



# The AAP's SUNSTAR Innovation Grant

OVERVIEW



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Thank you to SUNSTAR for the generous support allowing the AAP to offer a grant program supporting member research that aims to identify novel and innovative evidence-based periodontal treatment approaches to enhance patient care. As we reflect on the culmination of this endeavor, we celebrate six years of dedicated effort and hard work that have been invested into this program. The insights gained from these research endeavors have not only advanced our understanding of periodontal health but have also directly translated into improved treatment approaches. This booklet serves as a testament to the exceptional achievements that emerge when vision, dedication, and support converge in the pursuit of a common goal.



# 6 Research Grants

**Yvonne Kapila, DDS, PhD**

*Natural Bacteriocins as Pre/Pro-Biotics to Promote Oral Health and Prevent Periodontal Disease*

The initial support Dr. Kapila received for her research project has enabled her to initiate various projects that have led to several publications and two new NIH RO1 grants. The studies that have resulted (and extended) from this initial work encompass nisin's effects not only on biofilms, but also on periodontal disease, peri-implant disease, cancer-related applications and beyond.

## 2017 Sunstar Innovation Grant Recipient

**Yvonne Kapila, DDS, PhD**

*Natural Bacteriocins as Pre/Pro-Biotics to Promote Oral Health and Prevent Periodontal Disease*



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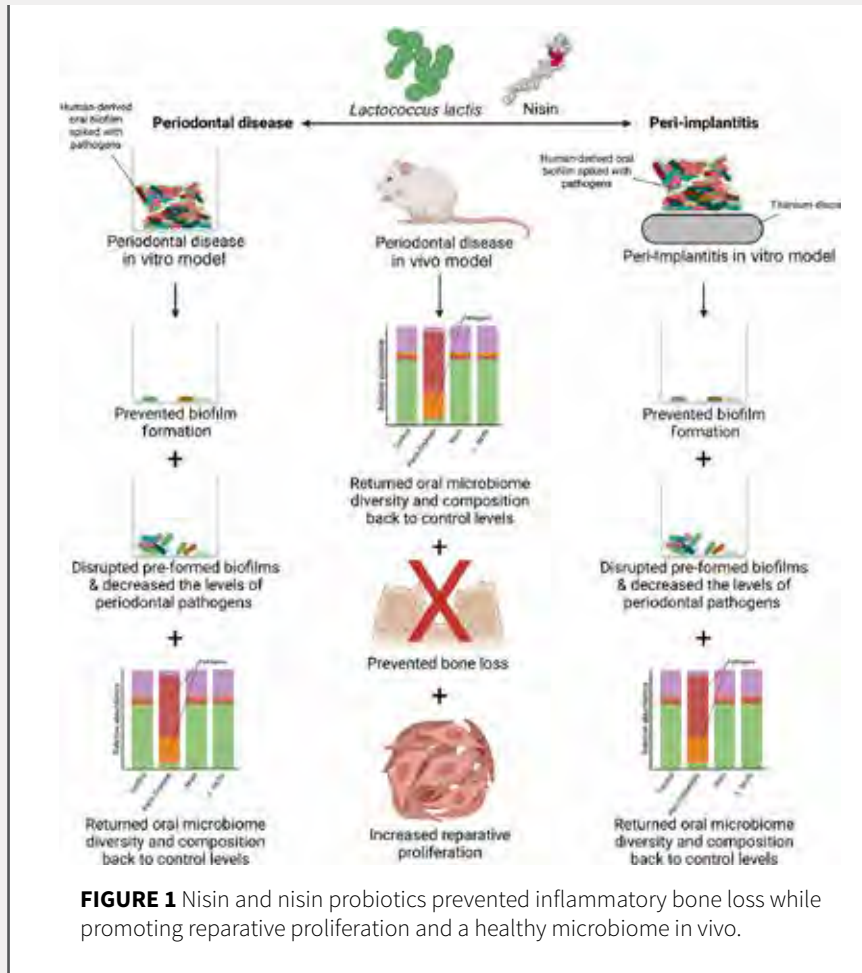


## ABSTRACT

### The next frontier: Shifting dysbiosis to eubiosis with nisin and nisin probiotics

Yvonne L. Hernandez-Kapila, University of California, Los Angeles, Los Angeles, CA, USA

Periodontal disease is a chronic oral inflammatory disease characterized by a dysbiotic microbiome that mediates destruction of the periodontium. Abrogating the pathogenic oral biofilm formation that underlies this dysbiosis is a crucial activity for restoring oral eubiosis and health. Yet, the rise of multidrug-resistant microbes and the scarcity of new antibiotics are growing concerns for new therapies. Thus, novel antimicrobial therapies to reduce the use of antibiotics for reestablishing a state of eubiosis and treating periodontal disease is warranted. One such antimicrobial is nisin, an antimicrobial peptide, made by the probiotic *Lactococcus lactis*, which can inhibit key periodontopathogenic bacteria. Therefore, the objective of this series of studies was to investigate the role of nisin in reestablishing a state of oral eubiosis from one of dysbiosis for mitigating periodontal disease and peri-implantitis. Using a series of in vitro and in vivo approaches, we discovered that nisin and a nisin-producing probiotic *L. lactis* can prevent oral biofilm formation and disrupt pre-formed biofilms. We further demonstrated that these treatments decreased the levels of periodontal pathogens within the biofilms and returned the diversity and composition of the oral microbiome back to control or “healthy” levels, from a state of dysbiosis to eubiosis. This same finding was true for oral biofilms grown on titanium discs; thus, nisin and nisin probiotics may be useful in treating dysbiosis in a peri-implantitis setting. Lastly, nisin and nisin probiotics prevented inflammatory bone loss while promoting reparative proliferation and a healthy microbiome in vivo (Figure 1). Thus, nisin and nisin probiotics can be used to treat disease-altered biofilms and promote healthier oral biofilms from a state of dysbiosis to eubiosis in vitro and in vivo, which may be useful for treating oral diseases and improving patient oral health.



## References

- Radaic A, Ye C, Parks B, et al. Modulation of pathogenic oral biofilms towards health with nisin probiotic. *J Oral Microbiol.* 2020;12(1):1809302. <http://doi.org/10.1080/2000.2297.2020.1809302>. PMID: 32944159; PMCID: PMC7482728.
- Radaic A, Brody H, Contreras F, et al. Nisin and nisin probiotic disrupt oral pathogenic biofilms and restore their microbiome composition towards healthy control levels in a peri-implantitis setting. *Microorganisms.* 2022;10(7):1336. <http://doi.org/10.3390/microorganisms10071336>. PMID: 35889055; PMCID: PMC9324437.
- Gao L, Kuraji R, Zhang MJ, et al. Nisin probiotic prevents inflammatory bone loss while promoting reparative proliferation and a healthy microbiome. *NPJ Biofilms Microbiomes.* 2022;8(1):45. <http://doi.org/10.1038/s41522-022-00307-x>. PMID: 35672331; PMCID: PMC9174264.



## Hsun-Liang (Albert) Chan, DDS, MS

*In-Situ Evaluation of Periodontal Inflammation with Ultrasonography*

The grant has helped Dr. Chan and his team with their goal of developing a point-of-care ultrasound device to diagnose and monitor periodontal and peri-implant tissue inflammation. Through this grant, they were able to publish a paper in the *Journal of Dental Research* with the lead author Dr. Shayan Barootchi about classifying peri-implant diseases with ultrasound imaging. Through knowledge and experiences gained from the Sunstar grant, another 4 NIH grants – among other foundational and industrial grants – were secured. Dr. Chan and his team will further explore and validate the efficacy of ultrasound on understanding intraoral wound healing and the disease process for providing better clinical care. They are currently piloting this innovative technology for clinical evaluation of periodontal and peri-implant tissue wound healing at the University of Michigan.

## 2018 Sunstar Innovation Grant Recipient

**Hsun-Liang (Albert) Chan, DDS, MS**

*In-Situ Evaluation of Periodontal Inflammation with Ultrasonography*



Through this grant, they were able to publish a paper in the *Journal of Dental Research* with the lead author Dr. Shayan Barootchi about classifying peri-implant diseases with ultrasound imaging. Through knowledge and experiences gained from the Sunstar grant, other 4 NIH grants – among other foundational and industrial grants – were secured. Dr. Chan and his team will further explore and validate the efficacy of ultrasound on understanding intraoral wound healing and the disease process for providing better clinical care.

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## **ABSTRACT**

### **Inflammatory vascular and tissue content profile for periodontal diagnosis using integrated quantitative ultrasonic imaging**

*Hsun-Liang Chan, Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA*

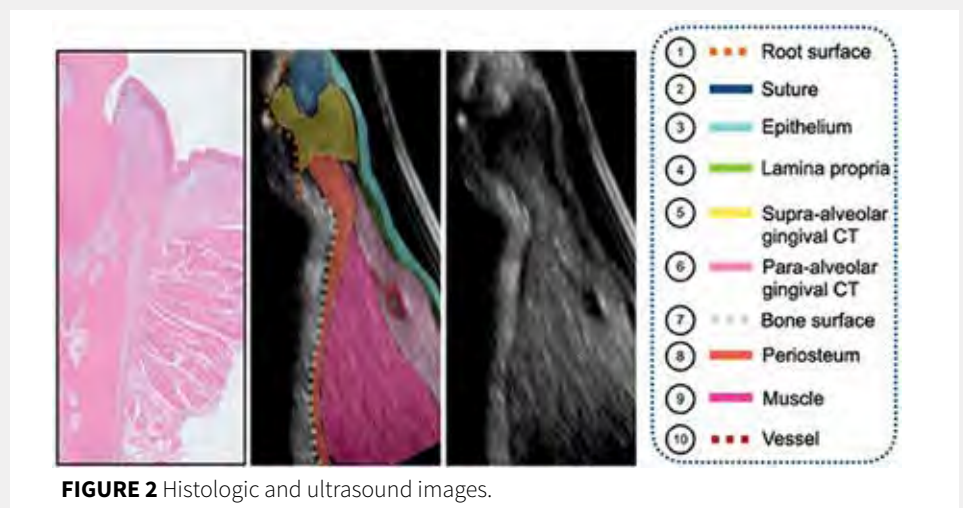
**Background:** Early manifestations of periodontitis are disruption of microcirculation and increases in extracellular fluid volume at the expense of reduction in collagen content. Detecting these subclinical changes could lead to early diagnosis of disease activity and timely intervention. Quantitative ultrasound parameters, including color pixel density, soft tissue elasticity, and ultrasonic backscatter, could be useful for indicating these changes. The aim of this project was to evaluate the feasibility of ultrasound for quantifying vascular and tissue quality changes due to periodontal inflammation.

**Methods:** Facial periodontium of the lateral incisor, canine, and second premolar on both sides of the mandible in six female miniature pigs were scanned with ultrasound at baseline. These teeth randomly received one of four treatments for creating various degrees of periodontal inflammation: no ligature, or ligature + *Porphyromonas gingivalis* for 2, 4, or 6 weeks. After each treatment, ultrasound scans were performed. After 6 weeks, the animals were euthanized, and samples were collected for histology. Ultrasound parameters were compared among the four disease groups. Additionally, the ultrasound parameters were correlated with histologic results.

**Results:** Ultrasound-derived anatomical macrostructures, including soft/hard tissue dimensions, correlated well with histology. Soft tissue microstructures, including epithelium, submucosa, lamina propria, periosteum, muscles, and suprapariosteal vessels, could be imaged with ultrasound. Ultrasound color flow, soft tissue elasticity, and backscatter were successfully recorded. Acute periodontal inflammation was observed within the first 2 weeks of ligature induction, evidenced by increased blood flow, and subsided subsequently (Figure 2).

**Conclusions:** Preliminary data demonstrated ultrasound is capable of imaging periodontal microstructures. Methods to quantify color pixel density, elasticity, and backscatter with ultrasound were established and subsequently applied to our NIH-funded R21 study. A longer disease induction period and a combination of various periodontal pathogens with frequent injections are needed for periodontal disease occurrence in this porcine model.

**Acknowledgments:** Oliver D. Kripfgans, Shayan Barootchi, Jad Majzoub, and J. Christopher Fenno, University of Michigan School of Dentistry, Ann Arbor, MI, USA contributed to this research.



**FIGURE 2** Histologic and ultrasound images.



### **Jeff C.W. Wang, DDS, DMSc**

*Development of Patient-friendly Oral Health Report with Customized Oral Hygiene Instructional Video for Enhanced Patient Education Modalities*

With the help of the grant, Dr. Wang and his team have created prototypes for a personalized oral health report to help patients understand their own oral health condition. Dr. Wang states this has been very successful because information about oral health is presented in a patient-friendly manner, with “clinical photos, noted radiographes, periodontal chart, plaque control heat map, and odontograms.” Extended active learning materials explaining their risk factors for caries and periodontal disease are included as well as a customized oral hygiene instructional video. The video was included as part of the package for the patient, which “tremendously improved the efficacy of the home care therapy that was catered to individual needs.” The grant has also supported Dr. Wang and his team in launching a proof-of-principle pilot clinical trial.

## **2018 Sunstar Innovation Grant Recipient**

**Jeff C.W. Wang, DDS, DMSc**

*Development of Patient-friendly Oral Health Report with Customized Oral Hygiene Instructional Video for Enhanced Patient Education Modalities*



“With the help of the grant, Dr. Wang and his team have created prototypes for a personalized oral health report to help patients understand their own oral health condition.”

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## **ABSTRACT**

### **Personalized oral health report impacts periodontal treatment outcome Preliminary results from a feasibility trial**

*Chin-Wei Wang, Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA; Department of Periodontics, Taipei Medical University Hospital, Taipei, Taiwan; Graduate Institute of Clinical Dentistry, National Taiwan University, Taipei, Taiwan; School of Dentistry, College of Oral Medicine, Taipei Medical University, Taipei, Taiwan*

**Background:** Patient education is vital for successful periodontal treatment yet limited customized educational material has been provided for patients to learn about their own oral health records and conditions. Therefore, this study aimed to develop a personalized oral health report (POHR) to enhance patient education during the initial phase of periodontal treatment as a feasibility trial.

**Methods:** Patient-friendly POHRs were created based on patients' oral health records, including odontograms, periodontal charts, newly developed plaque control heat maps, and marked radiographs. All the health records were transformed to a patient-friendly format and were explained to the patients, including basic radiographic findings. All the systemic/local risk factors were organized into a checklist with extended reading, and customized oral hygiene instructional videos were recorded in the patients' own mouths. Each provider delivered routine periodontal treatment as a control group before learning and integrating POHRs into patient care for the experimental group. Surveys were used to evaluate patient-reported outcomes and their oral health knowledge about systemic and local factors.

**Results:** A total of four providers completed eight paired cases. Preliminary data showed bleeding on probing reduction for the experimental group with POHRs was 2.47 times higher (30.75% vs. 76.02%; control vs. experimental group, respectively). Plaque Control Record score and Plaque Index in the control group were 2 and 2.7 times higher (81% vs. 40%; 1.6 vs. 0.6, respectively,  $p < .05$ ). Additionally, patients in the experimental group showed significantly better understanding of oral health knowledge and compliance.

**Conclusions:** Preliminary data showed that POHRs exert a positive influence on periodontal treatment outcomes. Larger trials with further development of POHRs should have huge potential for general implementation.

**Acknowledgments:** Hong-Ying Pan, Gunjeeta Diwaker, and Sara Tinawi, Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, MI, USA, contributed to this research.



**Kevin M. Byrd, DDS, PhD**

*An Atlas of Experimental Gingivitis in Humans at Single Cell Resolution*

Since receiving the grant funding, Dr. Byrd and his team have enmeshed themselves in the ever-growing community of singlecell and spatial biologists at the axis of data generation, data integration, standardized cell annotation, technology innovation, and ultimately application to the clinic in collaboration with computational scientists who can employ AI/ML strategies for data interpretation. Dr. Byrd informed *Periospectives* that the grant was a catalyst for his team's current leadership within the Human Cell Atlas Oral & Craniofacial Bionetwork, which now has transdisciplinary partnerships with over 60 labs across 5 continents.

## 2019 Sunstar Innovation Grant Recipient

Kevin M. Byrd, DDS, PhD

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## ABSTRACT

### SARSCoV2 infection of the oral cavity and saliva

Kevin M. Byrd, Division of Oral & Craniofacial Health Sciences, University of North Carolina Adams School of Dentistry, Chapel Hill, NC, USA; Department of Innovation & Technology Research, ADA Science & Research Institute, Gaithersburg, MD, USA

Despite signs of infection—including taste loss, dry mouth, and mucosal lesions such as ulcerations, enanthema, and macules—the involvement of the oral cavity in coronavirus disease 2019 (COVID-19) is poorly understood. To address this, we generated and analyzed two single-cell RNA sequencing datasets of the human minor salivary glands and gingiva (9 samples, 13,824 cells), identifying 50 cell clusters. Using integrated cell normalization and annotation, we classified 34 unique cell subpopulations between glands and gingiva. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral entry factors such as *ACE2* and *TMPRSS* members were broadly enriched in epithelial cells of the glands and oral mucosae. Using orthogonal RNA and protein expression assessments, we confirmed SARS-CoV-2 infection in the glands and mucosae. Saliva from SARS-CoV-2-infected individuals harbored epithelial cells exhibiting *ACE2* and *TMPRSS* expression and sustained SARSCoV-2 infection. Acellular and cellular salivary fractions from asymptomatic individuals were found to transmit SARS-CoV-2 ex vivo. Matched nasopharyngeal and saliva samples displayed distinct viral shedding dynamics, and salivary viral burden correlated with COVID-19 symptoms, including taste loss. Upon recovery, this asymptomatic cohort exhibited sustained salivary IgG antibodies against SARS-CoV-2. Collectively, these data show that the oral cavity is an important site for SARS-CoV-2 infection and implicate saliva as a potential route of SARS-CoV-2 transmission.

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## Mia L. Geisinger

*Development of Multimedia Educational Materials for Caregivers to Enable Optimal Oral Hygiene Provisions for Patients with Dementia*

The grant funding has helped Dr. Geisinger and her team parlay their work into programs they have used to train caregivers (both professional and familial) for individuals with moderate to severe dementia at over 10 facilities in the Birmingham area. The data they gathered indicates that utilizing the Managing Oral Hygiene Using Threat Reduction (MOUTH) protocol to reduce care-resistant behavior (CRB) results in substantially longer time spent on oral hygiene activities, reduction in CRB, and improved oral health outcomes. More recently, a secondary analysis revealed tailored strategies may be advantageous in subgroups of individuals living with dementia. Younger individuals who were less dependent upon caregivers for activities of daily living demonstrated less response to MOUTH intervention whereas older individuals with higher levels of dementia and taking more anti-psychotic medications demonstrated larger oral health benefits and reduction in CRBs when MOUTH protocols were used. Dr. Geisinger's group recently submitted a federal grant proposal to further evaluate the potential for development and validity testing of a scalable web-based application to provide training for CRB recognition and amelioration during the delivery of oral care in patients with dementia.

## 2019 Sunstar Innovation Grant Recipient

**Mia L. Geisinger, DDS, MS**

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**Mia L. Geisinger, DDS, MS**

*Development of Multimedia Educational Materials  
for Caregivers to Enable Optimal Oral Hygiene  
Provisions for Patients with Dementia*



## **ABSTRACT**

### **Multimedia tools for caregiver education and implementation of optimal mouth care in persons living with moderate to severe dementia**

*Mia L. Geisinger, University of Alabama at Birmingham, Birmingham, AL, USA*

**Background:** The act of providing mouth care to an older adult residing in a long-term care facility (LTC) can improve patient quality of life and prevent dental pain, gingival inflammation, and the concomitant systemic increase in pro-inflammatory mediators. Mouth care, specifically efficacious oral hygiene practices, is not consistently provided to persons with dementia because mouth care has been established as a trigger to careresistant behavior (CRB), particularly in individuals with moderate to severe dementia.

**Methods:** Multimedia tools were developed utilizing interactive modules and deployed to caregiver staff in LTCs with quick response (QR) code technology as a part of staff education and calibration as well as onboarding of newly employed caregivers. Mouth care completion rates and CRB incidence were recorded during oral care delivery before and after multimedia Managing Oral Hygiene Using Threat Reduction (MOUTH) training.

**Results:** Caregiver assessment demonstrated that 78% of caregivers who received MOUTH training with novel multimedia tools strongly agreed or agreed that such training improved their ability to deliver effective mouth care for persons living with dementia. Multimedia training for MOUTH also improved mouth care completion rates and decreased CRB incidence, although the differences were only significant for morning delivery of mouth care.

**Conclusions:** Multimedia tools can provide an effective training protocol for caregivers to improve mouth care for persons living with medication. Further research should focus on scalable and formative calibration for professional and familial caregivers and the ability to create individualized oral care plans based upon patient characteristics and trajectory analysis.





## **Chun-Teh Lee, DDS, MS, DMSc**

*Improving Periodontal Health through a Precision Periodontal Health Care Chart*

With the help of the Sunstar Innovation Grant, Dr. Lee and his team were able to develop the Precision Periodontal Health Care Chart (PPHCC) in the electronic health record system and share it with other institutions. The PPHCC is an electronic form containing risk factors and risk assessment for periodontitis. The dental care provider answers the required questions in PPHCC, and then the PPHCC provides the summary of the periodontal charting, a suggested periodontal diagnosis, a periodontal risk profile, and the risk factor information. This project has been further extended to create algorithms to suggest a preliminary periodontal diagnosis based on the information collected by the PPHCC, as well as develop a deep learning model to assess radiographic bone level to assist clinical diagnoses. According to the results of a survey done by Dr. Lee and his team, dental care providers and patients are highly satisfied with the PPHCC. Patients are better educated and motivated to receive treatments and follow instructions after reading the evidencebased information of risk factors. Clinicians can create a proper treatment plan for patients based on the risk assessment results. The treatment outcomes have improved, and the risk of disease progression has reduced with the use of PPHCC.

## **2019 Sunstar Innovation Grant Recipient**

**Chun-Teh Lee, DDS, MS, DMSc**

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**SUNSTAR**







## **ABSTRACT**

### **Using precision periodontal health care chart to improve periodontal care**

*Chun-Teh Lee, Department of Periodontics and Dental Hygiene, The University of Texas Health Science Center at Houston School of Dentistry, Houston, TX, USA*

**Background:** There is a lack of tools delivering clinical and educational information to help patients understand periodontitis and motivate them to control the disease. This study aimed to develop a Precision Periodontal Health Care Chart (PPHCC) available in the electronic health record system and evaluate its clinical use and effects on clinical outcomes.

**Methods:** An electronic form, the PPHCC, which contains information on periodontitis risk factors, risk assessment, and clinical examination results, was created. A survey with questions based on the System Usability Scale (SUS) and additional questions was used to evaluate the satisfaction of patients and care providers with the PPHCC before and after non-surgical periodontal therapy. The clinical outcomes, including probing depth, clinical attachment level (CAL), and bleeding on probing, in the patients who used the PPHCC (PC group) were compared to those in the patients without using the PPHCC (controls).

**Results:** The mean scores of SUS questions at the initial periodontal examination were  $74.26 \pm 18.89$  ( $n = 37$ ) for patients and  $88.31 \pm 14.14$  ( $n = 37$ ) for care providers. The mean scores of SUS questions at reevaluation were  $74.84 \pm 17.78$  ( $n = 16$ ) for patients and  $89.63 \pm 13.48$  ( $n = 20$ ) for care providers. The changes in the percentages of teeth with CAL1 to 2mm ( $p=0.01$ ) and CAL3 to 4mm ( $p=0.04$ ) were significantly different between the PC and control groups, but the other parameters were not.

**Conclusions:** Both patients and care providers were satisfied with using the PPHCC in the clinic. However, the differences in short-term clinical outcomes between the PC and control groups were inconclusive.

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