College of Dentistry Research Day
Research Presentation Abstracts

Abstract Title:	**Systemic Antibody Responses to Oral Bacteria with Aging**
Author(s):	D. Dawson III, Center for Oral Health Research, Div. of Periodontics, College of Dentistry, U of Kentucky S. Kirakodu, Center for Oral Health Research, College of Dentistry, U of Kentucky M. J. Steffen, Center for Oral Health Research, College of Dentistry, U of Kentucky R. Hamzah, Center for Oral Health Research, Division of Periodontics, College of Dentistry, U of Kentucky M. Al-Sabbagh, Division of Periodontics, College of Dentistry, U of Kentucky M.J. Novak, Center for Oral Health Research, Division of Periodontics, College of Dentistry, U of Kentucky J.L. Ebersole, Center for Oral Health Research, Division of Periodontics, College of Dentistry, U of Kentucky

Abstract: Substantial evidence has demonstrated that adaptive immune responses are affected by aging, specifically focused on “newly acquired” responses in naïve aged individuals. However, responses to oral bacteria in aging provide a different set of conditions, in which the host has a pre-existing immune response to bacteria that have colonized the individual’s oral cavity over many decades. OBJECTIVE: This investigation examined the characteristics of serum antibody in a cohort of human subjects related to age, oral health, and specific bacterial burden in the oral cavity. METHODS: Serum IgG and IgG subclass antibody responses to oral bacteria were evaluated by ELISA from 447 subjects (age range: 21-80): healthy (H; N=61); gingivitis (G; N=87); periodontitis (PD; N=299). Subgingival plaque samples were evaluated for specific bacteria using qPCR. RESULTS: Antibody to the oral bacteria were not altered related to aging alone, but reflected the increased prevalence of periodontitis with aging. Generally, antibody levels to periodontal pathogens did not correlate significantly with aging. Interestingly, antibody to the pathogens was inversely correlated with clinical disease in younger individuals, but positively correlated with levels of disease in the older patients. Pg levels were decreased in diseased and healthy sites of the older population. Additionally, the level of antibody to Pg was positively correlated with the specific microbial burden, except in the >50 age group. Finally, aging effects on IgG subclass antibody distribution was noted, with both IgG1, IgG3 and IgG4 increasing with aging, although IgG2 levels contributed the largest proportion of total IgG antibody. These differences were also reflected with periodontitis, and related to the severity of the disease. CONCLUSIONS: These findings suggest that aging alterations in antibody responses to oral bacteria that have “primed” the immune system are different than responses to naïve antigens and indicate that the affects related to gender, subclass, and microbial burden may have some role in disease changes with aging.

Supported by: NIH awards: GM110778, UL1TR000117, RR020145, GM103538

Primary Presenter / email: **Dawson III, D.** / drdaws0@uky.edu
Mentor / e-mail: Dawson III, D. / drdaws0@uky.edu

College of Dentistry Research Day
Research Presentation Abstracts

Abstract Title:	**P. gingivalis-induced PLA2-IIA involves Notch-1 activation in oral epithelial cells**
Author(s):	Y. Alimova, Center for Oral Health Research, College of Dentistry, U of Kentucky A. Al-Attar, Center for Oral Health Research, College of Dentistry, U of Kentucky S. Kirakodu, Center for Oral Health Research, College of Dentistry, U of Kentucky J.L. Ebersole, Center for Oral Health Research, College of Dentistry, U of Kentucky O.A. Gonzalez, Center for Oral Health Research, College of Dentistry, U of Kentucky

Abstract: Global gene expression analysis in oral epithelial cells (OECs) exposed to P. gingivalis (Pg) led us to identify phospholipase 2-group IIA (PLA2-IIA) as a potential candidate associated with Pg-driven dysbiosis. The mechanisms involved in PLA2-IIA production remain unclear; however, intestinal expression of Notch-1 receptor was recently correlated with PLA2-IIA production. Herein we sought to determine the ability of Pg to specifically induce the expression of PLA2-IIA in OECs, and the role of Notch-1 activation in this response. Oral epithelial cells (OKF6) were challenged with Pg or other oral bacterial species. The mRNA and protein levels for PLA2-IIA and Notch-1 were evaluated by qPCR, ELISA, and flow cytometry. Notch-1 activation was tested by determination of HES-1 transcription. The Notch-1/gamma-secretase inhibitors DAPT and JLK6 were used to test the role of Notch-1 in Pg-induced PLA2-IIA. The role of gingipains in Pg-induced PLA2-IIA was evaluated using a triple mutant Pg strain (rgpA-rgpB-kgp-). Pg induced a 500-fold increase in mRNA levels of PLA2-IIA in OECs. Accordingly, PLA2-IIA protein levels were elevated in cell lysates, but not cell supernatants. Other oral species failed to induce similar PLA2-IIA responses. Pg increased the activation of Notch-1 and this response correlated with Pg-induced PLA2-IIA expression. Both Notch-1/gamma-secretase inhibitors completely abrogated Pg-induced PLA2-IIA. Pg mutant for gingipains failed to induce PLA2-IIA expression. PLA2-IIA production in OECs is strongly and specifically induced by Pg in a mechanism that seems to involve Notch-1 activation and gingipains. Based on the PLA2-IIA-associated antimicrobial and immunoinflammatory effects, we hypothesize that activation of Notch-1/PLA2-IIA axis could be involved in Pg-induced oral dysbiosis.

Supported by: NIH/NIDCR grant 1R21DE024804-01 and Center for Oral Health Research, University of Kentucky

Primary Presenter / email: **Gonzalez, O.A.** / ogonz2@uky.edu
Mentor / e-mail: Gonzalez, O.A. / ogonz2@uky.edu

College of Dentistry Research Day
Research Presentation Abstracts

Abstract Title:	**Appalachian Rural Dental Education Partnership (ARDEP)**
Author(s):	S. Burch, College of Dentistry, U of Kentucky J. Aalboe, College of Dentistry, U of Kentucky P. Stein, College of Dentistry, U of Kentucky M.R. Mullins, College of Dentistry, U of Kentucky G. DeMoss, Morehead State U, Morehead, KY

Abstract: Background: Oral health disparities with adverse economic outcomes across the lifespan are well documented in Kentucky's rural Appalachian counties. Children, adults and seniors have very poor oral health and oral health literacy, with indicators near or at the lowest in the nation. A comprehensive, long-term development strategy is needed to improve health, education and economic outcomes for the region. Objectives: Develop a strategic partnership between Morehead State University and the University Of Kentucky College Of Dentistry under the auspices of the Kentucky Oral Health Network, which leverages the strengths of each university and also public health, community health and other non-profit organizations in this region of Appalachia. Methods: The Appalachian Rural Dental Education Partnership (ARDEP) was established in 2013 to increase opportunities for Kentuckians from Appalachian counties to pursue dental education and practice as a career choice, improve the numbers and distribution of dentists practicing in Kentucky's Appalachian counties, improve oral health literacy and demand for care, and develop financially sound oral health models to benefit the economic base and societal improvements in Appalachia. Results: By 2015 the innovative ARDEP has established a variety of sustainable projects. These consist of a strong in-region K-12 early dental pipeline program, an MSU Campus Dental Pipeline Program including for credit online oral health courses, and a regional oral health literacy and dental services program with university and community partners. Conclusion: The MSU/UK ARDEP partnership is providing important new models to guide infrastructure development that helps improve oral health and workforce capacity in Appalachia.

Supported by: Supported by a grant from the Appalachian Regional Commission

Primary Presenter / email: **Burch, S.** / sharlee.burch@uky.edu
Mentor / e-mail: Burch, S. / sharlee.burch@uky.edu

College of Dentistry Research Day
Research Presentation Abstracts

Abstract Title:	**Digital Removable Prosthodontics, a simple technology for everyday clinical practice**
Author(s):	A. Kutkut, Div. of Prosthodontics, Dept. of Oral Health Practice, College of Dentistry, U of Kentucky

Abstract: Computer Aided Design – Computer Aided Manufacturing (CAD/CAM) technology has made significant improvement in modern dentistry. CAD/CAM applications in dentistry include fabrication of inlays, onlays, crowns, fixed partial dentures, and implant abutments/prostheses. Recently, computer-aided technology is a new method commercially available for fabricating removable prostheses. This system facilitates impressions, interocclusal records, and tooth selection to be completed in one appointment. The dentures are then fabricated using CAD/CAM technology and placed in the second appointment. 2 commercial manufacturers in the United States are currently fabricating removable prostheses with computer-aided design and computer-aided manufacturing (CAD/CAM) technology for clinicians world-wide. These manufacturers have definitive protocols and offer exclusive dental materials, techniques, and laboratory support. CAD/CAM technology allows the clinician to design removable prostheses and create natural looking superstructures. The CAD/CAM technique provides precise fit, reduces number of visits and the cost of the procedure, and eliminates dimensional inaccuracies due to conventional processing techniques. The aim of this presentation is to describe a simple technique for removable prosthesis procedure using CAD/CAM technology.

Supported by:

Primary Presenter / email: **Kutkut, A.** / aku227@uky.edu
Mentor / e-mail: /

College of Dentistry Research Day
Research Presentation Abstracts

Abstract Title:	**Adaptive Immune Responses in Periodontitis: Mucosal Tissue Responses to a Complex Microbial Ecology in Aging**
Author(s):	J.L. Ebersole. Center for Oral Health Research, College of Dentistry, U of Kentucky S. Kirakodu, Center for Oral Health Research, College of Dentistry, U of Kentucky M. J. Novak, Center for Oral Health Research, College of Dentistry, U of Kentucky L. Orraca, Caribbean Primate Research Center, Sebana Seca, PR J. Gonzalez-Martinez, Caribbean Primate Research Center, Sebana Seca, PR L.L. Cunningham, Division of Oral and Maxillofacial Surgery, College of Dentistry, U of Kentucky M.V. Thomas, Division of Periodontics, College of Dentistry, U of Kentucky O.A. Gonzalez, Center for Oral Health Research, College of Dentistry, U of Kentucky

Abstract: Evidence has shown activation of T and B cells in gingival tissues in experimental models and in humans diagnosed with periodontitis. The results of this adaptive immune response are noted both locally and systemically with antigenic specificity for an array of oral bacteria, including periodontopathic species, e.g. P. gingivalis, A. actinomycetemcomitans. It has been recognized through epidemiological studies and clinical observations that the prevalence of periodontitis increases with age. OBJECTIVE: This report describes our studies evaluating gingival tissue transcriptomes in humans and a nonhuman primate model of naturally-occurring periodontitis to delineate gingival mucosal tissue gene expression profiles focusing on the B cells and plasmacytes critical for development of humoral adaptive immune responses. METHODS: Gingival tissue samples were obtained from healthy (N=3) and chronic adult periodontitis (N=4) human subjects. Similar samples were obtained from 34 Macaca mulatta primates with 23 healthy tissues of different age groups from ~3-22 years of age and 11 naturally-occurring periodontitis. RNA was prepared from all tissues and microarray analysis (Affymetrix) was used to identify variations in transcriptome profiles. RESULTS: Patterns of B cell and plasmacyte genes were altered in aging healthy gingival tissues. Substantial increases in a large number of genes reflecting antigen-dependent activation, B cell activation, B cell proliferation, and B cell differentiation/maturation were observed in periodontitis in adults and aged animals. Finally, evaluation of the relationship of these gene expression patterns with those of various tissue destructive molecules (MMP2, MMP9, CTSK, TNF□, RANKL) showed specific clusters of gene responses that characterized correlations in healthy tissues versus periodontitis tissues. CONCLUSIONS: These results are consistent with B cell response activities in healthy tissues potentially contributing to muting the effects of the tissue destructive biomolecules responding to oral bacterial colonization, whereas with periodontitis this relationship is adversely affected and enables a progression of tissue destructive events.

Supported by: NIH awards: GM110778, UL1TR000117, RR020145, GM103538.

Primary Presenter / email: **Ebersole, J.L.** / jleber2@uky.edu
Mentor / e-mail: Ebersole, J.L. / jleber2@uky.edu