PETRAGEN

novel therapeutics for periodontal disease

LIFE SCIENCE STARTUP & DOMAIN EXPERTISE

Petragen was founded Aug. 2020; Closed on >$1m of seed capital in Mar. 2021

Based on biology developed by Dr. Braddock; also basis for the spinout Inozyme

Demetrios Braddock, MD, PhD

- Associate Professor of Pathology, Yale University
- Scientific Founder, Inozyme (NASDAQ: INZY)
- Founder & CSO, Petragen, Inc.
- Expert in ENPP1 biology (our target)

David Kolb, MBA

- 10+ yrs life science investment banking; 3 yrs equity research
- 12 yrs as life science entrepreneur and executive
- Founder of 3 previous university spinouts (2 exited; 1 active)
- Founder & CEO, Petragen, Inc.

Martha Somerman, DDS, PhD

- Former Director of the National Institute of Dental and Craniofacial Research (NIDCR) at NIH
- Chief of the Laboratory of Oral Connective Tissue Biology at the National Institute of Arthritis and Musculoskeletal and Skin Diseases
- Co-inventor on Petragen IP

Enrique De La Cruz, PhD

- Professor and Chair of Molecular Biophysics and Biochemistry; Head, Branford College
- Co-inventor on Petragen IP

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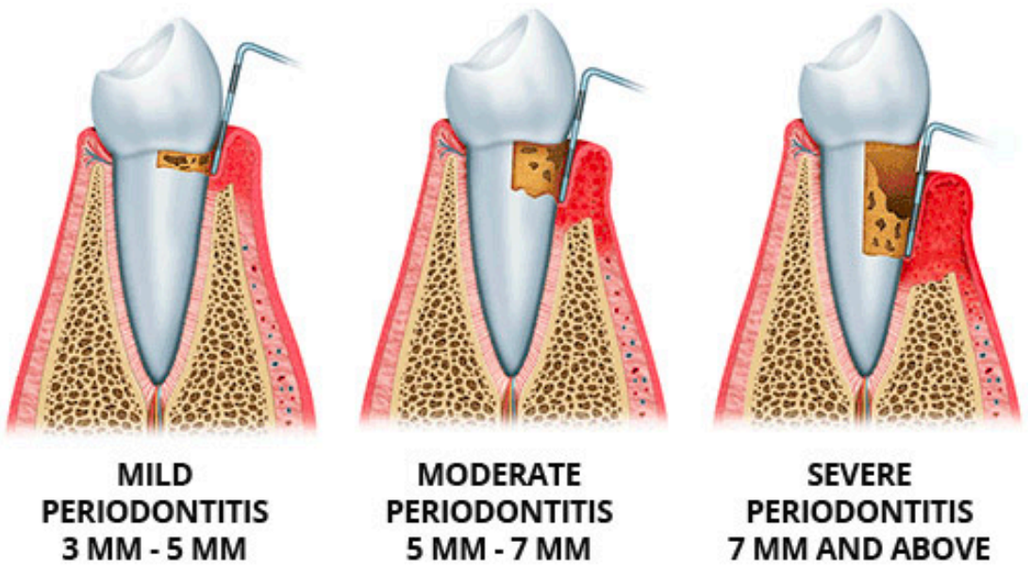
WHAT PROBLEM ARE WE TRYING TO SOLVE?

PERIODONTAL DISEASE: NOT SEXY BUT STILL A BIG PROBLEM

The Disease



26.8 million
≥2 tooth/pt

7.6 million
≥1 tooth/pt

$5 Billion Est. Opportunity In the U.S. Alone

Standard of Care

Procedure: Scaling & Root Planing (SRP)
Cost: ~$370; Benefit: ~1mm

Pocket depth = Clinical endpoints

Arestin® minocycline HCl 1mg Microspheres

Therapeutic: Arestin® (minocycline)
Cost: ~$87/tooth; Benefit: ~0.3mm

Lack of care can lead to implants ($10K+), nutritional issues and other diseases.

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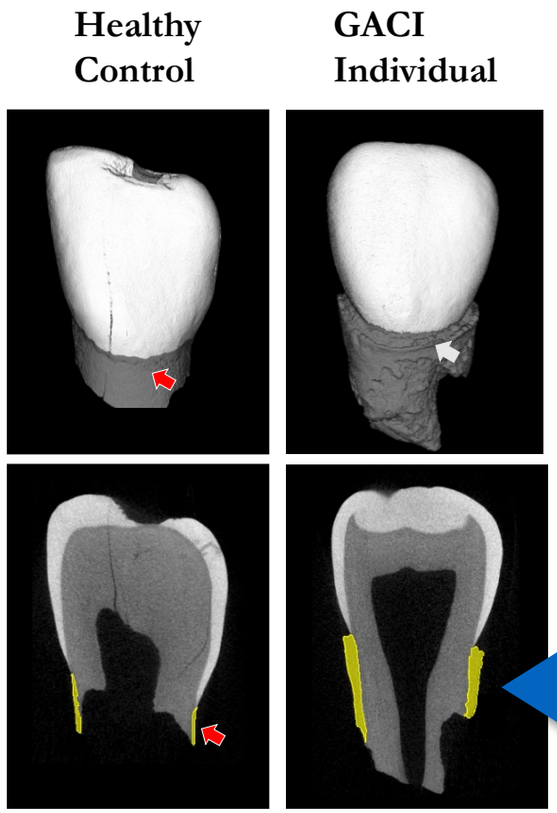
EXTENDING HUMAN PROOF OF CONCEPT

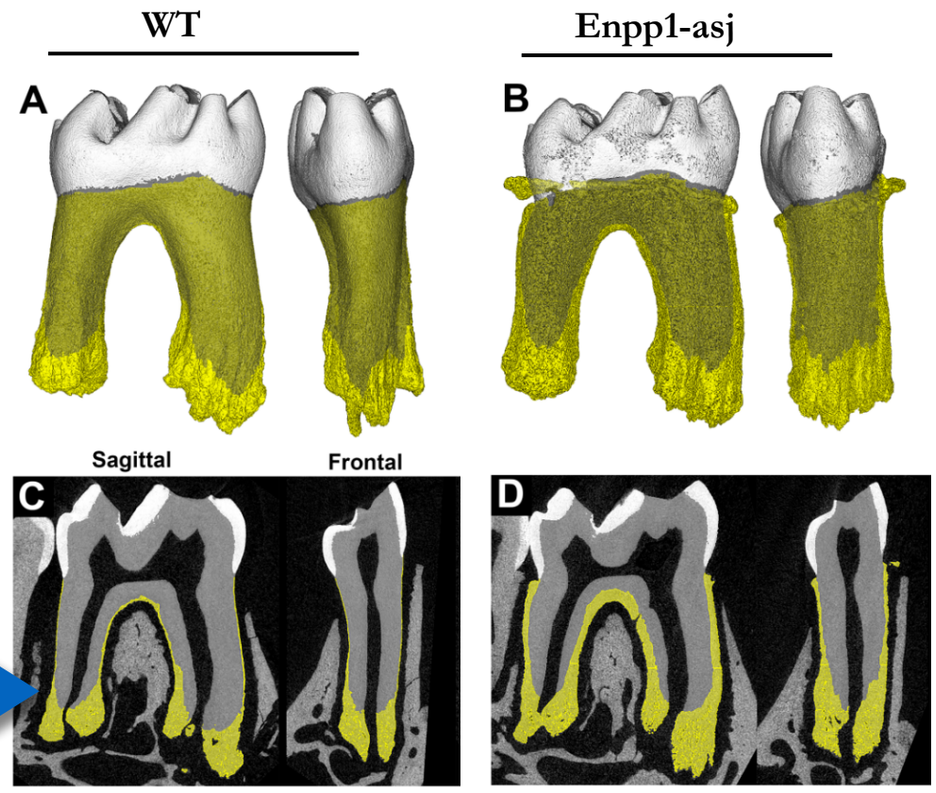
HUMAN PROOF OF CONCEPT
HUMAN



Observed cementum build-up in ENPP1 mutant patients

cementum

MURINE VALIDATION OF TARGET
Mouse Model



Missense Mutation of *Enpp1* gene leads to severe osteoarthritis but also an observable buildup of cementum

asj = ages with stiffening joints

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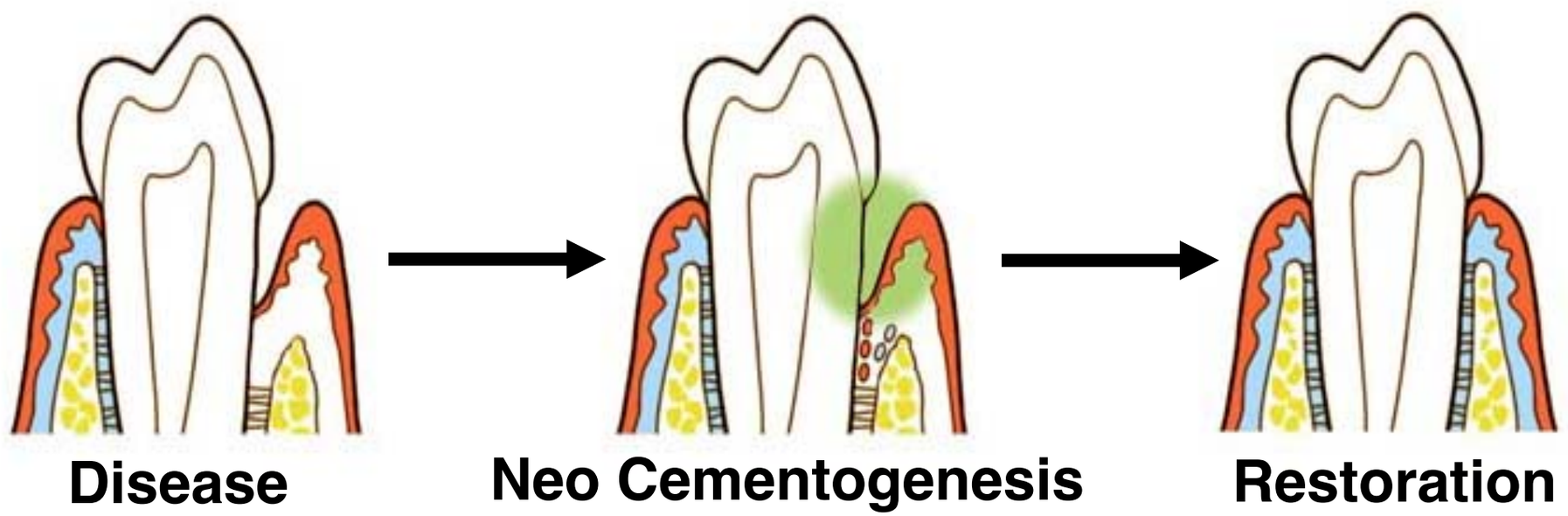
SO WHAT'S THE THERAPEUTIC STRATEGY?

Replicate the known ENPP1 inhibition phenotype LOCALLY . . .
. . . and drive neocementogenesis in the periodontal pocket



We expect that by avoiding systemic distribution and by using a micro-dose of inhibitor we should avoid any systemic toxicities

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IN A NUTSHELL (WHAT TO REMEMBER)

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- ✓ Human proof of concept
- ✓ Known inhibitors in hand; optimization ongoing
- ✓ IP portfolio covers (current/in process) method of use, composition of matter, formulation and dosing
- ✓ Standard of care not getting it done
- ✓ $5B U.S. opportunity (+ animal health)
- ✓ Known regulatory path and endpoints
- ✓ Limited capital needs; value inflection points near

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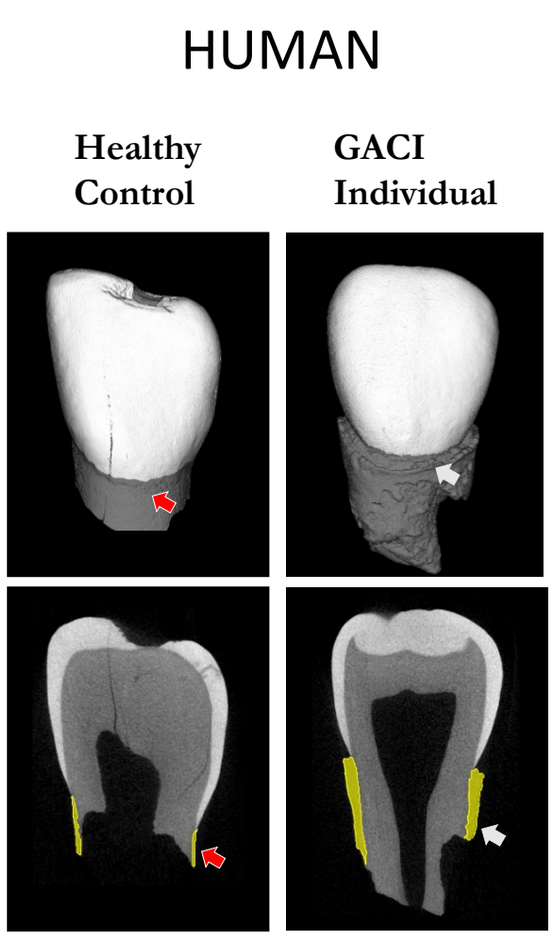
Backup slides

WHY PERIODONTAL DISEASE?
WELL THIS PROBLEM FOUND US

- Dr. Braddock's lab had been focused on an ENPP1-mutated rare disease called GACI which leads to significant calcification of the heart and arteries
- His work led to the founding and funding of Inozyme, now a public company (July 2020) with over $250m in investor funding
- It also led to the discovery that GACI patients had very thick cementum around their teeth which led to strong periodontal ligament (gum) attachment
- He believed this might be an interesting solution for periodontal disease and brought in the dental experts at the NIH to test the hypothesis and help develop a therapeutic



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ARESTIN "EFFICACY" DATA FROM PIVOTAL STUDIES

LOW REGULATORY AND COMPETITIVE BAR TO HURDLE

Table 1: Probing Pocket Depth at Baseline and Change in Pocket Depth at 9 Months From 2 Multicenter US Clinical Trials

Time	Study OPI-103A (N=368)			Study OPI-103B (N=380)		
	SRP+ Alone n=124	SRP+ Vehicle n=123	SRP+ ARESTIN® n=121	SRP Alone n=126	SRP + Vehicle n=126	SRP+ ARESTIN® n=128
PD (mm) at Baseline [Mean ± SE]	5.88 ±0.04	5.91 ±0.04	5.88 ±0.04	5.79 ±0.03	5.82 ±0.04	5.81 ±0.04
PD (mm) Change from Baseline at 9 Months [Mean ± SE]	-1.04 ±0.07	-0.90 ±0.54	-1.20*†† ±0.07	-1.32 ±0.07	-1.30 ±0.07	-1.63**†† ±0.07
Change over SRP Alone			**0.16 mm**			**0.31 mm**

SE = standard error; SRP = scaling and root planing; PD = pocket depth.
Significantly different from SRP *($P \leq 0.05$); **($P \leq 0.001$).
Significantly different from SRP + vehicle †($P \leq 0.05$); ††($P \leq 0.001$).

In these 2 studies, an average of 29.5 (5-114), 31.7 (4-137), and 31 (5-108) sites were treated at baseline in the SRP alone, SRP + vehicle, and SRP + ARESTIN® groups, respectively. When these studies are combined, the mean pocket depth change at 9 months was -1.18 mm, -1.10 mm, and -1.42 mm for SRP alone, SRP + vehicle, and SRP + ARESTIN®, respectively.

https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/050781s020lbl.pdf

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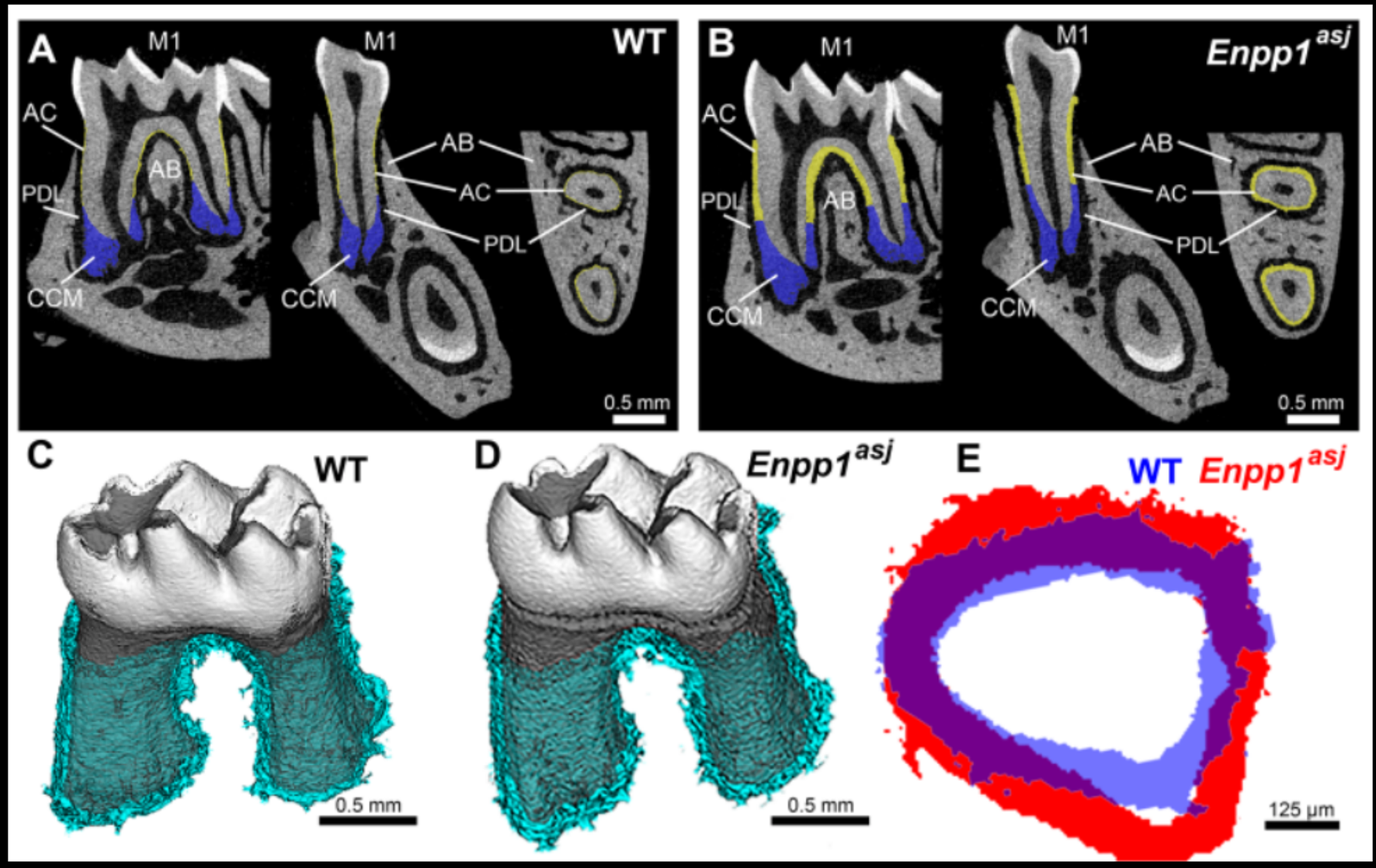

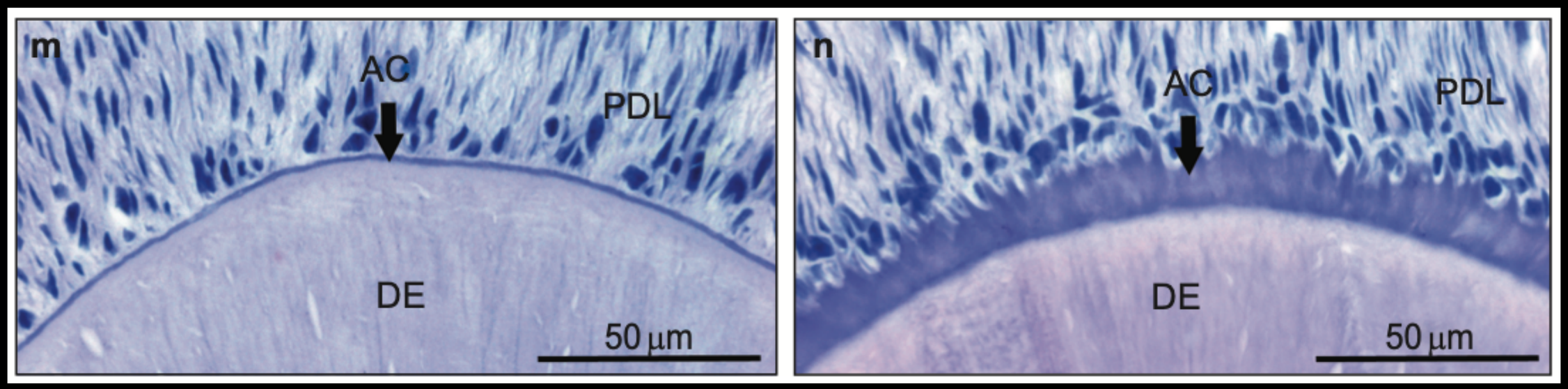

Int J Oral Sci. 2015 Mar; 7(1): 27–41.
J Dent Res. 2018 Jul; 97(8): 937–945.

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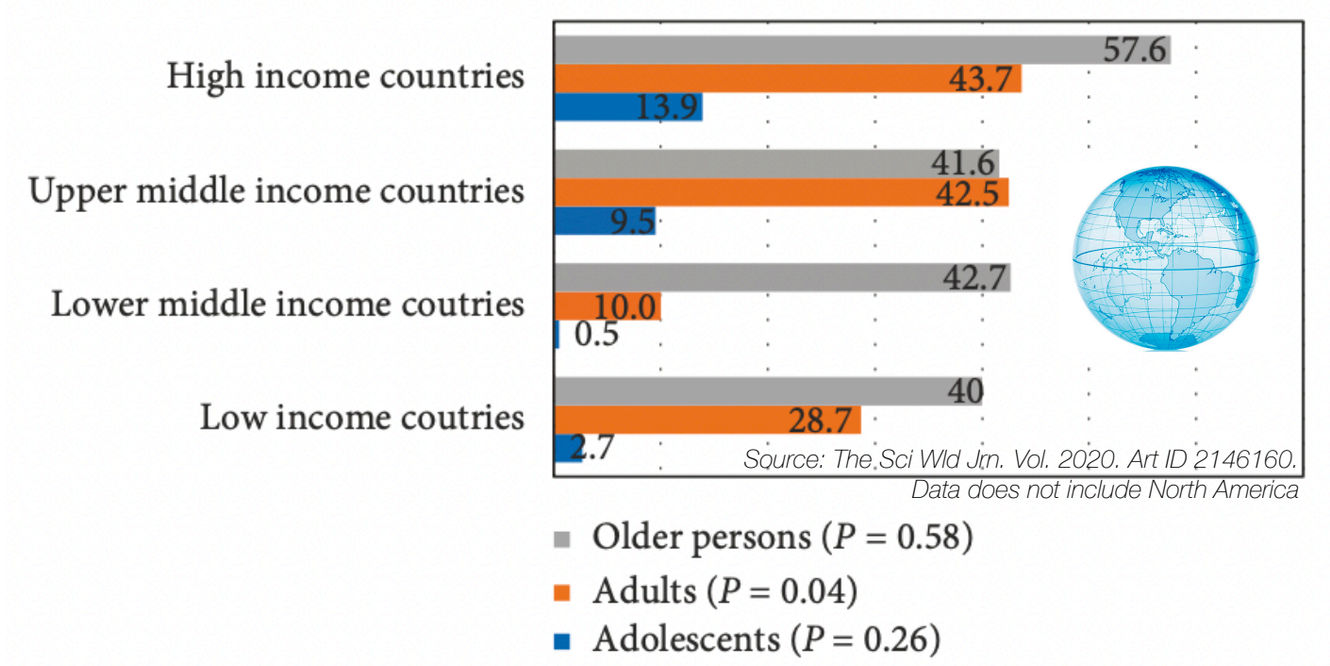
OPPORTUNITIES BEYOND THE U.S. HUMAN POPULATION



Source: The Sci Wld Jrn. Vol. 2020. Art ID 2146160.
Data does not include North America

Globally the prevalence of moderate/ severe periodontal disease is quite significant; India, the EU, China and South America represent large market opportunities

It is estimated that over 40 million dogs in the U.S. have periodontal disease, leading to a potential therapeutics market of over $3 billion

Source: VCA Hospitals reports.

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