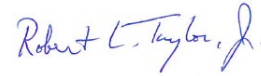


MEMORANDUM

TO: Richard Rhodes, PhD
Executive Director
NERA

FROM: Robert L. Taylor, Jr., PhD
Administrative Advisor, NE-1834



DATE: April 25, 2023

RE: Project Renewal NE-1834 (NE_TEMP2334) *Genetic Bases for Resistance and Immunity to Avian Diseases*

The renewal for the NE-1834 project renewal *Genetic Bases for Resistance and Immunity to Avian Diseases* has been reviewed by four external reviewers. The document has been revised in accordance with the reviewers' suggestions. Below please find the responses to these comments and the action taken. The renewal committee and I hope that these changes will be satisfactory. Three reviewers recommended *Approve/continue project* whereas the fourth reviewer recommended *Approve/continue project with revision*.

Thank you for the opportunity to revise and renew this project.

Reviewer 1 (received 04/05/23)

Comments: *Understanding the underlying causes and developing strategies for enhanced resistance to avian diseases will require a multidisciplinary approach involving genetics, genomics, immunology, cell and molecular biology, infectious disease, microbiology, nutrition, physiology and poultry medicine. During disease outbreaks (e.g., HPAI) and changing consumer demands (e.g., antibiotic-free), a better basic understanding is needed to develop novel strategies to address these challenges. The members of the proposed multistate project have expertise in a variety of complementary disciplines and have a documented record of collaboration not only within but also outside of the multistate project. Significant scientific contributions to our fundamental understanding of avian diseases will result from this multistate project.*

Your Recommendation: *Approve/continue project*

Action: **none required**

Reviewer 2 (received 04/10/23)

Comments: *Multi-hurdle approaches are urgently needed to address the interdisciplinary nature of avian diseases that continue to pose significant threat to both public and economic health. The team that comprises this multi-state project has shown strong collaborative efforts that successfully leverage team-member individual expertise into effective multidisciplinary approaches that maximize understanding of avian diseases. This multi-state project has demonstrated significant progress in addressing several such avian diseases, and the continuation of this research project is highly likely to result in novel solutions that solve important remaining challenges.*

Your Recommendation: *Approve/continue project*

Action: **none required**

Reviewer 3 (received 04/11/23)

Comments: *The first objective to be addressed will be to understand how genetics, epigenetics and gene regulation influences innate and adaptive immune responses. The work will include well characterized infection models to identify genes important in viral transmission, and delineate the immune pathways activated in response to bacterial infection. Work will also continue with well defined disease resistant and susceptible chicken lines to evaluate the role of regulatory sequences in the genome in response to infection. Defined genetic lines will also be used to identify genes encoding chicken alloantigens.*

The second objective will examine the influence of nutrition, the microbiome and postbiotic supplements on the development of innate and adaptive immunity in poultry. Immune dysregulation will be evaluated with viral and parasite infection models, and with chickens that develop autoimmune disease. These studies will further clarify how systemic inflammation contributes to immune dysfunction.

The third objective seeks to assess basic immune function in poultry using lines selected for resistance and susceptibility to economically important diseases and with animal models of autoimmune disease. Use of these valuable genetic resources in characterization of immune defense mechanisms in the responses to viral and bacterial infections will help identify genes controlling immune responses in poultry.

This research is essential to understand basic mechanisms of innate and adaptive immune responses in poultry. The collaborative effort involves investigators with integrated expertise that were very productive in the last 5-year period with an impressive 165 peer reviewed publications, 203 abstracts submitted, and 10 book chapters published.

Your Recommendation: *Approve/continue project*

Action: **none required**

Reviewer 4 (received 04/21/23)

Comments: *Well written proposal from a productive group. Projects planned should meet goals and enable excellent research to be conducted and published. Some suggestions for improvement of the proposal are as follows:*

Consider revising Objective 1 to include “poultry” as the area of focus (i.e., To determine how genetics, epigenetics and gene regulation influences innate and acquired immune functions in poultry). As written, the current objective is quite broad, which could lead to new members thinking they can contribute efforts focused on non-poultry immune function. It is unlikely that this was the intent of the current multistate project members.

Action: **Edited as requested**

Objective 1. To determine how genetics, epigenetics and gene regulation influences innate and acquired immune functions in poultry.

Portions of the Methods contain limited descriptions, making it challenging to evaluate the technical approach. For instance, for Objective 1, “...will explore some methods and tools in poultry health, making them available for community use” is not particularly informative or insightful. Consider revising to contain more explicit details about methodology. These concerns notwithstanding, in general, most of the methods do contain sufficient detail, should be feasible, and will provide valuable information.

Action: **Edited as requested**

Objective 1. To determine how genetics, epigenetics and gene regulation influences innate and acquired immune functions in poultry.

In the Outcomes or Projected Impacts and Milestones sections some further editing is needed for consistency in the bullet points. For instance, the first 3 bullets (Identification of..., Identification of..., Knowledge of...) read like outcomes or impacts. The next 2 bullets (Enhance poultry..., Characterizing genes...) do not. Suggest revising the latter, and others like them to be consistent. For instance, “Identification of alloantigen genes that improve the immune response to vaccine and pathogens, facilitating breeding for improved immune response in poultry and other species.” “Characterization of genes, and their regulation, in disease susceptible and resistant lines that will provide genetic biomarkers for selective breeding of chickens with high production traits and a robust immune system.”

Action: **Edited as requested (edits underlined)**

Identification of genes that are associated with resistance to heat stress and Newcastle disease virus and can be used to genetic enhancement of disease resistance of chicken in adaption to hot climate.

Identification of cellular factors important for transmission of MDV will allow better strategies to prevent and control MDV in poultry houses, as well as provide marker-assisted

selection and breeding.

Knowledge of associations of biomarkers with specific immune traits will allow genetic selection to enhance innate disease resistance in poultry, thus improving bird health and production.

Identification of alloantigen genes that improve the immune response to vaccine and pathogens, facilitating breeding for improved immune response in poultry and other species.

Characterization of genes, and their regulation, in disease susceptible and resistant lines that will provide genetic biomarkers for selective breeding of chickens with high production traits and a robust immune system.

Assessing the impact of microbial components and vaccine antigens on the direction and quality of the immune response, for application to modulate and optimize immune system function.

Classifying fundamental mechanisms of virulence evolution of Marek's disease virus via exosome studies that are essential to the understanding how these vesicles affect systemic immunity.

Interpreting the obtained results to better determine how disease occurs, identify the most effective means of prevention or mitigation at the tissue or cellular level and to develop targeted intervention.

Establishing mechanistic links between the microbiome, its metabolites and immune function to facilitate new ways of controlling the immune response of production birds

Identifying the mechanisms, magnitude, dose and duration of probiotics, acidifiers, and vaccine schedules to decrease incidence of important enteric or foodborne pathogens of poultry

Designing an effective vaccine against coccidiosis using T data for -cell subpopulations and their functions during coccidia infection in chickens

Publishing refereed papers, symposia, invited lectures and informal discussions at regional, national and international workshops and meetings to disseminate information to stakeholders and the public.

Similar issues exist in Milestones. Milestone 2023 is fine. The others should be edited for consistency. For instance, (2024) Detection of distinct alloantigen genotypes.... For (2025) A defined role for CHIR in infectious disease and reproduction in poultry. And so on....

Action: Edited as requested (edits underlined)

Milestones 2024

Detection of distinct alloantigen genotypes and their interactions that affect immune function.

Completion of functional annotation of chicken genome in selected cells and tissues.

Establishing immune response profiles to microbial components for phenotyping innate immune response capabilities in poultry populations.

Determining how mutations in Meq increase MDV virulence.

Establishing an in vitro system for evaluating identified metabolites' ability to regulate function of individual immune cells.

Measuring the dPCR response after infection.

Identifying the mechanism through which probiotics, acidifiers, and vaccine schedules decrease incidence of enteric pathogens of poultry
Submitting papers for publication

Milestones 2025

Examining data to better comprehend the range of factors and agents affecting the poultry immune system.

Establishing a definition of the CHIR role in infectious disease and reproduction.

Modeling key effectors of MDV virulence in vitro and in vivo.

Characterizing markers of immune response

Developing an in vivo system for validating the impact of identified metabolites on immune system regulation.

Identifying the magnitude of protection of probiotics, acidifiers, and vaccine schedules against enteric pathogens of poultry

Publishing papers in peer-reviewed journals

Milestones 2026

Characterizing gene regulation in infectious disease, differentiation of immune cells and reproduction, specifically enhancers.

Developing strategies to block MDV spread in poultry houses.

Targeting key immune responses with feed interventions

Characterizing the immunometabolism of negative responses.

Submitting papers for publication.

There is a growing trend for multistate groups to develop symposia at regional or national meetings where extension educators will be present to aid outreach efforts. It is unclear if the current Outreach Plan in which the technical committee invites industry stakeholders to attend also includes extension educators, but should be considered to help enhance the outreach goals.

Action: Edited by adding two sentences (underlined) to paragraph 1 of the outreach plan
The Technical Committee invites industry stakeholders to attend the annual project meetings. The frequent attendance of these stakeholders facilitates information exchange. Project members learn of the emerging problems which can be examined through experiments. Poultry breeding companies can learn of genetic impacts in the immune system. The information exchange often leads to successful collaborations. Additional extension personnel and other potential collaborators will be invited. The project scientists will disseminate their new data using refereed publications, symposia, invited lectures, informal discussions and online data bases of genetic lines and genome/transcriptome information. Participants will work to develop a symposium at a national meeting. The cooperative effort among project members and other researchers will include sharing scientific expertise and genetic resources held at numerous project stations will continue. This cooperation has enabled members to make significant scientific contributions to the improvement of poultry immune responses as well as the genetics of disease resistance.

Your Recommendation: Approve/continue project with revision