

Immune System Basics

Sore Joints and Bad Breath: What is Going on?



Felipe Andrade, M.D., Ph.D.

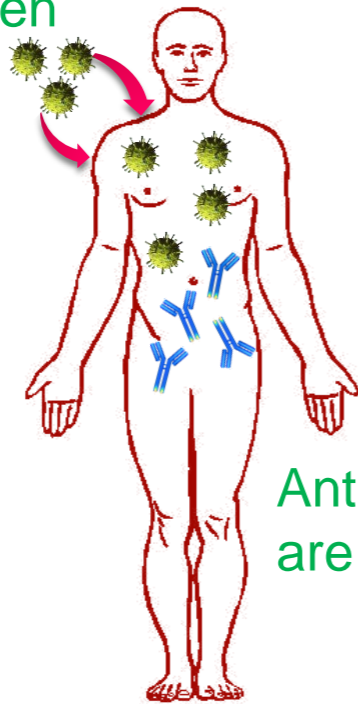
Associate Professor of Medicine



Autoimmune Diseases: When your body turns on you

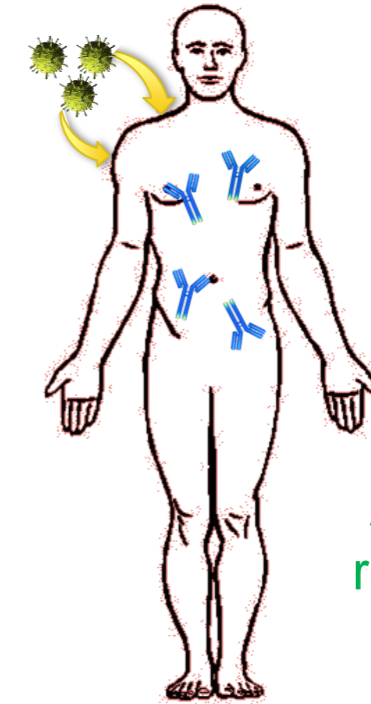
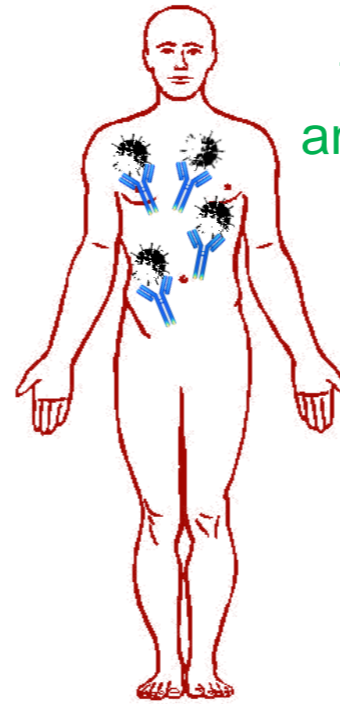
Normal
Immune
Response

Foreign
antigen



Antibodies
are made

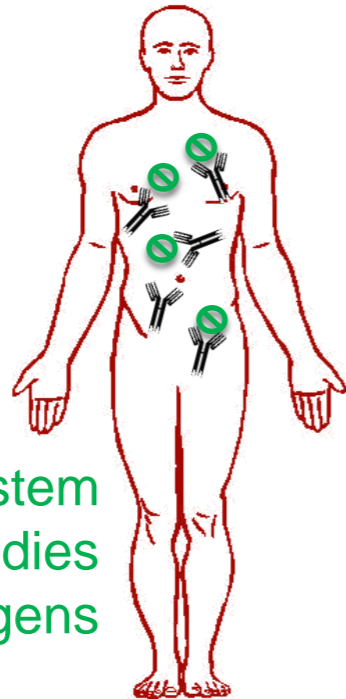
Antibodies
clear
foreign
antigens



Antibodies
remain and
protect

Autoimmune
Disease

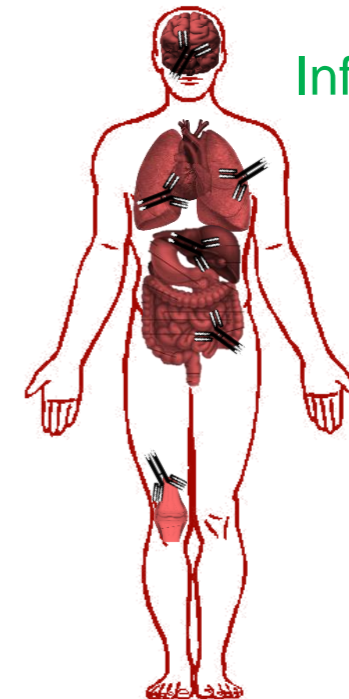
Immune system
forms antibodies
to self-antigens



Autoantibodies
attack different
organs



Inflammation
and tissue
damage



Systemic autoimmune rheumatic diseases

Systemic Lupus Erythematosus



Rheumatoid Arthritis



Scleroderma



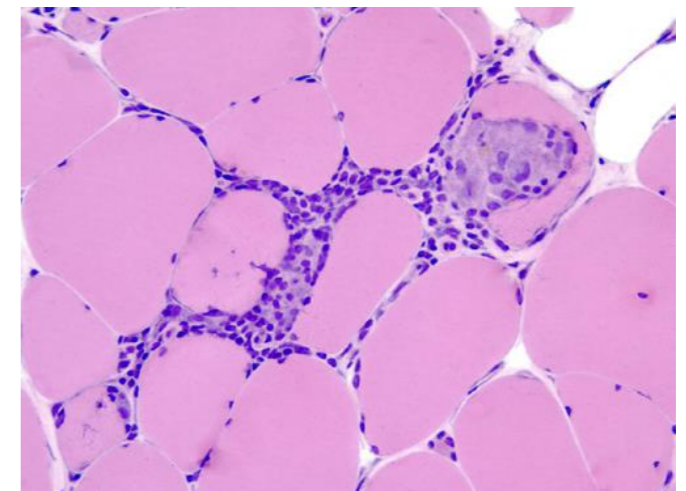
Sjögren's Syndrome



Vasculitis



Myositis

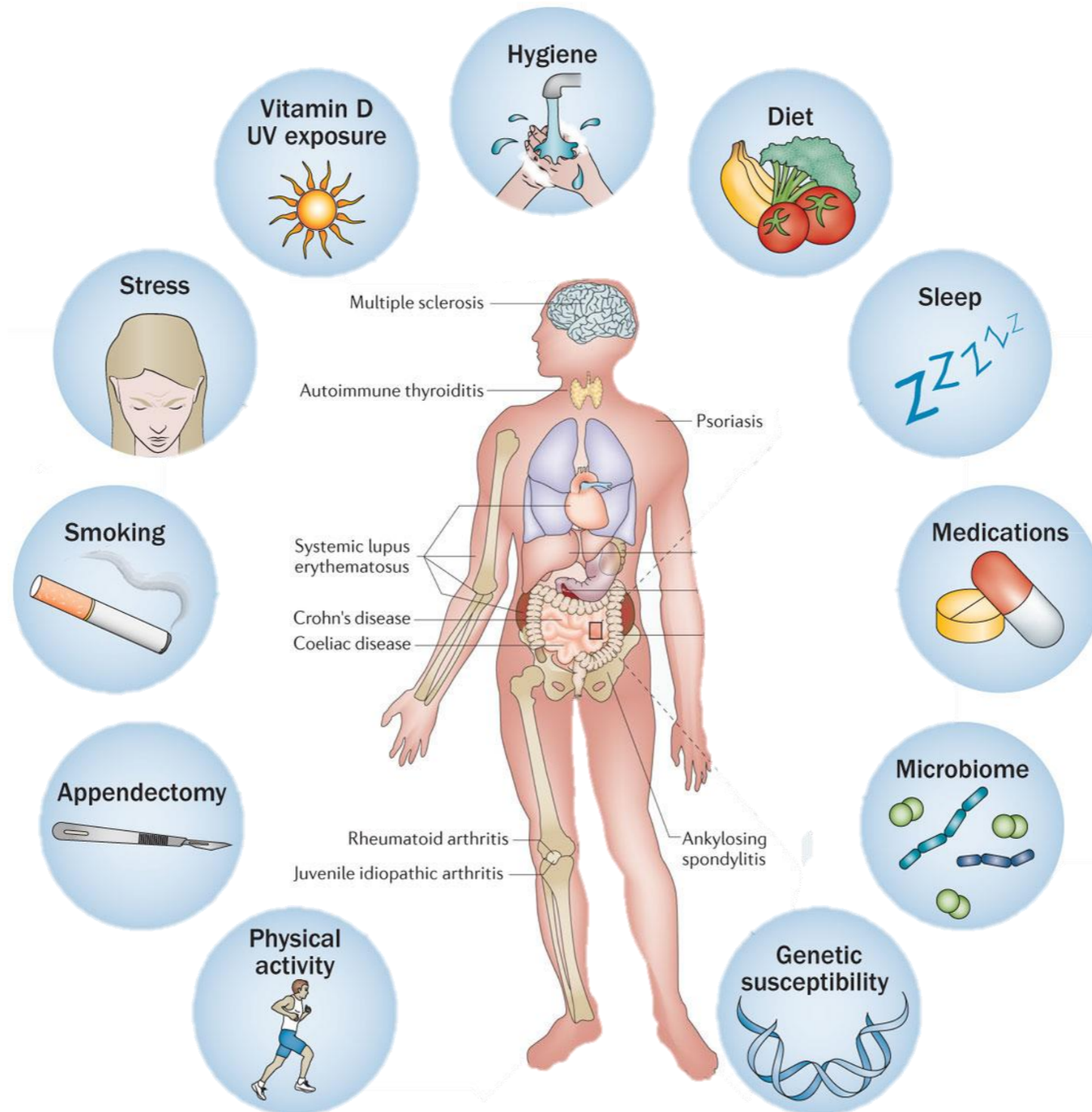


Rheumatoid Arthritis

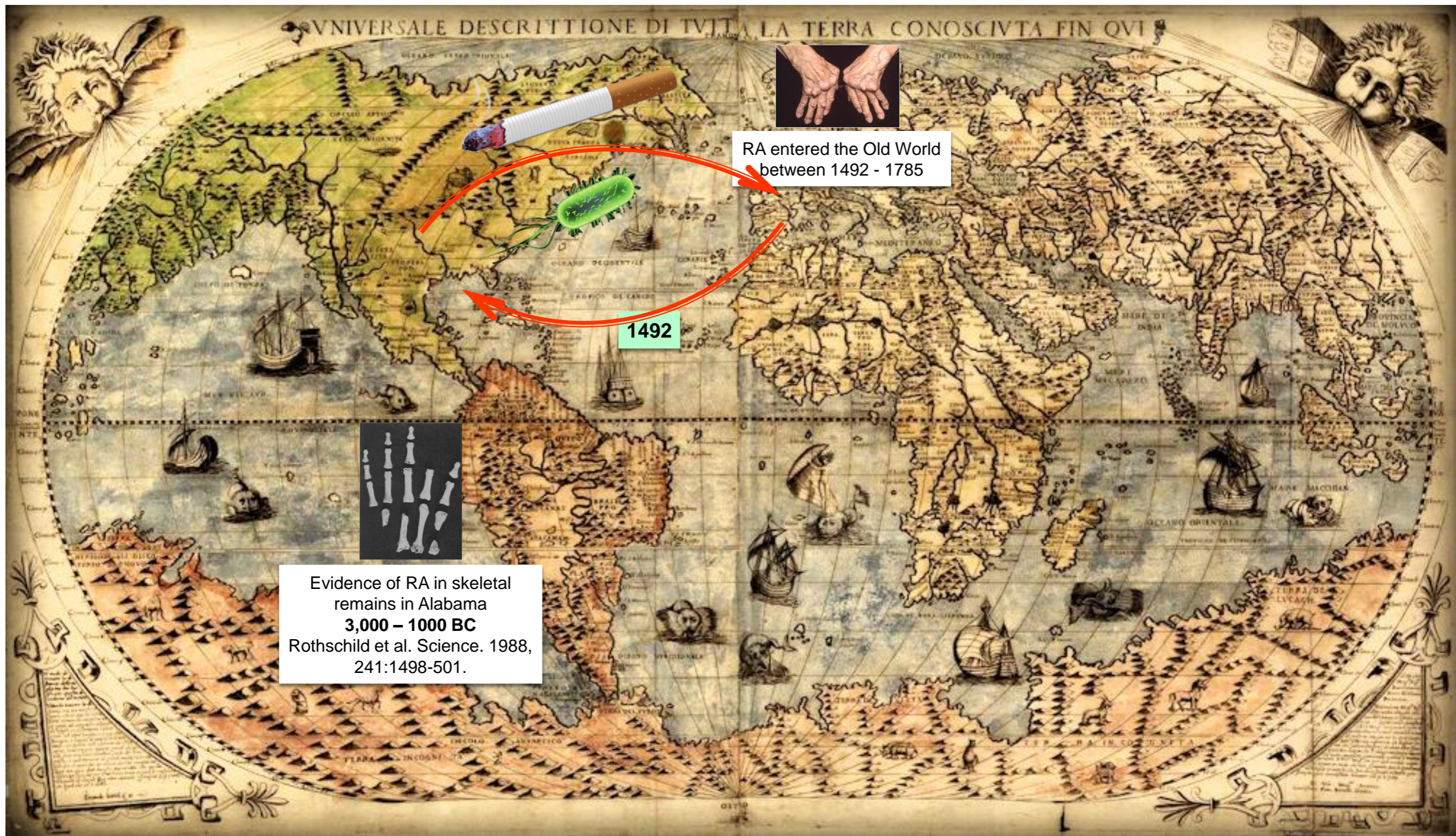
- Rheumatoid arthritis (RA) affects 1% of the adult population worldwide.
- About 1.3 million Americans have RA, mainly women over 40.
- RA is associated with increased mortality.



Rheumatoid Arthritis: The interaction between genetics, immunology and environment



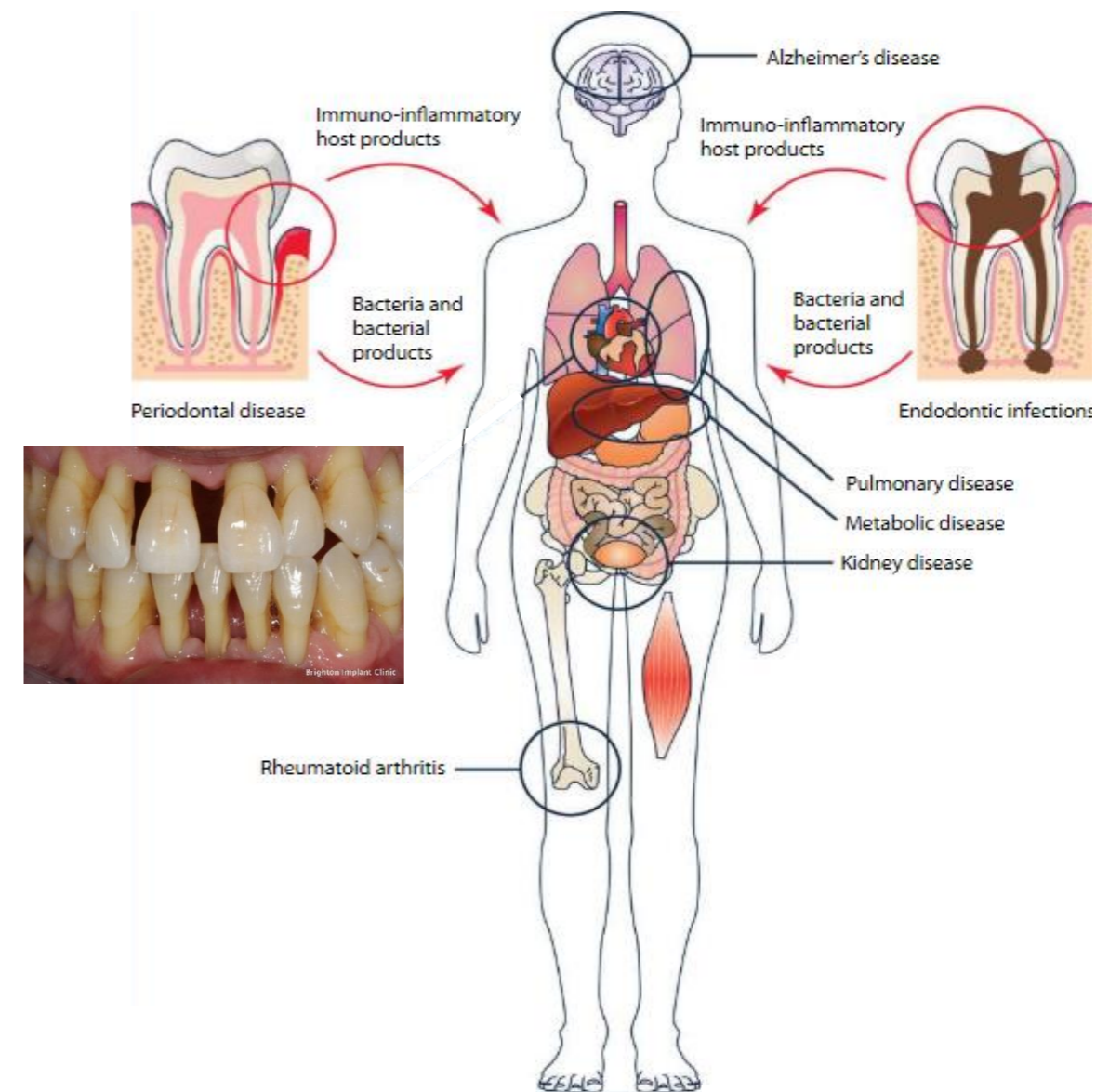
Rheumatoid Arthritis: An infectious disease from the New World?



Rheumatoid Arthritis and Periodontal Disease

“Infection from carious teeth has been considered as one of the causes of rheumatoid arthritis.”

- *J. Lambert, 1908*



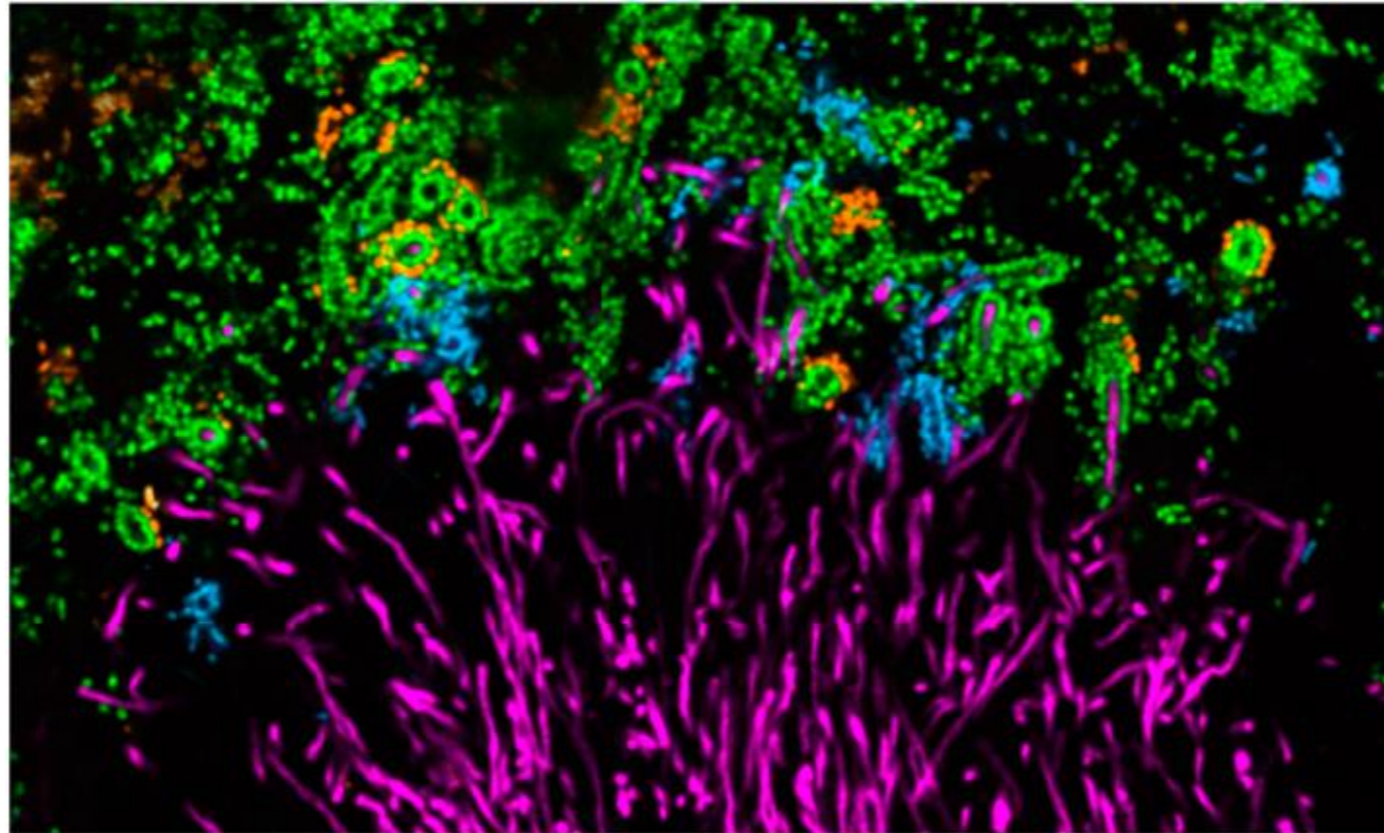
Dunbar LL. JAMA 1895, 24:75-77

Hunter W. Br Med J 1900, 2:215-216

Lambert J. Bulletin of the Committee for the Study of Special Diseases 1908, 2:83-94

Kumar PS. J Physiol 2017, 595:465-476

Over 1000 different bacteria have been detected in the oral cavity.



Bacteria in dental plaque

How to identify those bacteria associated with RA?

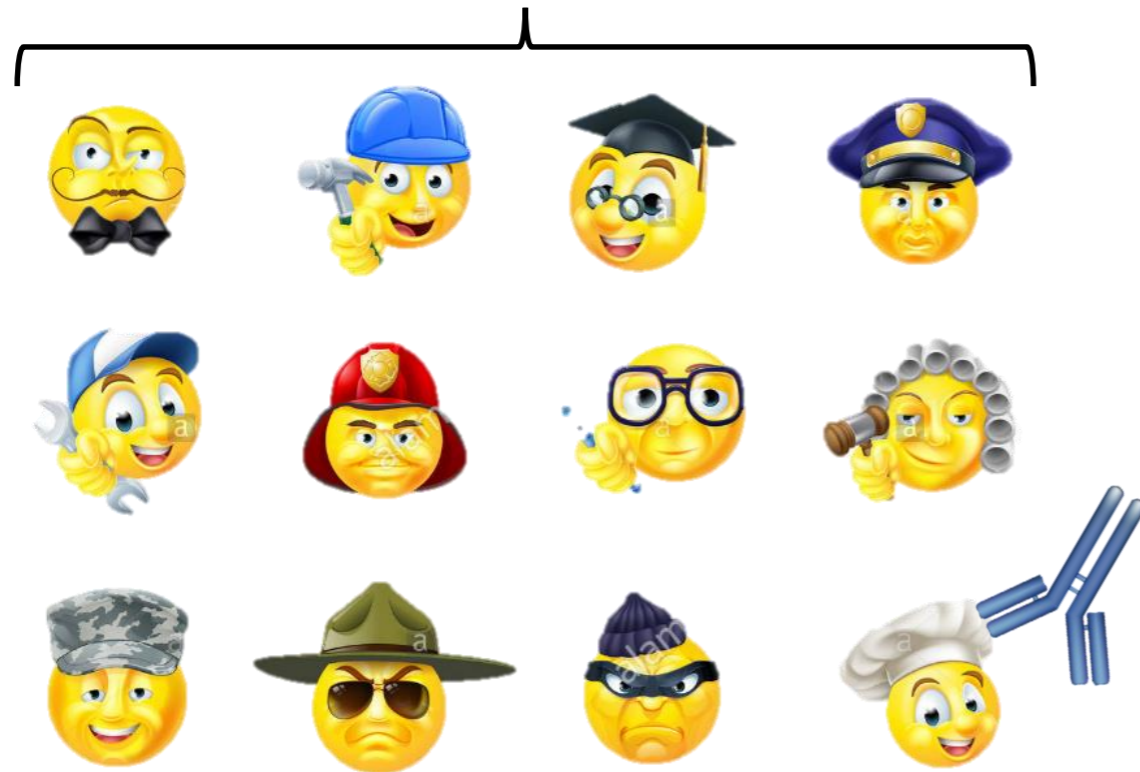
Ge et al. PLoS ONE 2013,8:e65520

Peterson et al. PLoS ONE 2013,8:e58487

Mark Welch et al. Proc Natl Acad Sci U S A. 2016,113:E791-800

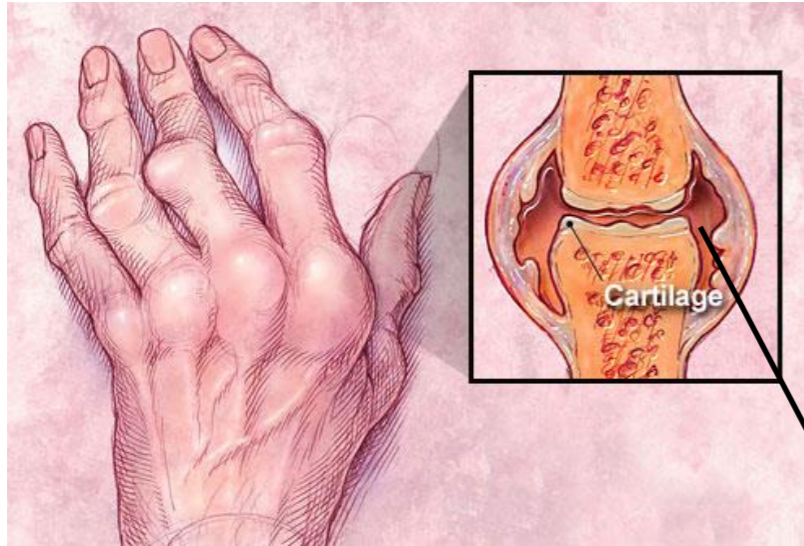
Patients with RA have antibodies to citrullinated proteins

Proteins normally “dress in different costumes” (modifications) to diversify their function

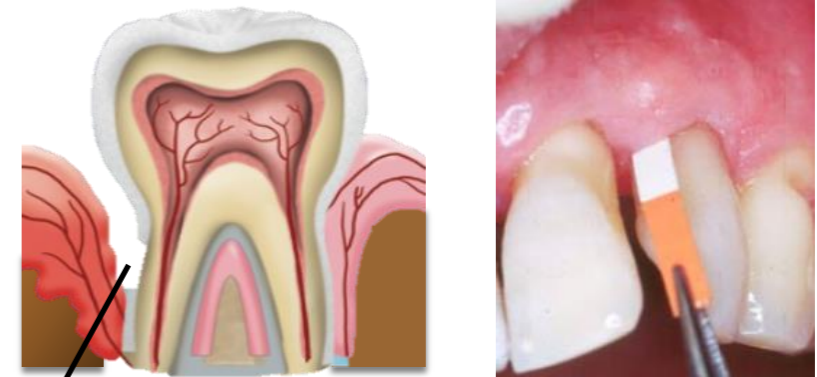


Citrullination is a modification (“a costume”) in proteins that is attacked by antibodies in RA

Periodontitis mirrors citrullination in the RA joint

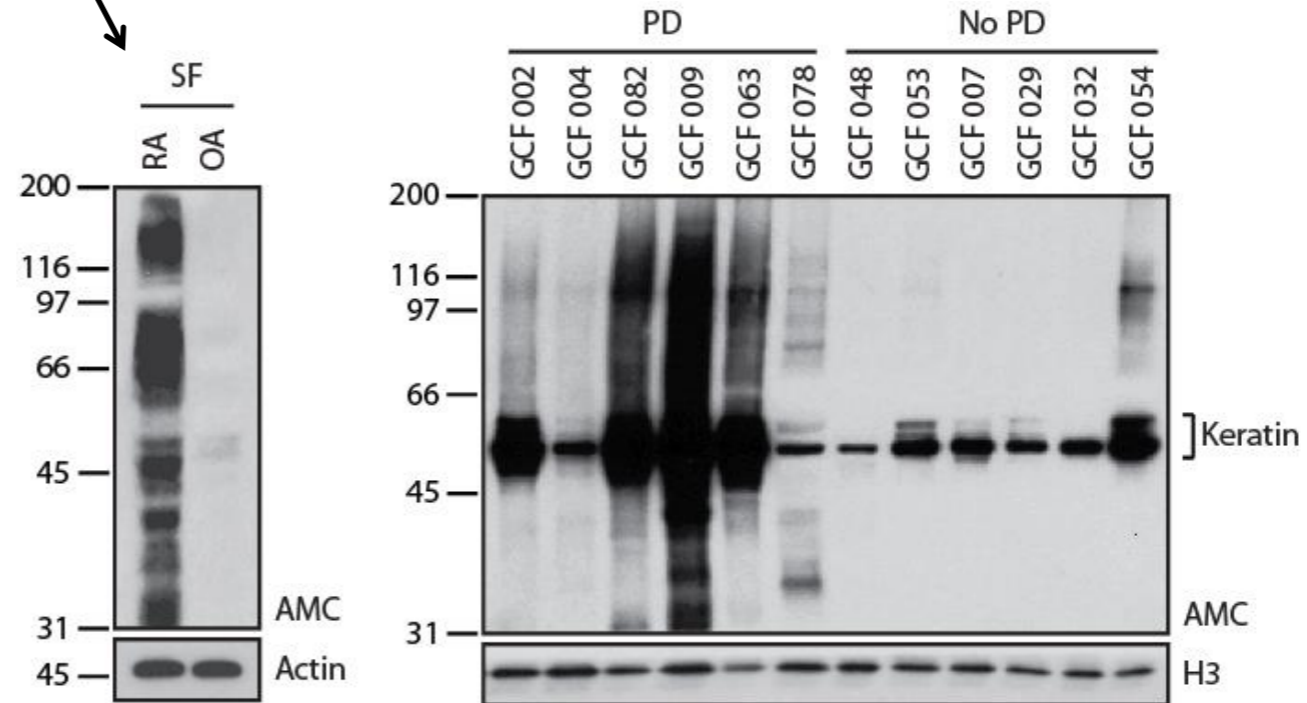


Synovial Fluid

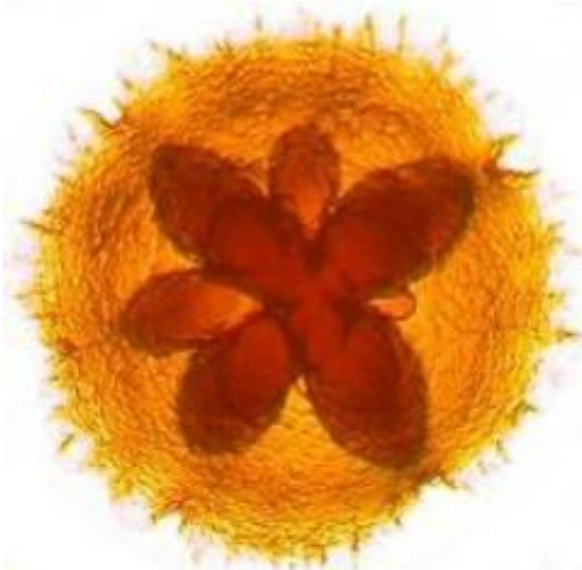


Gingival Crevicular Fluid

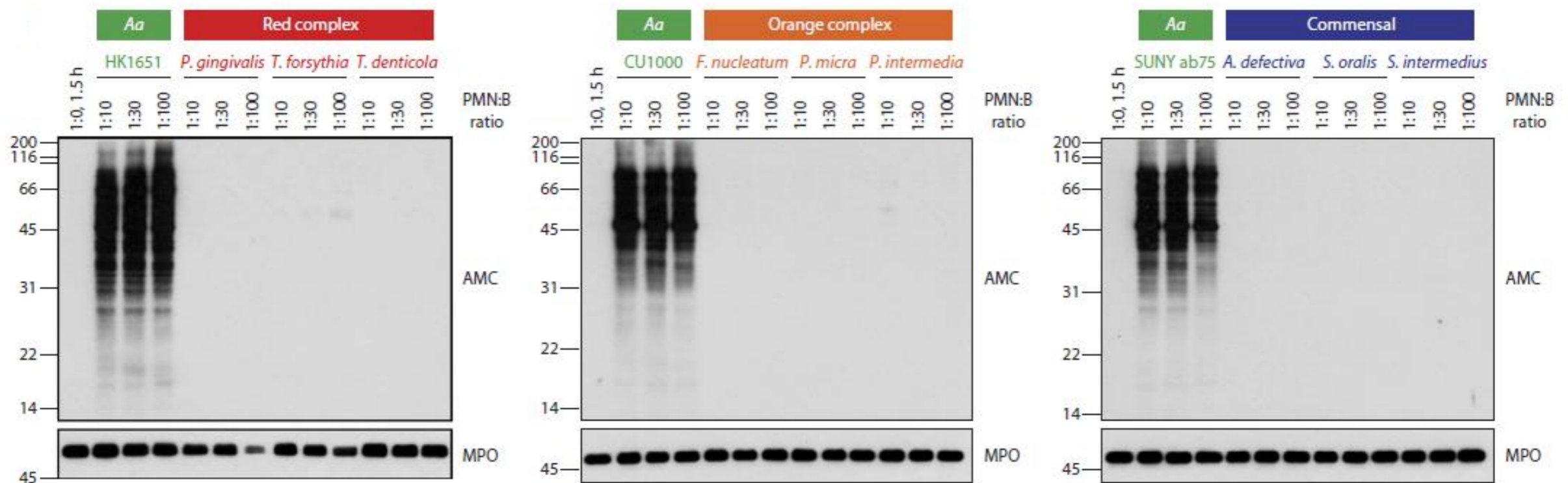
Citrullination is abundant both in the RA joint and periodontal disease



What bacteria may be the cause of citrullination in periodontal disease?

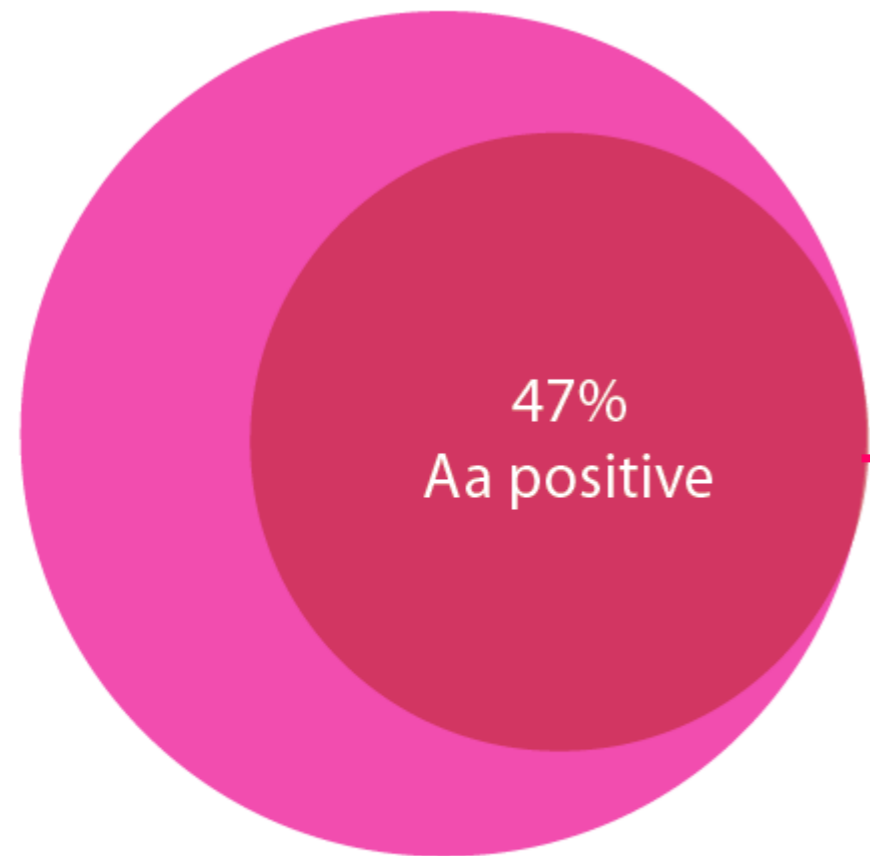


Aggregatibacter actinomycetemcomitans (Aa)



Almost half of patients with RA had evidence of infection by *Aa*

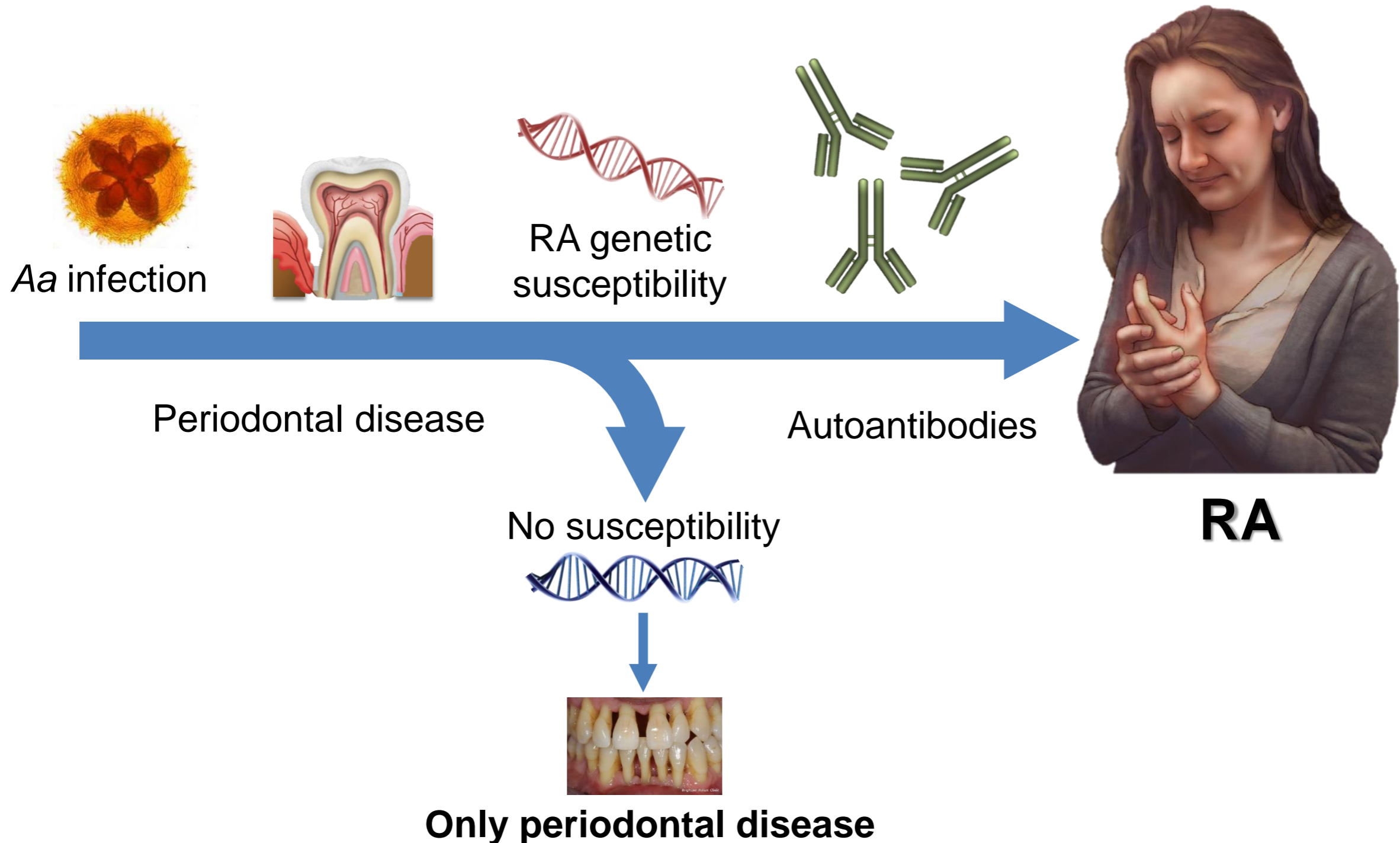
196 patients with RA



92/196; 47%

More than 90% of *Aa* positive patients are genetically susceptible to RA and are positive for autoantibodies

Aa is a candidate bacterial trigger of autoimmunity in RA



Acknowledgements

Johns Hopkins University (Andrade's Lab)

- Maximilian F. König
- Kevon Sampson

Johns Hopkins University

- Antony Rosen

Columbia University Medical Center

- Jon Giles
- Joan Bathon

Harvard Medical School

- Peter Nigrovic

Aarhus University, Denmark

- Jesper Reinholdt

NIH

- Niki M. Moutsopoulos
- Loreto Abusleme
- Robert J. Palmer

Stanford University School of Medicine

- Jeremy Sokolove

Forsyth Institute

- Ricardo P. Teles

Funding

- The Donald B. and Dorothy L. Stabler Foundation
- Jerome L. Greene Foundation
- NIH