

**SUMMARY STATEMENT**

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( Privileged Communication )

**Release Date:** 08/10/2025

**Revised Date:**

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**Application Number:** 1K99DE035581-01

**Principal Investigator**

**MAKKAR, HARDIK**

**Applicant Organization:** UNIVERSITY OF PENNSYLVANIA

**Review Group:** ZRG1 MSOS-F (80)  
Center for Scientific Review Special Emphasis Panel  
Mentored, Career Transition, and Mid-Career K Awards

**Meeting Date:** 07/22/2025  
**Council:** OCT 2025  
**Requested Start:** 12/01/2025

**Opportunity Number:** PA-24-194  
**PCC:** L5R1

**Dual IC(s):** AI

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**Project Title:** Probing the Mechanical Regulation of Inflammation in Periodontal Health and Disease  
**SRG Action:** ++  
**Next Steps:** Visit [https://grants.nih.gov/grants/next\\_steps.htm](https://grants.nih.gov/grants/next_steps.htm)  
**Human Subjects:** 10-No human subjects involved  
**Animal Subjects:** 30-Vertebrate animals involved - no SRG concerns noted

| Project<br>Year | Direct Costs<br>Requested |
|-----------------|---------------------------|
| 1               | 127,850                   |
| 2               | 130,936                   |
| 3               | 249,000                   |
| 4               | 249,000                   |
| 5               | 249,000                   |
| <b>TOTAL</b>    | <b>1,005,786</b>          |

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**++NOTE TO APPLICANT:** Members of the Scientific Review Group (SRG) were asked to identify those applications with the highest scientific merit, generally the top half. Written comments, criterion scores, and preliminary impact scores were submitted by the assigned reviewers prior to the SRG meeting. At the meeting, the more meritorious applications were discussed and given final impact scores; by concurrence of the full SRG, the remaining applications, including this application, were not discussed or scored. The reviewers' comments (largely unedited by NIH staff) and criterion scores for this application are provided below. Because applications deemed by the SRG to have the highest scientific merit generally are considered for funding first, it is highly unlikely that an application with an ND recommendation will be funded. Each applicant should read the written critiques carefully and, if there are questions about the review or future options for the project, discuss them with the Program Contact listed above.

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**1K99DE035581-01 Makkar, Hardik****ADMINISTRATIVE NOTE**

**DESCRIPTION (provided by applicant):** This award will train Dr. Hardik Makkar, a dentist-scientist, at the intersection of tissue mechanics and mechanobiology in periodontal health and disease. It will support his transition to an independent research career focused on developing novel mechano-immune therapeutics for periodontal disease. While microbial dysbiosis and immune responses in periodontitis are well-studied, the impact of mechanical properties of gingival tissue on immune regulation during disease progression remains underexplored. During periodontal disease, the collagenous ECM of the gingiva degrades, impairing tissue stiffness and disrupting immune homeostasis. There is an unmet clinical need to identify mechanisms by which gingival ECM stiffness regulates host homeostasis. This proposal hypothesizes that changes in mechanical properties of gingival tissue during periodontal disease progression alter immune responses, exacerbate inflammation, and promote a pro-inflammatory environment. The project will investigate mechanobiological pathways driving gingival fibroblasts (GFs) to adopt pro-inflammatory phenotypes, uncovering novel therapeutic targets. A gingival ECM mimicking model has been developed with tunable stiffness, replicating both healthy and diseased ECM. Preliminary data show stiff ECM reduces cytokine responses, downregulates matrix metalloproteinase gene expression, and enhances TGF $\beta$  signaling and matrix-related genes. Additionally, stiffer matrices promote the differentiation of myeloid progenitors into antigen-presenting cells. These findings suggest ECM stiffness supports tissue homeostasis and fibroblast-myeloid interactions. I hypothesize that reduced tissue stiffness in periodontal disease disrupts fibroblast function, impairing matrix and immune homeostasis. This hypothesis will be tested using a gingival ECM-mimicking hydrogel and a mouse model of periodontitis. The research will address two specific aims: 1) Investigate how ECM stiffness regulates the epigenetic state of gingival fibroblasts, and 2) Examine how ECM stiffness influences stromal-myeloid cell crosstalk. During the K99 mentored phase, I will gain expertise in 1) multimodal approaches to study tissue mechanics in periodontal health and disease, 2) mouse model of bone marrow transplantation with ligature induced periodontitis, proficiency in spatial transcriptomics, and 3) enhance my teaching, grant writing, and scientific communication skills. In the independent R00 phase, the Makkar lab will study ECM stiffness-dependent fibroblast-myeloid crosstalk using in vitro and in vivo models. This research will improve understanding of ECM's role in periodontal inflammation, with potential for ECM-targeted therapies to promote healing and prevent disease progression. In conclusion, this proposal will investigate the changing mechanobiology of gingival ECM during periodontal disease, leading to new insights and novel therapeutic targets for disease management. I aim to secure an R01/35 grant by the end of the award period, supporting my transition to an independent career as a dentist-scientist integrating mechanobiology, tissue engineering, and infection biology to advance oral health care.

**PUBLIC HEALTH RELEVANCE:** Periodontitis is one of the most prevalent chronic inflammatory conditions, affecting over one billion people worldwide. We found that stiff gingival tissue promotes tissue homeostasis which is reversed in periodontitis with concomitant microscale ECM degradation with altered mechanics. This study aims to dissect the regulation matrix stiffness dependent immunological homeostasis in periodontal health and disease. of

**CRITIQUE 1**

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Candidate: 2

Career Development Plan/Career Goals /Plan to Provide Mentoring: 6

Research Plan: 5

Mentor(s), Co-Mentor(s), Consultant(s), Collaborator(s): 4

Environment Commitment to the Candidate: 2

### **Overall Impact:**

Dr. Makkar, a clinician-scientist and postdoctoral fellow at the University of Pennsylvania under the R90 institutional program, has submitted this K99/R00 application to investigate the role of extracellular matrix (ECM) biomechanics in periodontal disease. His research focuses on fibroblast-immune cell crosstalk using an engineered ECM construct with tunable mechanical properties. With a background in bioengineering and biomaterials, Dr. Makkar aims to strengthen his expertise in imaging, biomechanics, and in vivo modeling through this proposal. He presents a focused and feasible research plan and has identified mentors who can support his technical development. However, there are concerns regarding the mentoring team's experience and the lack of sufficient detail on mentoring objectives, milestones, and evaluation metrics, which raises uncertainty about Dr. Makkar's ability to transition to independence. Additionally, the proposal lacks critical experimental details, contains inaccuracies in the description of prior work, and does not fully address experimental rigor, which diminishes confidence in the project's successful execution.

### **1. Candidate:**

#### **Strengths**

- The candidate is a clinician, endodontist (BDS) - scientist (PhD) trained in India and Singapore, with background in biomaterials and bioengineering.
- Significant publication record in the field, first author.
- Was involved in translational aspects of research.
- Currently a postdoctoral fellow at UPenn NIDCR-R90 fellowship.
- Has immersed himself also in the biotechnology industry.

#### **Weaknesses**

- Clinical training in a field that is distant from the research field.

### **2. Career Development Plan/Career Goals & Objectives:**

#### **Strengths**

- Career goals are well crafted.
- Weakness areas are well identified and are focused to enhance the candidates knowledge and ability to pursue and independent research plan.
- The candidate has knowledge in fabrication of connective tissue constructs and investigating the immune response, adding knowledge in controlling the mechanical properties of such constructs would enable Dr. Makkar to successfully establish the groundwork for the proposed research plan.
- Leadership development together with immersing himself in a focused research group on mucosal immunology will augment his current clinical knowledge.

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### **Weaknesses**

- Grantsmanship training is not detailed.
- Main mentor is not experienced in successfully transition candidates into a tenured academic position.
- Defined milestones are lacking.
- The cadence of meeting with mentors and advisory committee specifically with the most senior member Dr. Hajishengallis is not clear.

### **3. Research Plan:**

#### **Strengths**

- The effect of ECM biomechanics on the onset and progression of periodontal disease is of importance and significance.
- The research design timeline is adequate.
- The R00 phase is well built upon training and skills development during the K99 phase.

#### **Weaknesses**

- Rigor of prior research and weaknesses are not well explained.
- Not clear which region in the periodontium are the gingival fibroblasts representing.
- In experiment 2 it is mentioned that transglutaminase will be injected to promote x-linking and tissue stiffening, this is an enzyme that does the opposite of what is written.
- Mechanical testing methods of in-vivo models is not clear.

### **4. Mentor(s), Co-Mentor(s), Consultant(s), Collaborator(s):**

#### **Strengths**

- Mentoring team and advisors have complementary and relevant skills in the areas that the candidate wishes to develop.
- There is a clear separation between the mentors research and the candidate's.

#### **Weaknesses**

- Mentoring plan is not clear without designated roles and objectives.

### **5. Environment and Institutional Commitment to the Candidate:**

#### **Strengths**

- Excellent environment.
- Excellent support from mentors and the institution.

#### **Weaknesses**

- None noted.

### **Protections for Human Subjects:**

Not Applicable (No Human Subjects)

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**Vertebrate Animals:**

YES, all criteria addressed

**Biohazards:**

Not Applicable (No Biohazards)

**Training in the Responsible Conduct of Research:**

Acceptable

**Resource Sharing Plans:**

Acceptable

**Authentication of Key Biological and/or Chemical Resources:**

Acceptable

**Budget and Period of Support:**

Recommend as Requested

**CRITIQUE 2**

Candidate: 2

Career Development Plan/Career Goals /Plan to Provide Mentoring: 3

Research Plan: 4

Mentor(s), Co-Mentor(s), Consultant(s), Collaborator(s): 2

Environment Commitment to the Candidate: 2

**Overall Impact:** This K99/R00 application is submitted by a dentist-scientist who demonstrates exceptional training and expertise in oral biology/bioengineering. The project aims to elucidate how extracellular matrix mechanics influence gingival fibroblast epigenetics and stromal, myeloid cell interactions, addressing critical and clinically relevant aspects of periodontitis pathogenesis. Robust preliminary data, coupled with a well-articulated career development plan and targeted training, substantiate the feasibility of the research. The institutional environment is exceptional, complemented by a structured career mentoring committee designed to ensure the candidate's progression and resource availability. The proposal encompasses a wide range of techniques and milestones, which may pose challenges. Additionally, the proposed research presents potential overlap with mentor's research. There are some methodological concerns relate to the need for strengthened statistical power justifications, relevance of circulating monocyte in the coculture model, and need for more rigorous controls to clearly differentiate experimental findings from hydrogel digestion artifacts. However, the applicant's strong career trajectory and the innovative, significant scientific objectives position this project as a medium-high priority.

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### **1. Candidate:**

#### **Strengths**

- Applicant has a robust dual training (DDS Ph.D. in Oral Sciences/Bioengineering).
- Applicant has multiple publications.
- Applicant demonstrated evidence of leadership and mentoring.

#### **Weaknesses**

- Applicant has less than 2 years of post-doctoral experience; independent track-record still maturing.

### **2. Career Development Plan/Career Goals & Objectives:**

#### **Strengths**

- Coherent plan and matching skill gaps including hands-on training in nano-indentation, spatial transcriptomics, mouse marrow-chimera periodontitis, leadership and grant-writing courses.
- Quarterly advisory-committee reviews, defined milestones (manuscript, R01 submission).

#### **Weaknesses**

- Timeline is ambitious (two publications and an R01 in Year 1).
- Contingency plans for delays (e.g., spatial-omics troubleshooting) are not described.

### **3. Research Plan:**

#### **Strengths**

- Compelling hypothesis that loss of gingival stiffness skews fibroblast epigenetics and stromal-myeloid crosstalk, exacerbating inflammation.
- Established in-vitro hydrogel system validated with preliminary mechanistic data.
- Sex as a biological variable is addressed.

#### **Weaknesses**

- Vertebrate-animal sections do not state group sizes or power calculations; reviewers may judge the study under-powered or unable to detect sex-specific effects.
- The project bundles epigenetic profiling, spatial transcriptomics, rheology, AFM, multi-photon SHG imaging, and bone-marrow chimeras in a single K99 aim. Each carries high failure risk and together they may exceed bandwidth of a new trainee.
- Ligature-induced periodontitis model may not capture ECM-softening etiology.
- No matrix-only monoculture controls. Without GF-free and monocyte-free conditions, it will be impossible to disentangle direct matrix effects from GF-secreted factors. Hydrogel digestion step confounds read-outs. Collagenase and alginate-lyase strip surface proteins such as CD14, CD80 and PD-L1 that are central outcome measures.
- Differential enzymatic kinetics across stiffness conditions may create artifactual differences during flow-cytometry.

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- Monocytes are generated ex vivo with potent drivers of dendritic differentiation that can mask mechanotransductive cues. Basal cytokine supplementation differs from the low-cytokine marrow micro-environment experienced by naïve monocytes.

#### **4. Mentor(s), Co-Mentor(s), Consultant(s), Collaborator(s):**

##### **Strengths**

- Primary mentor (Vining) is an early-stage PI with Nature Materials and ACS awards and >15 years of mechanobiology experience; co-mentor (Wells) is a senior mechanobiologist and AAAS Fellow, providing balance.
- Advisory committee includes internationally recognized leaders in periodontology, immunology and engineering, each providing explicit commitment letters and resources.

##### **Weaknesses**

- Both mentor and candidate study immuno-mechanobiology, and it is not clear how the applicant will differentiate himself from the mentor. Stronger delineation of proprietary reagents/datasets would help.
- Primary mentor is very accomplished but a new faculty, assistant professor recruited at 2022 and has limited mentoring experience.

#### **5. Environment and Institutional Commitment to the Candidate:**

##### **Strengths**

- Penn Dental/CiPD offers exemplary environment for this project.
- Vice-Dean letter guarantees ≥75 % effort, dedicated space, seed funding opportunities and travel support.

##### **Weaknesses**

- None noted.

#### **Protections for Human Subjects:**

Not Applicable (No Human Subjects)

#### **Vertebrate Animals:**

YES, all criteria addressed

#### **Biohazards:**

Not Applicable (No Biohazards)

#### **Training in the Responsible Conduct of Research:**

Acceptable

#### **Select Agent Research:**

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Acceptable

**Resource Sharing Plans:**

Acceptable

**Authentication of Key Biological and/or Chemical Resources:**

Acceptable

**Budget and Period of Support:**

Recommend as Requested

**CRITIQUE 3**

Candidate: 2

Career Development Plan/Career Goals /Plan to Provide Mentoring: 2

Research Plan: 4

Mentor(s), Co-Mentor(s), Consultant(s), Collaborator(s): 2

Environment Commitment to the Candidate: 2

**Overall Impact:** This new K99/R00 application is submitted by a dedicated and motivated dentist-scientist who is currently an NIDCR R90 postdoctoral fellow at the Center for Innovation & Precision Dentistry (CiPD) at the University of Pennsylvania. The main goal of the proposal is to understand how changes in the mechanobiology of the gingival extracellular matrix (ECM) contribute to the development of periodontitis, focusing on the role of ECM disruption by host and microbial proteases in disease progression. In healthy gingiva, gingival fibroblasts (GFs) and a crosslinked collagen type I ECM provide tissue stiffness and resistance to stretching. The candidate aims to compare how ECM mechanics influence myeloid immune responses via GFs in healthy versus diseased tissue. For Aim 1 (K99 phase), the project will test whether differences in ECM stiffness are linked to epigenetic changes in GFs, using an ECM hydrogel model to study inflammation. Preliminary data show that increased ECM stiffness reduces cytokine and chemokine responses. Aim 2 (R00 phase) will examine how ECM stiffness affects stromal-myeloid interactions, hypothesizing that stiffer ECM in healthy gingiva supports GF regulation of myeloid cell fate, while softer ECM in periodontitis disrupts this. This will be tested with a co-culture model and validated in vivo using a mouse model of ligature-induced periodontitis. The goal is to identify mechano-immune targets and develop new therapeutics for oral inflammatory diseases. The candidate and mentoring team have a strong track record, and the career development plan, mentorship, and institutional environment are excellent. However, the proposal is heavily focused on the interaction between gingival fibroblasts and collagen type I fibers, overlooking the roles of other important gingival cells such as oral keratinocytes (which form the gingival epithelium and protect against the oral environment) and junctional epithelial cells (which are crucial for tooth attachment and are lost during periodontitis progression). The study's rationale would be strengthened by considering how initial disruptions in GF-collagen interactions might lead to epigenetic changes in oral keratinocytes and junctional epithelial cells, which are also key players in periodontal disease. Overall, despite the weaknesses in the research plan, the project still generates a moderate-high level of interest.



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### **1. Candidate:**

#### **Strengths**

- Dr. Makkar is a highly productive and skilled postdoctoral fellow, as demonstrated by his strong record of first author and co-authored publications included in this application.
- One of his mentors' notes, "He frequently provides feedback on my grants and projects," highlighting Dr. Makkar's active engagement and expertise. This feedback underscores that Dr. Makkar has developed a rigorous training and research plan, leveraging his extensive background in periodontal disease research.
- Dr. Makkar currently leads the bio-subgroup in Dr. Kyle's research group meetings, demonstrating his leadership and initiative. Dr. Makkar will also participate in a variety of seminars and meetings. This highlights his capacity to lead independent research.
- Candidate is working with highly productive team of mentors and co-mentors in the field.
- The mechanobiology of gingival tissue at the host-microbe interface has not been explored by either my mentor, Dr. Kyle Vining, or co-mentor, Dr. Rebecca Wells, which also reflects about his progression towards independent pathway of research- very distinct from his mentors.

#### **Weaknesses**

- None noted.

### **2. Career Development Plan/Career Goals & Objectives:**

#### **Strengths**

- Dr Makkar is dentist-scientist, NIDCR R90 postdoctoral fellow at the Center for Innovation & Precision Dentistry (CiPD) of the University of Pennsylvania. Dr Makkar's goal has well-defined goal: to become a tenured professor and independently establishing a lab focused on immuno-mechanobiology and Tissue Engineering to study periodontitis and develop next-generation mechano-immune therapeutics.
- His commitment towards developing non-animal technologies for studying chronic oral inflammatory diseases and lead a collaborative team that encourages creativity and innovation. He also mentions his intention for Academia-industry partnerships to translate his innovative research into clinical solutions.
- Under the mentorship of Dr. Kyle Vining (primary mentor) and Dr. Rebecca Wells (Co-mentor), Dr Makkar will develop a deep understanding of biomaterial characterization and mechanically tunable hydrogel models, LIP model and cutting-edge molecular biology technologies.
- To develop leadership skills, Dr Makkar is committed to participate in the "Leadership Essentials Program" at the Perelman School of Medicine, University of Pennsylvania.
- His proposed work and expertise gained will make him distinct from his present mentors and co-mentors and therefore will greatly help him take the next step toward independent research.

#### **Weaknesses**

- A bioinformatician with expertise in high-throughput epigenomics would be helpful in training how to accurately assess the molecular changes during periodontitis progression.

### **3. Research Plan:**

#### **Strengths**

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- The project fills a critical knowledge gap by investigating the mechanobiology of the gingival extracellular matrix (ECM), an area that has been largely overlooked in periodontitis research.
- While microbial dysbiosis and host immune responses in periodontitis are well-studied, the immunological effects of changes in gingival tissue mechanics due to matrix degradation remain unclear. This grant aims to address this gap.
- The central hypothesis is well-founded and addresses a critical aspect of periodontal biology. By focusing on the role of gingival fibroblasts (GFs) in maintaining tissue integrity through the regulation of TIMPs and MMPs, the study highlights the importance of the balance between extracellular matrix remodeling and immune responses.
- The use of advanced ECM hydrogel models that mimic healthy and diseased gingival tissue allows for precise control and study of tissue stiffness, providing physiologically relevant insights.
- The results of this proposal will provide a solid basis for developing new therapeutic approaches that target fibroblast-mediated pathways in periodontal disease.
- The experimental design integrates cutting-edge technologies, which will enable a deeper and more precise investigation of the research questions.
- Strong preliminary data supports the rationale of the proposed study.
- Transcriptome analysis of GF encapsulated in soft and stiff hydrogels shows a robust shift in transcriptional response upon TLR2 treatment. This strongly supports the rationale proposed and will identify mechanistic details on GF response under different physiological conditions.
- Preliminary data presented in Fig 5, interestingly showed that TLR2 activation in stiffer hydrogels increased expression of the co-inhibitory molecule PD-L1 on GFs which promoted the emergence of M2-like macrophage signatures evidenced by higher double-positive expression of CD163 and CD206. Based on this, co-culture of GFs and HSC-derived monocytes in 3D gels of various degree of stiffness and their activation TLR2 agonist for 24 hours will enable to study how immune responses adapt to changing tissue mechanics in periodontal health and disease.

### Weaknesses

- Rationale of aim 1: the basis of study epigenetic modification is not clearly mentioned but seemingly worth to study.
- Figure 1 is not very clear authentication about immune infiltrates. Multi-parametric flow cytometry and RT-qPCR of their respective markers are needed to be presented here.
- The candidate mentioned that GFs respond to microbial and non-microbial stimuli by upregulating cytokines, chemokines, and matrix metalloproteinases (MMPs), with toll-like receptor 2 (TLR2) signaling for immune activation. But GF expresses TLR2, 4 and 9. There is no explanation TLR 2 expression and signaling is preferred over other TLRs.
- In Figure 3, agonists for additional TLRs, as well as LPS derived from periodontal pathogens, should be included to better represent the full spectrum of inflammatory signaling.
- To establish a basis for epigenetic evaluation, it will be suitable to perform either DNA methylation analysis using methylation-specific PCR (MSP) with pyrosequencing, or ChIP analysis of key GF remodeling genes in diseased versus healthy controls.
- The candidate plans to assess the pro-inflammatory environment by measuring IL-6, IL-8, CCL-2, CCL-5, and IL-1 $\beta$  using multiplex ELISA. However, it is unclear why other key cytokines involved in periodontitis, such as TNF $\alpha$  and IL-17, were not included in the analysis.

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- The scatter plots presented for flow cytometry do not clearly demonstrate proper gating or the induction of M2 macrophage-specific markers.
- For Aim 2, the candidate has not provided any in vivo data and only mentions plans to develop a ligature-induced periodontitis model. All figures in the proposal are based on in vitro data, which may not accurately reflect in vivo disease conditions. As a result, Aim 2 currently appears largely hypothetical.
- There is also no evidence that the candidate has successfully developed the in vivo ligature-induced periodontitis (LIP) model, which is essential for Aim 2.
- Isolating gingival fibroblasts from the LIP model and demonstrating epigenetic changes would only suggest these cells' involvement in periodontitis, without providing definitive evidence of their specific role.
- No justification for the power analysis (for animal size) provided based on the proposed experiments.

#### **4. Mentor(s), Co-Mentor(s), Consultant(s), Collaborator(s):**

##### **Strengths**

- A well-balanced team of one primary mentor and three co-mentors.
- Dr. Kyle H. Vining (Assistant Professor, Center for Innovation and Precision Dentistry) will mentor Dr. Makkar in biomaterial characterization, focusing on tunable hydrogel models and advanced techniques such as rheology, nanoindentation, AFM, and multi-photon microscopy, along with career development and job search support. Dr. Vining has mentored numerous students and postdocs across various disciplines and has the resources to support Dr. Makkar's training.
- Co-mentor Dr. Rebecca G. Wells (Professor and Co-Director, Center for Engineering Mechanobiology) will train Dr. Makkar in gingival tissue mechanics, ECM analysis, and histology in the mouse LIP model, as well as support his career development. CEMB's resources and collaborations will further strengthen Dr. Makkar's research.
- The Scientific Advisory Committee includes: Kang I Ko, DMD, DScD, who will support in vitro experiments as a board-certified periodontist and researcher; George Hajishengallis, DDS, PhD, who will advise on mouse bone marrow transplantation, spatial transcriptomics, and career development; Michael C. Abt, PhD, who will provide expertise in immune-microbiome interactions and germ-free mouse models; and Michel (Hyun) Koo, DDS, MS, PhD, and Kathleen J. Stebe, PhD, who will offer access to Penn resources and guidance on collaborations and career advancement.
- Recommendation letters of support from Dr. Sriram, Dr. Bottino, Dr. Rose, Dr. Lim, and Dr. Bostanci.

##### **Weaknesses**

- A bioinformatician with a strong publication record in high-throughput epigenomics and data analysis is needed as a consultant to help the candidate interpret complex data from various high-throughput analyses.

#### **5. Environment and Institutional Commitment to the Candidate:**

##### **Strengths**

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- Both the mentor and co-mentor (Dr. Rebecca Wells) are committed to meeting with Dr. Makkar every two weeks to discuss research, review progress, and assist with academic job preparation. This regular support will help Dr. Makkar complete his project and transition successfully to a faculty position.
- The letters of support state that Dr. Makkar will meet with mentors and scientific advisory committee to discuss strategies to advance his training and research. During these meetings, the mentors will also review and advise on his career development plans and how to achieve them.

**Weaknesses**

- None noted.

**Protections for Human Subjects:**

Not Applicable (No Human Subjects)

**Vertebrate Animals:**

YES, all criteria addressed

**Biohazards:**

Not Applicable (No Biohazards)

**Training in the Responsible Conduct of Research:**

Acceptable

**Resource Sharing Plans:**

Acceptable

**Authentication of Key Biological and/or Chemical Resources:**

Acceptable

**Budget and Period of Support:**

Recommend as Requested

**THE FOLLOWING SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE, OR REVIEWERS' WRITTEN CRITIQUES, ON THE FOLLOWING ISSUES:**

**UNALLOWED HYPERTEXT ADMINISTRATIVE NOTE:** During the review of this application, unallowed hypertext was noted in the application as only doi (digital object identifier) and .gov sites are allowed. Hypertext, hyperlinks, and URLs are only allowed when specifically noted in funding

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opportunities or application instructions. NIH is tracking this warning and has the authority to withdraw future noncompliant applications ([NOT-OD-20-174](#)).

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Footnotes for 1K99DE035581-01; PI Name: Makkar, Hardik

NIH has modified its policy regarding the receipt of resubmissions (amended applications). See Guide Notice NOT-OD-18-197 at <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-197.html>. The impact/priority score is calculated after discussion of an application by averaging the overall scores (1-9) given by all voting reviewers on the committee and multiplying by 10. The criterion scores are submitted prior to the meeting by the individual reviewers assigned to an application, and are not discussed specifically at the review meeting or calculated into the overall impact score. Some applications also receive a percentile ranking. For details on the review process, see [http://grants.nih.gov/grants/peer\\_review\\_process.htm#scoring](http://grants.nih.gov/grants/peer_review_process.htm#scoring).

## MEETING ROSTER

**Center for Scientific Review Special Emphasis Panel  
CENTER FOR SCIENTIFIC REVIEW  
Mentored, Career Transition, and Mid-Career K Awards**

**ZRG1 MSOS-F (80)  
07/22/2025 - 07/23/2025**

**Notice of NIH Policy to All Applicants:** Meeting rosters are provided for information purposes only. Applicant investigators and institutional officials must not communicate directly with study section members about an application before or after the review. Failure to observe this policy will create a serious breach of integrity in the peer review process, and may lead to actions outlined in NOT-OD-22-044 at <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-22-044.html>, including removal of the application from immediate review.

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