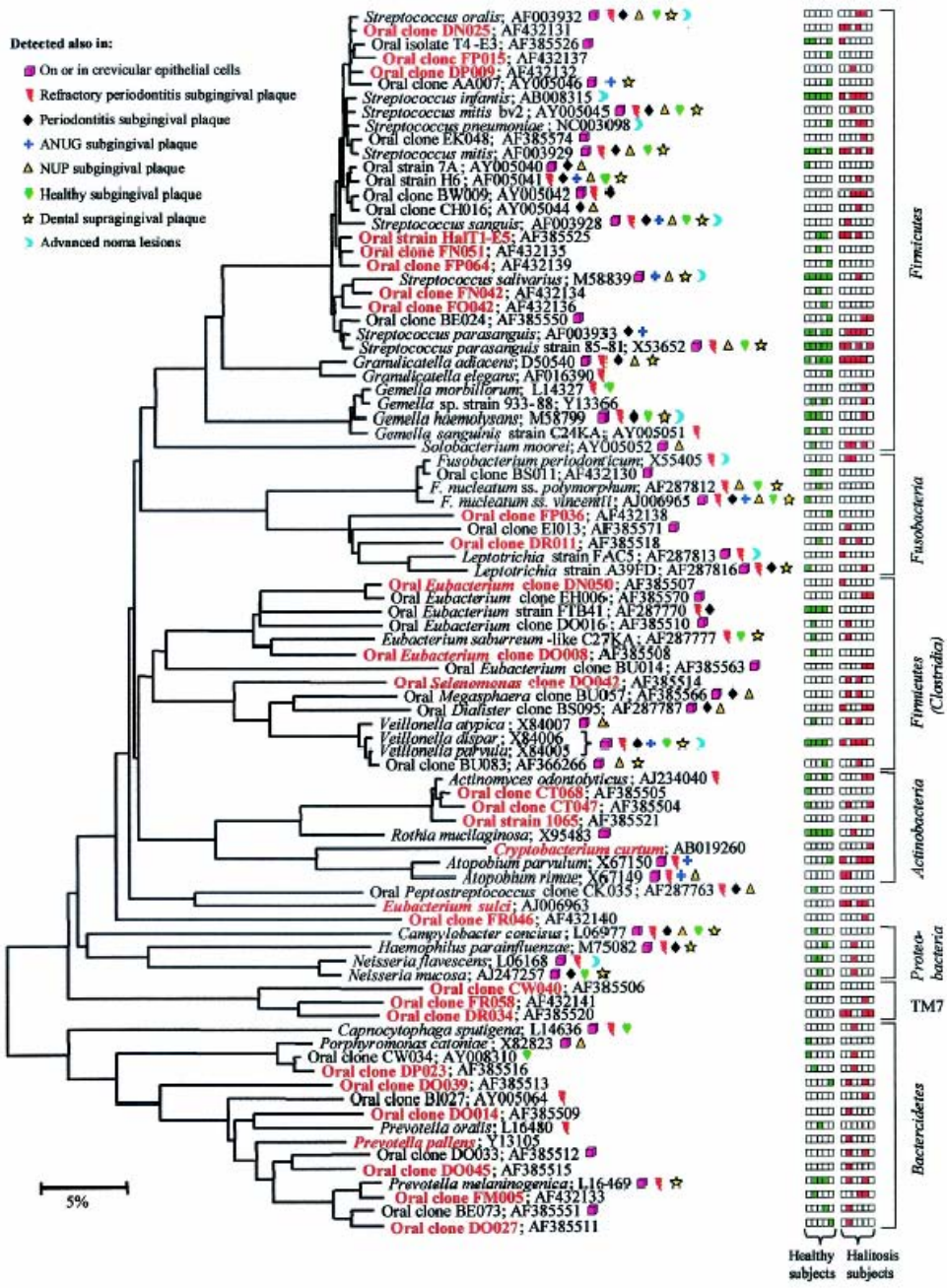
Acids

Plaque formation



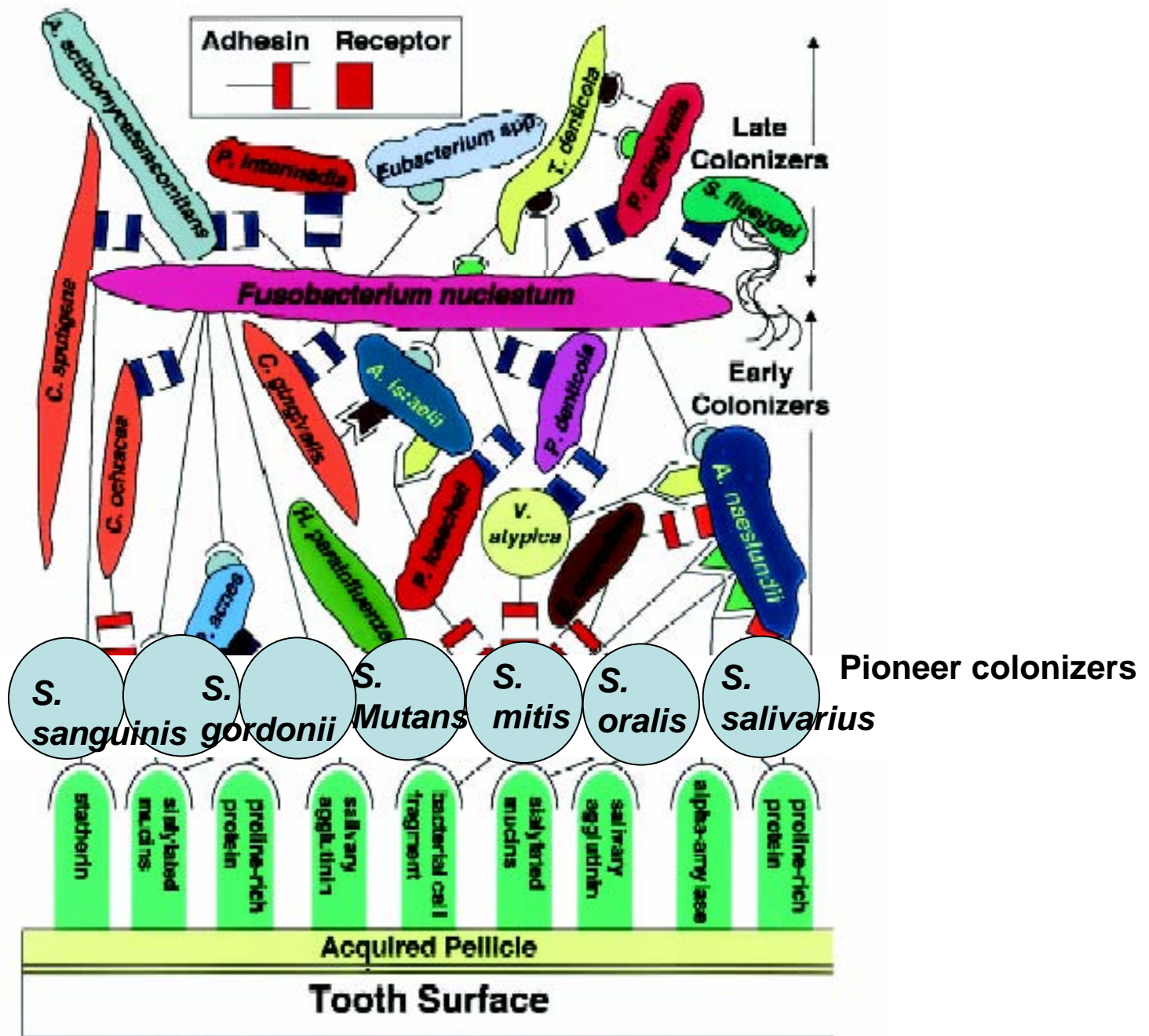
Demineralization





**Phylogenetic tree of bacterial species or phlotypes identified by 16s DNA sequencing from the samples from oral cavity**

**Individual: ~200 species**  
**Population: >700 species**  
**Cariogenic: 3 genus, 12 species**



# Some amazing new discovery on dental plaque

- Signal transduction
- Quorum sensing
- Biofilm
- Inter-species interactions
- ...

# Today's dentistry



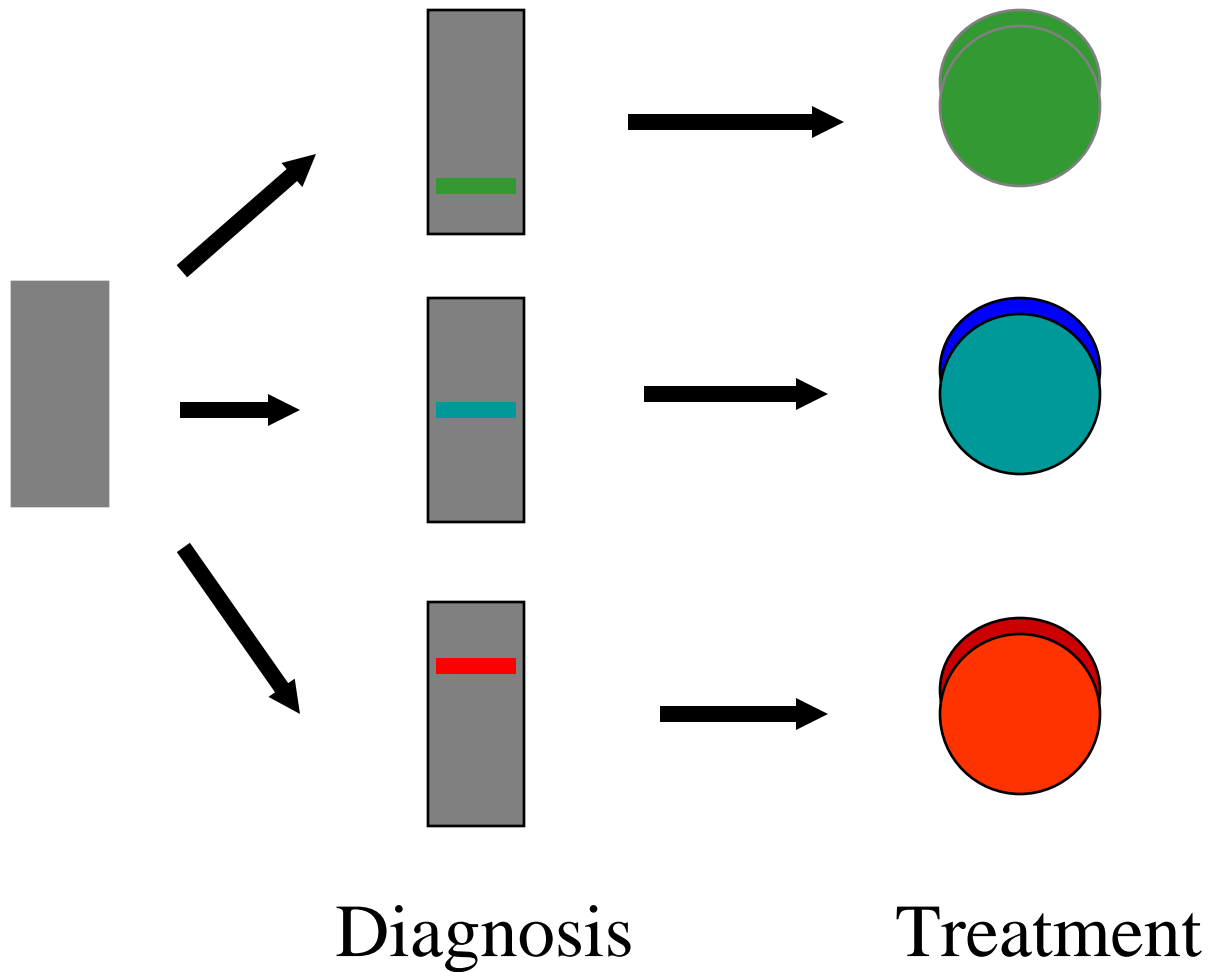
## **Diagnosis**

*-X-ray*

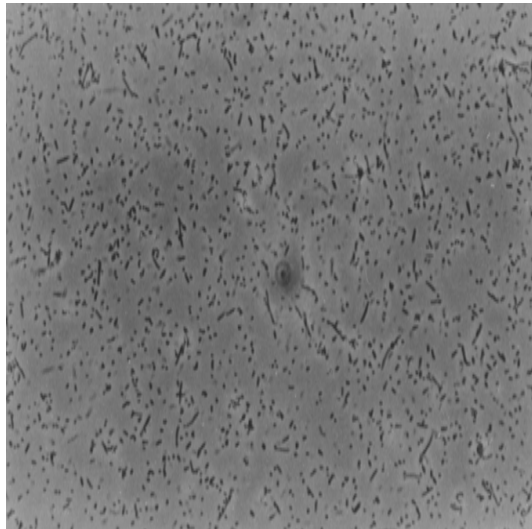
## **Therapeutics**

*-Drilling and filling*

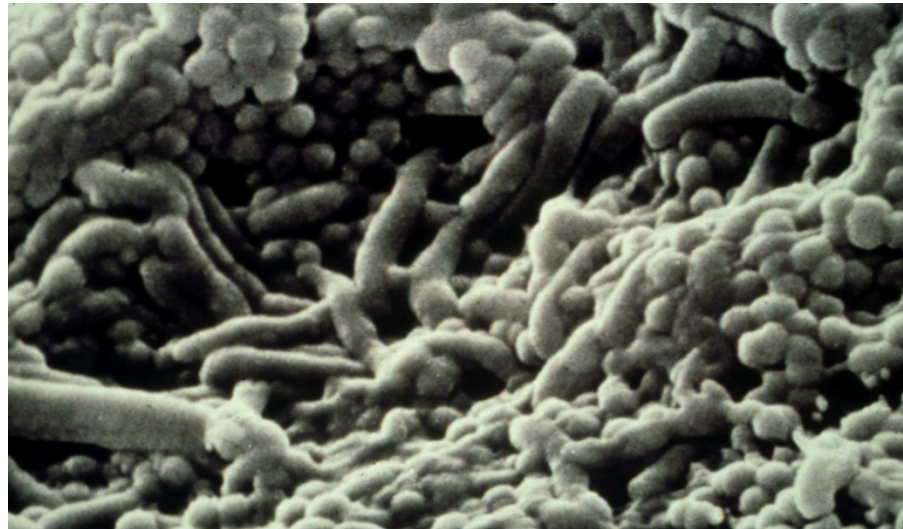
# A medical approach to dentistry



# How to detect oral pathogens in saliva or dental plaque?



Bacteria in saliva



Bacteria in plaque

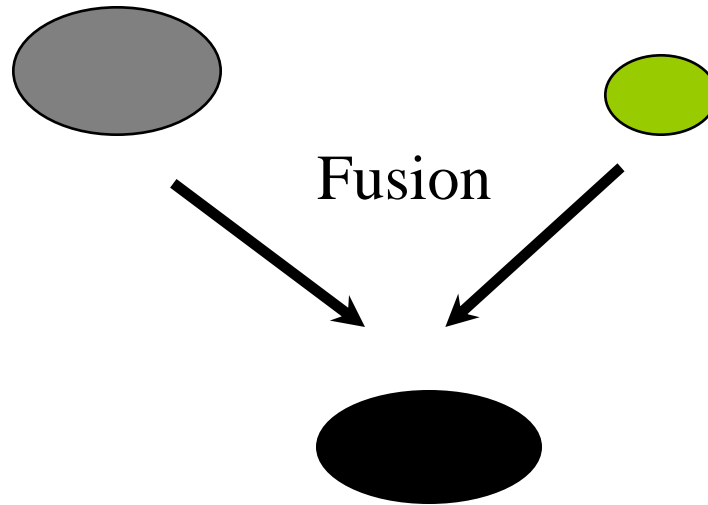
# **Biology based bacterial detection**

- **Cell based detection**
  - **Selective culture (e.g. CRT test)**
- **DNA based**
  - **Polymerase chain reaction**
  - **Southern blotting**
- **Protein based detection**
  - **Monoclonal antibody**

# Making Monoclonal Antibody

A normal B lymphocyte

A tumor cell



A hybridoma that secretes a monoclonal antibody

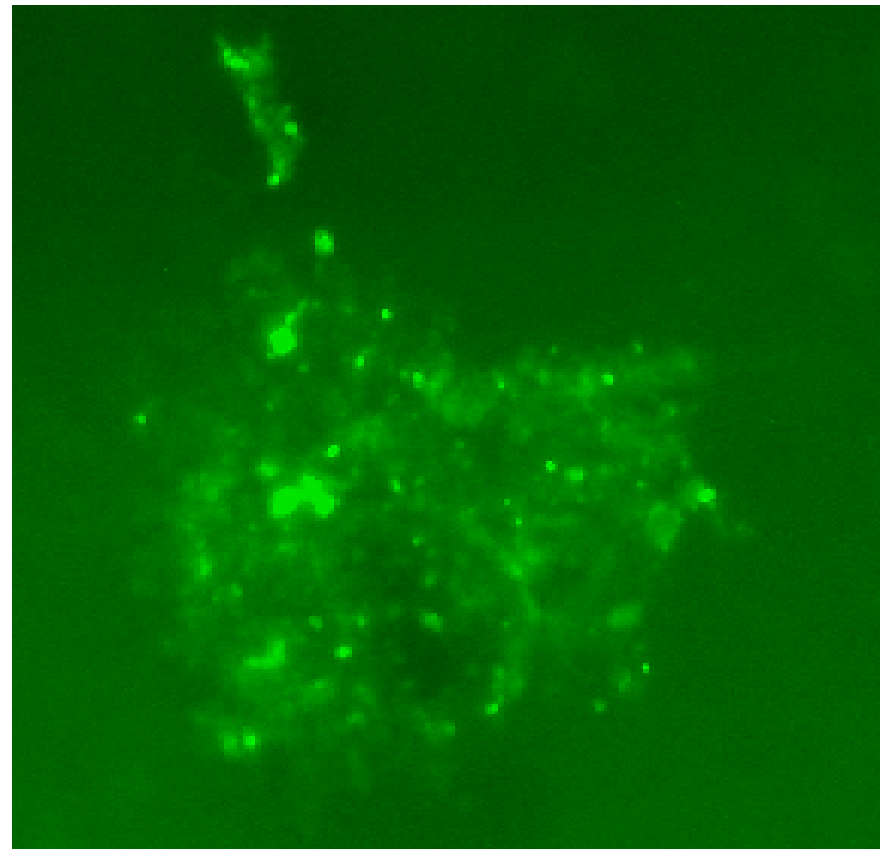
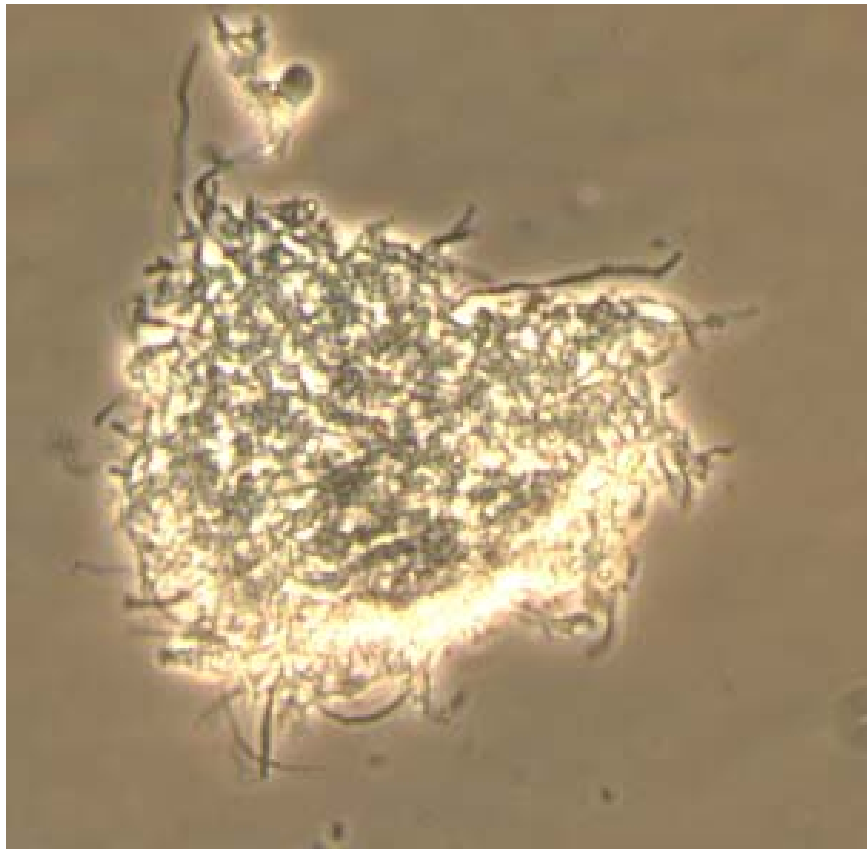
# Monoclonal Antibody-Based Bacterial Detection Techniques

- Linkage to fluorescent dyes      Fluorescence
- Linkage to color particles      Color change
- Linkage to enzymes      Color change
- Linkage to latex beads      Agglutination

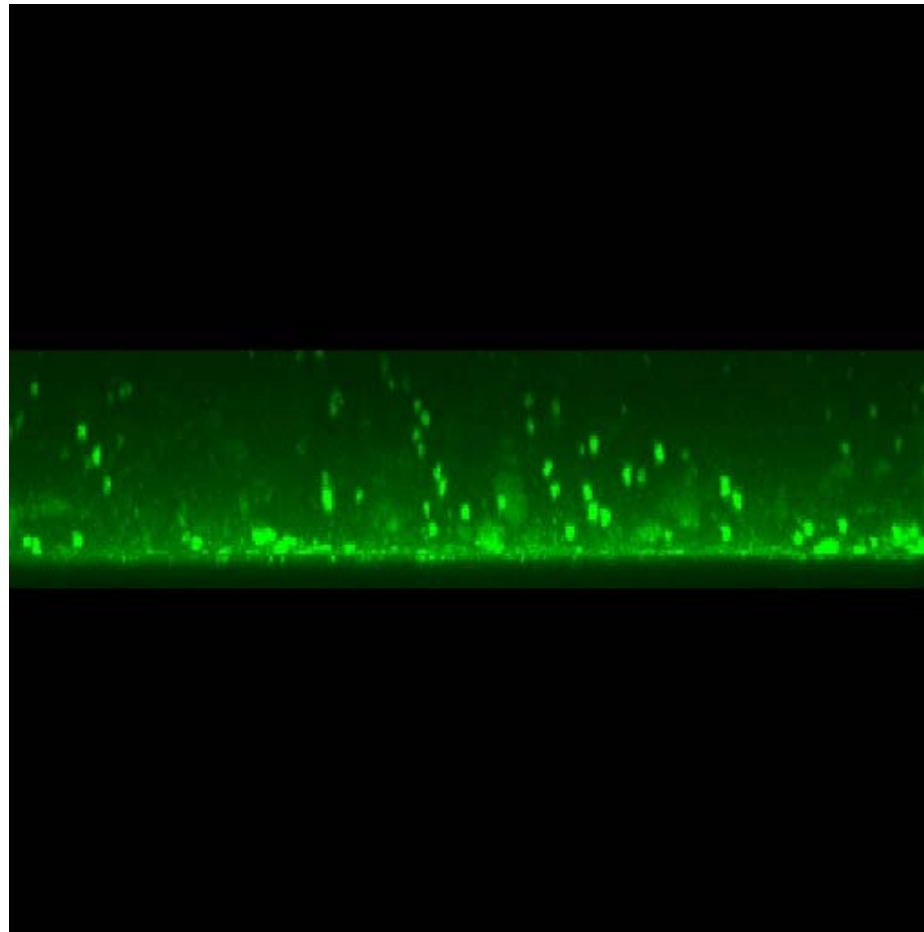
## *S. mutans*-specific monoclonal antibodies

Species	Strain name	Cross-reactivity		
		SWLA1	SWLA2	SWLA3
<i>Streptococcus mutans</i>	<b>ATCC25175</b>	+	+	+
	<b>LM7</b>	+	+	+
	<b>OMZ175</b>	+	+	+
<i>Streptococcus rattus</i>	ATCC19645	-	-	-
<i>Streptococcus gordonii</i>	ATCC10558	-	-	-
<i>Streptococcus mitis</i>	ATCC49456	-	-	-
<i>Streptococcus sobrinus</i>	ATCC33478	-	-	-
<i>Streptococcus sanguis</i>	ATCC10556	-	-	-
<i>Streptococcus anginosus</i>	ATCC33397	-	-	-
<i>Lactobacillus acidophilus</i>	ATCC4356	-	-	-
<i>Lactobacillus casei</i>	ATCC4646	-	-	-
<i>A. actinomycetemcomitans</i>	ATCC33384	-	-	-
<i>Porphyromonas gingivalis</i>	ATCC33277	-	-	-
<i>Prevotella intermedia</i>	ATCC49046	-	-	-
<i>Bacteroides forsythus</i>	ATCC43037	-	-	-
<i>Eikenella corrodens</i>	ATCC23834	-	-	-
<i>Fusobacterium nucleatum</i>	ATCC25586	-	-	-

# Detecting *S. mutans* in dental plaque with species-specific monoclonal antibody

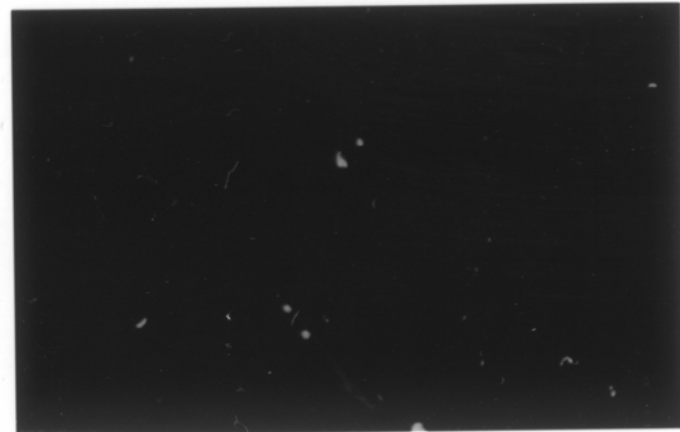
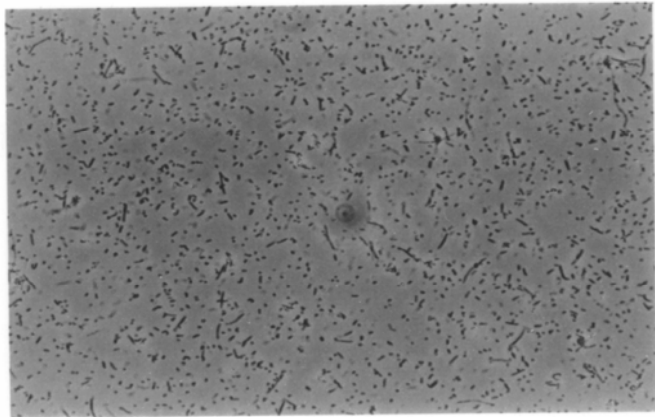


# 3D imaging of *S. mutans* in dental plaque

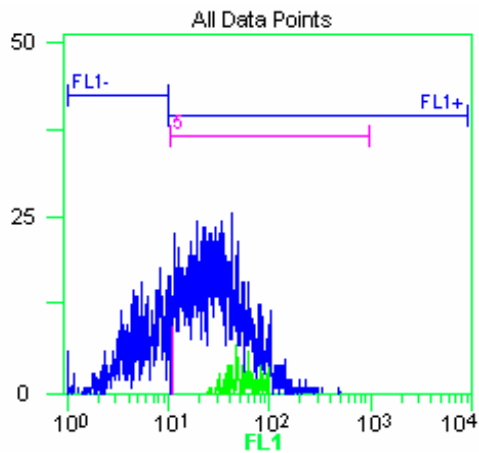
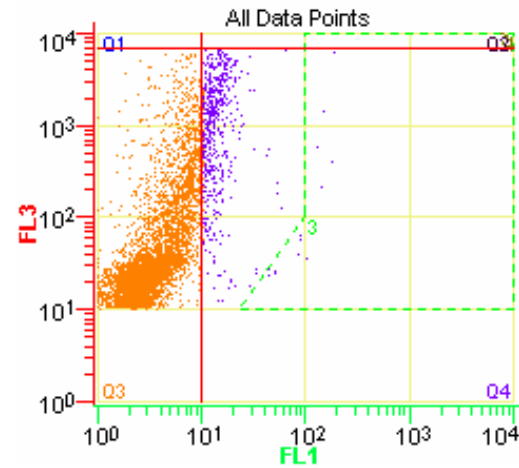
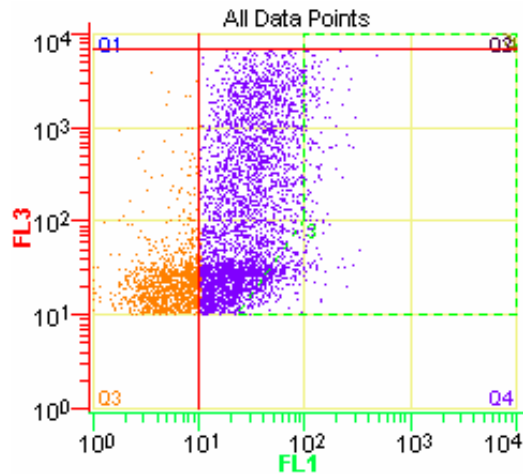


Green: *S. mutans* cells

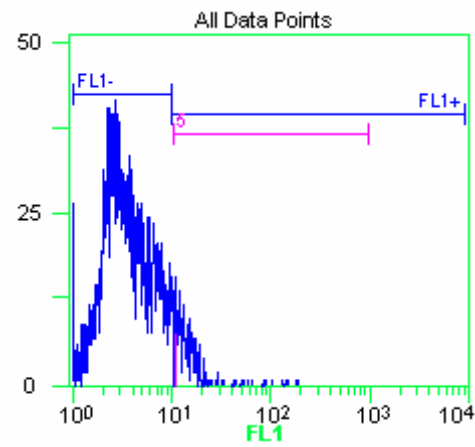
# Detection of *S. mutans* with Monoclonal Antibodies and Fluorescent Microscopy



# Saliva diagnosis

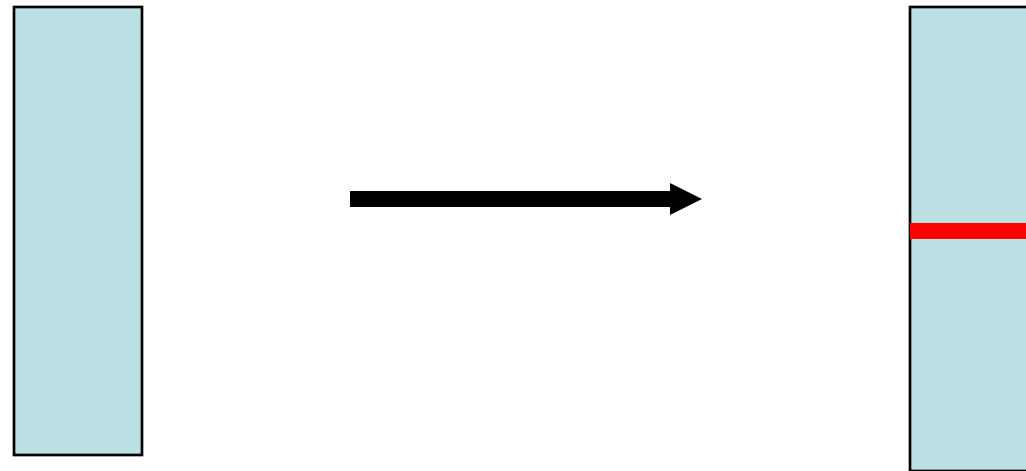


Saliva with high *S. mutans* content

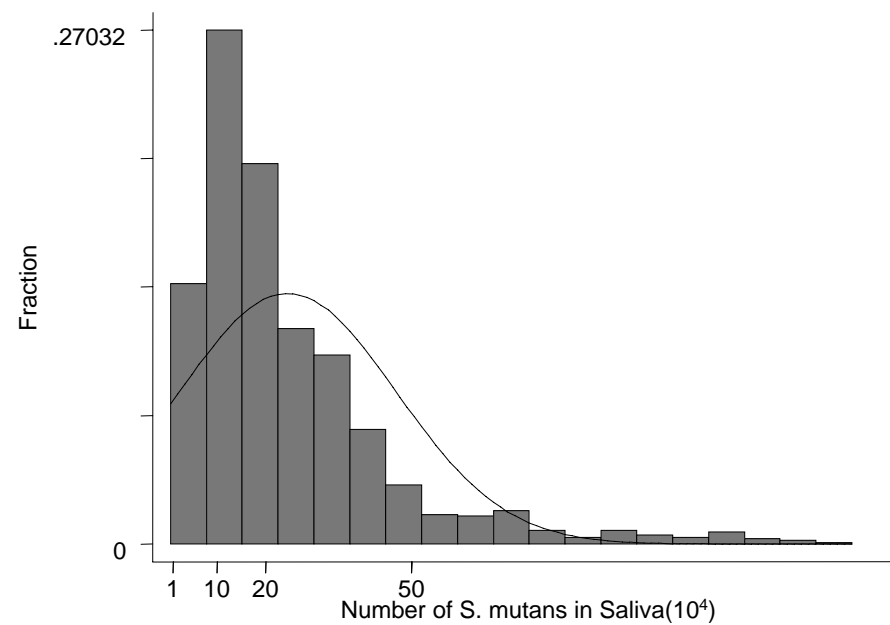


Saliva with low *S. mutans* content

# Membrane strip instant test for *S. mutans*



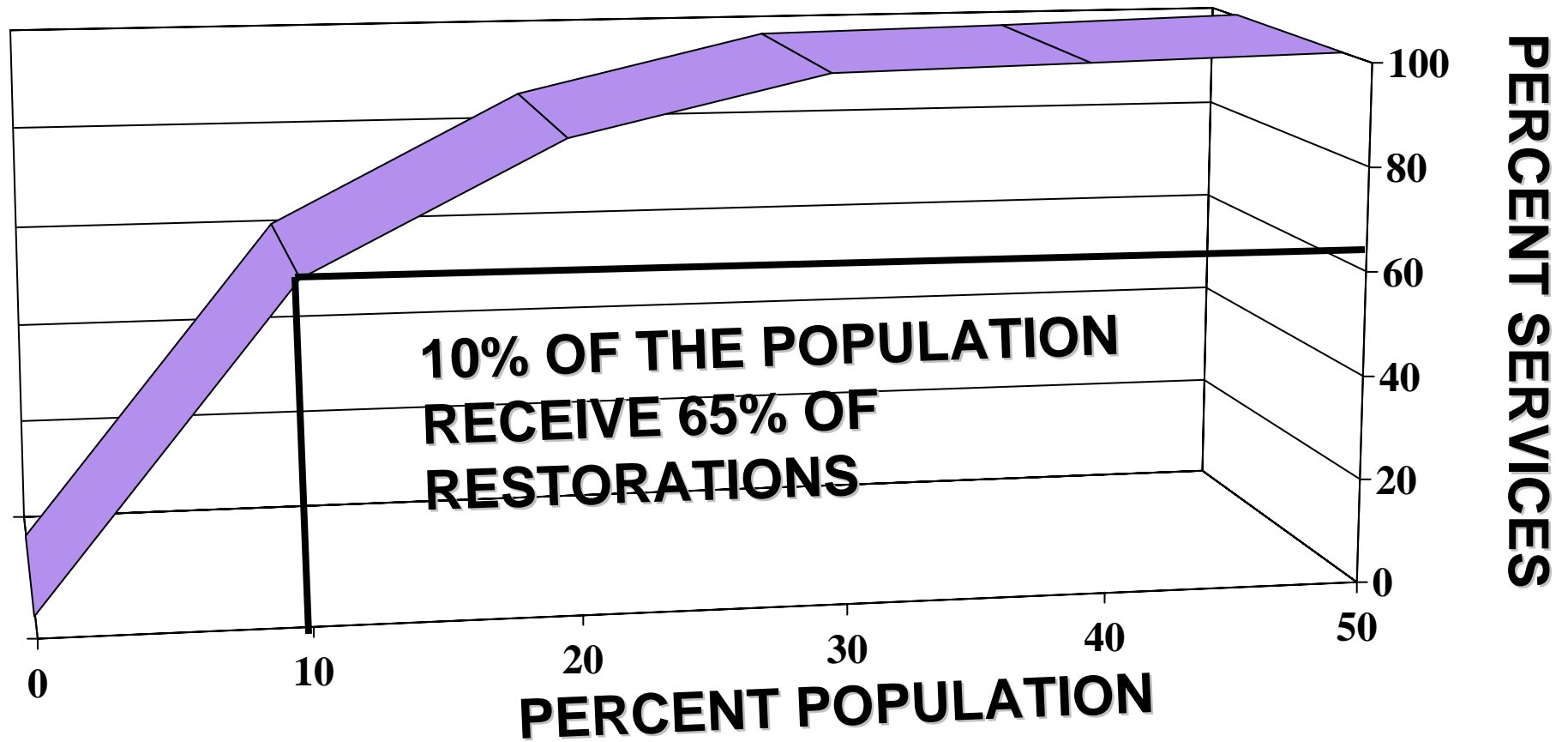
# Summary of salivary counts of *S. mutans* in >4000 human saliva samples tested



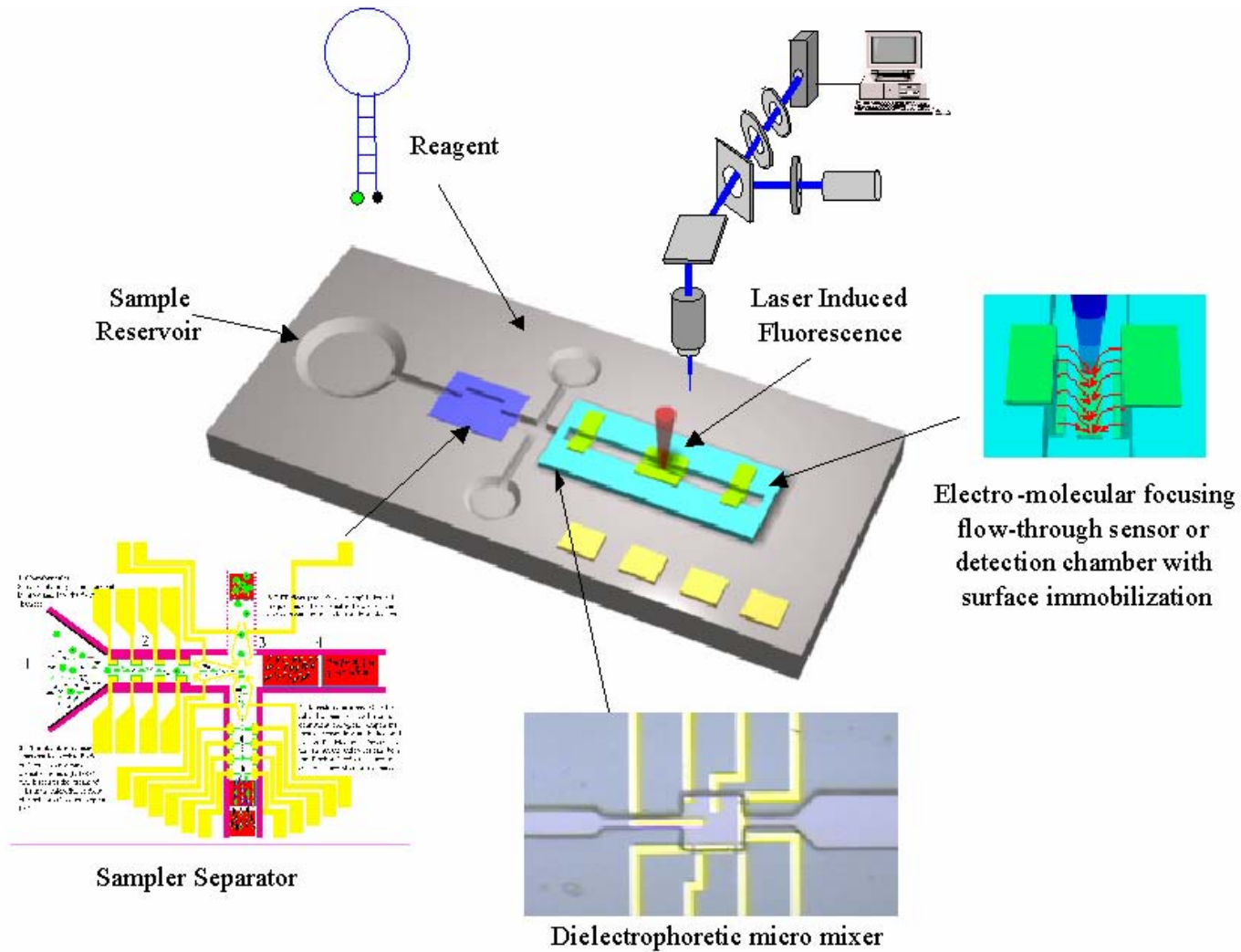
# Distribution of *S. mutans* in an USA population

- >2,000,000 *S. mutans* cells/ml ~2%
- >1,000,000 *S. mutans* cells/ml ~5%
- > 500,000 *S. mutans* cells/ml ~20%
- > 250,000 *S. mutans* cells/ml ~40%
- > 100,000 *S. mutans* cells/ml ~70%

# DISTRIBUTION OF RESTORATIVE SERVICES



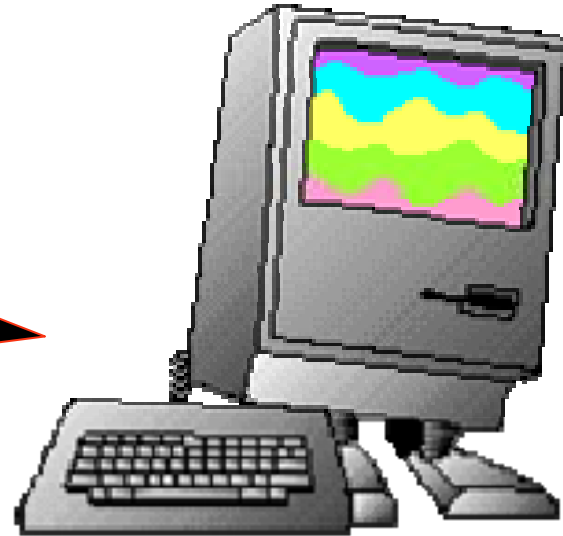
# Microelectromechanical/Nanoelectromechanical systems for detection of biomarkers in oral fluids



# Hand Held Saliva Diagnostic Device



# The Next Generation of E-Tooth

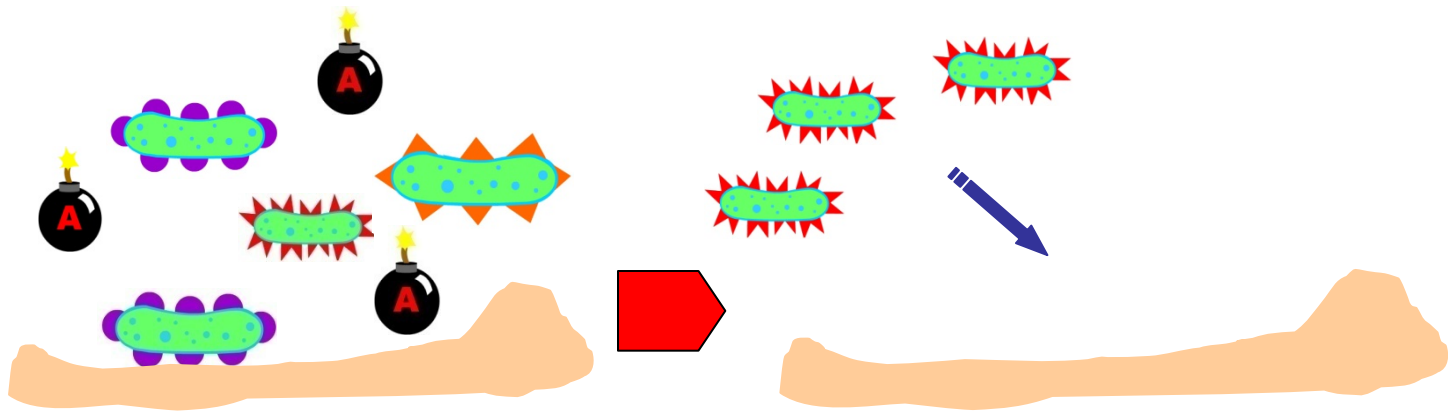


Go wireless!

# What to do when someone has high level of cariogenic bacteria?

- Mechanical removal with frequent cleaning
- High concentration of fluoride
- CHX
- Listerine
- Triclosan
- Povidone-iodine
- Bleaching agents
- Antibiotics
- Antimicrobial peptides

# Problem with current antimicrobial treatments



- Broad spectrum killing to disrupt normal microbial flora

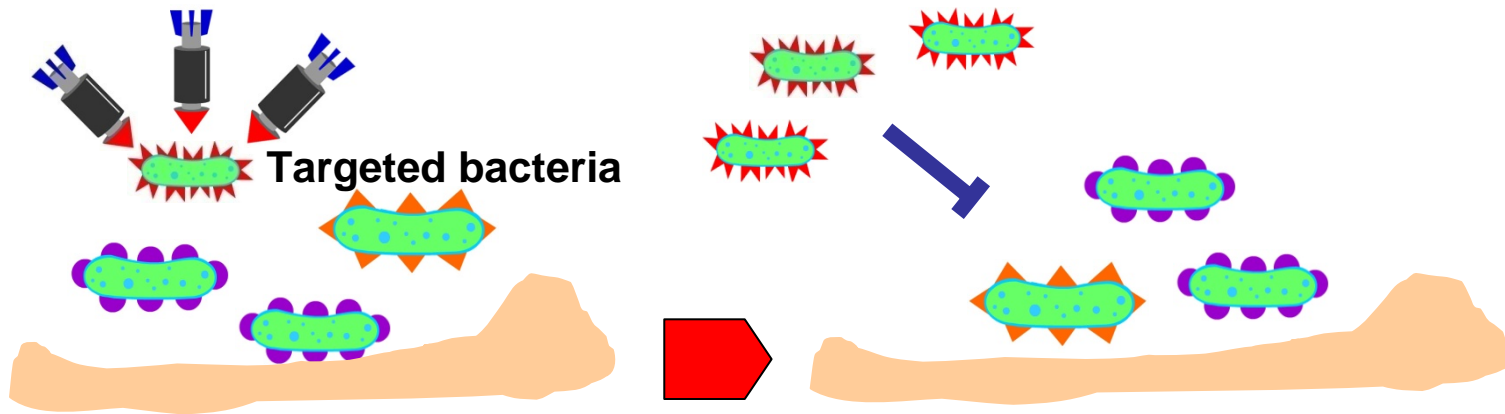
# Dental plaque formation



**What would be the better way  
to approach the problem?**

# Seeking A Better Solution

## A targeted approach



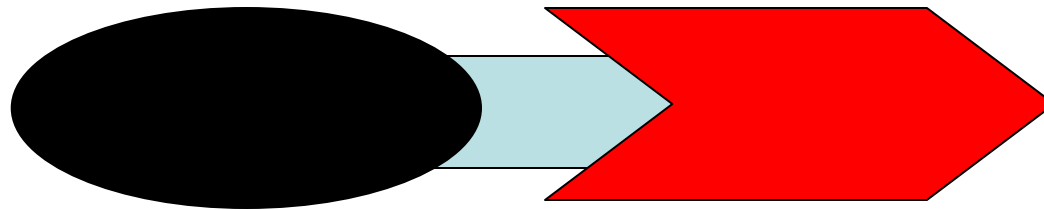
# How to achieve a targeted therapy?

- Vaccination (active or passive)
- Replacement with non-acidic *S. mutans*
- Enhancement of base-producing bacteria
- Targeted phage therapy

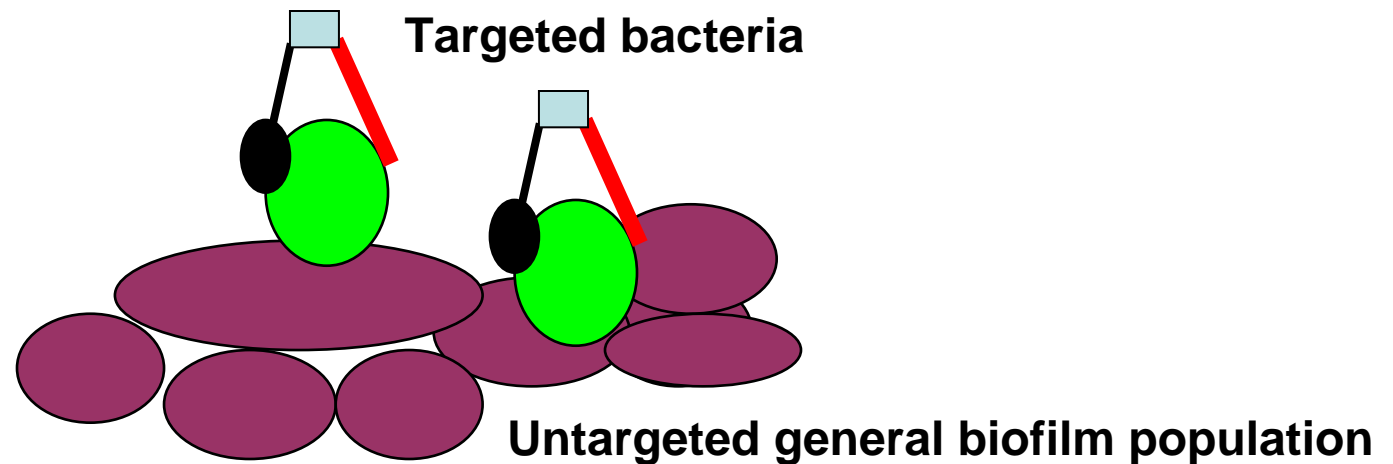
## The new technologies developed in my lab

- Smart bombs
- Medicinal herbs

# The New Technology Platform at C3 Jian Specifically Targeted Anti-Microbial Peptide **STAMP™**

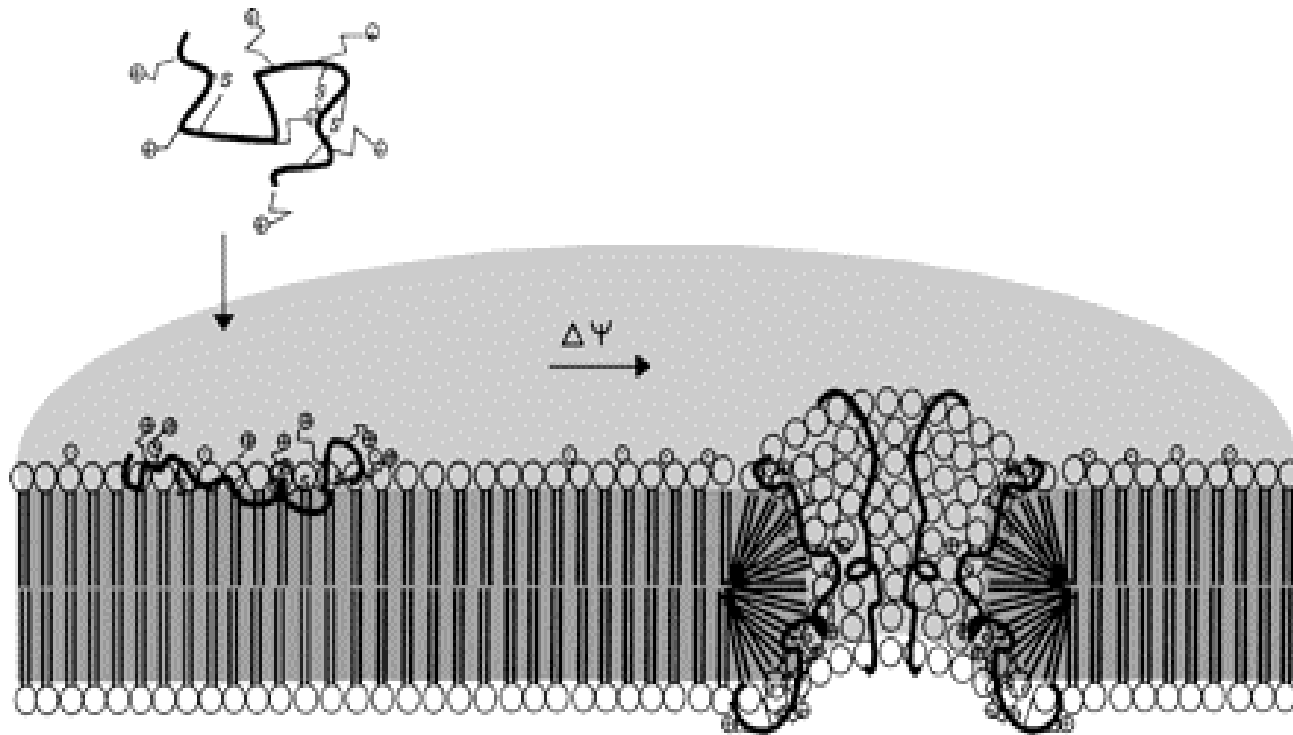


Antimicrobial peptide \* Linker peptide \* Targeting peptides

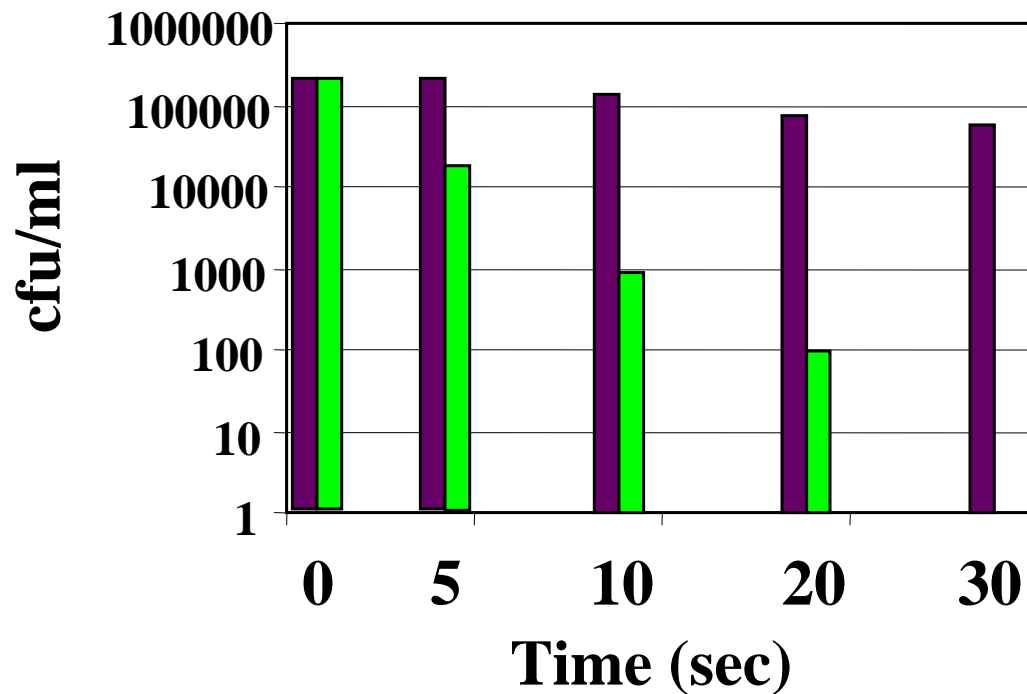


# The killing molecule: antimicrobial peptide

Mode of Action of peptide antibiotic on  
gram-positive bacteria  
(pore formation)



# A smart bomb (30 a.a) in action



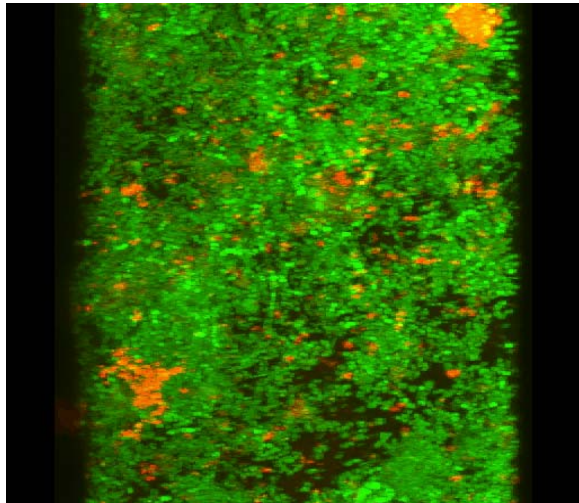
*S. mutans*



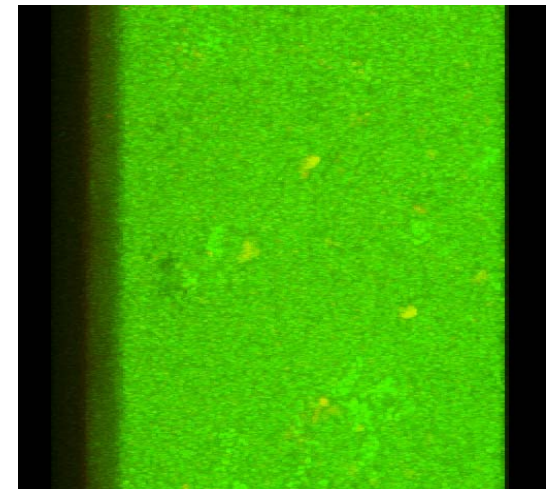
*S. sanguis*

Selective killing of *S. mutans* over *S. sanguis*

# Conversion of a bad plaque to a good plaque



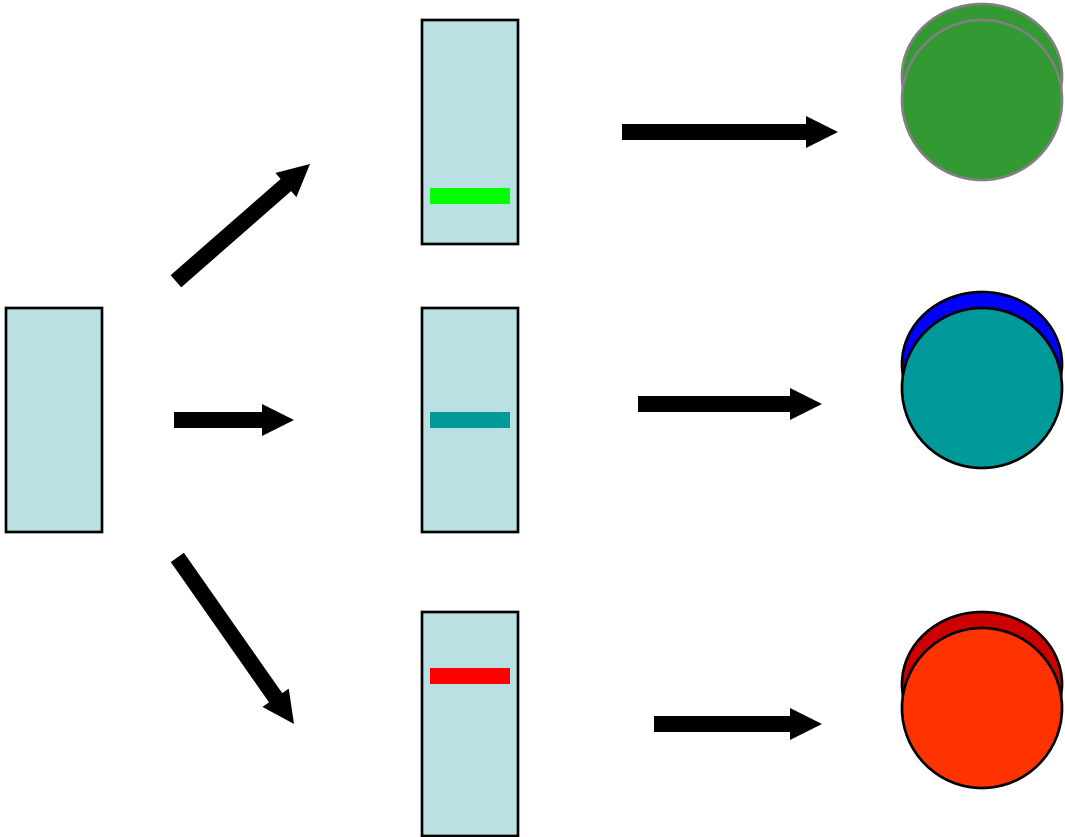
Smart bombs  
against *S. mutans*



An antibiotic-probiotic approach



# A Medical Approach to Dentistry



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