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INTRODUCTION

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Introduction to ecoimmunology: An integrative approach

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1 | INTRODUCTION

The immune system is critical for protecting animals from a litany of diseases, including established pathogens and parasites (e.g., influenza, malaria), as well as newly emerging infectious diseases such as Zika Virus. Although researchers have long recognized the importance of immunity within ecological research, only recently with the establishment of the field of ecological immunology (ecoimmunology), has it received formal empirical attention. To say it has been a challenge to study the immune system in groups of non-model organisms would be an understatement. This challenge is due, in no small part, to the fact that, unlike many other regulatory systems that show some degree of conservation across groups, a hallmark of the immune system is its diversity. This diversity is important for responding to both previously encountered and novel pathogens, but it also allows for specialization of immune responses within the broader contact of environmental, life history, and evolutionary forces an animal has experienced. While classic, model organisms have provided an important base of information on the organization of the immune system and its more specific mechanistic actions, efforts to understand the immune system in more natural contexts including its inherent variability have catalyzed the field of ecological immunology, which has grown tremendously in the past decade. Unlike traditional immunology, ecoimmunology is focused on understanding how the immune system responds in an environmentally relevant context. Often times, ecoimmunology studies are conducted in the field where animals are exposed to a myriad of ecologically relevant challenges that may affect their immune response. However, a number of critical studies also rely on more controlled, laboratory experiments that allow for more direct examination of immune function in response to interactive challenges, but always with ecological relevancy in mind.

In conversations with other ecoimmunologists over the years, we have found that there is tremendous excitement for the field (as evidenced by the increasing number of publications in the field and the recently established Division of Ecoimmunology and Disease Ecology at the Society for Integrative and Comparative Biology). Despite the substantial increase in research with an ecoimmunological focus, it remains challenging to find an appropriate venue to publish one's findings. There is a gap among ecological journals, immunology or physiology journals, and the more taxonomically focused venues that are home to many non-model organism publications. This special issue on ecoimmunology was conceived, in part, to illustrate the breadth of research questions being addressed by ecoimmunologists, and to highlight recent advances in methods that may be of use to those in the field or interested in pursuing related questions. An additional, equally important goal is to introduce the *Journal of Experimental Zoology Part A: Ecological and Integrative Physiology* as a venue that is welcoming to ecoimmunology research. Consistent with this mission, the journal was recently renamed *Ecological and Integrative Physiology*, replacing its former subtitle, *Ecological Genetics and Physiology*, to reflect its focus on emerging areas of integrative research including ecoimmunology. Contributions for this special issue were solicited from established leaders in the field as well as from newer laboratories that are adding to the rich diversity and integrative nature that characterizes ecoimmunology.

2 | TAXONOMIC APPROACHES

Papers in this special issue help illustrate the breadth of taxonomic systems of study and the immunological approaches being employed in these systems, as well as the diversity of important ecological and theoretical questions being addressed. To just give a brief idea of taxonomic diversity, species of study range from many different regions and include invertebrate to avian, and reptilian to mammalian. Invertebrate species investigated in this current issue are the bumblebee (*Bombus impatiens*), the weevil (*Curculio* sp., Coleoptera), the gallfly (*Eurosta solidaginis*, Diptera), and larvae of the lepidopteran *Pyrrharctia isabella* (Czerwinski & Sadd, 2017; Ferguson & Sinclair, 2017). Avian species include the house wren (*Troglodytes aedon*), the golden eagle (*Aquila chrysaetos*), the song sparrow (*Melospiza melodia*), the European starling (*Sturnus vulgaris*), and the zebra finch (*Taeniopygia guttata*) (Bowers, Sakaluk, & Thompson, 2017; Grindstaff & Merrill, 2017; Kelly et al., 2017; MacColl et al., 2017; Pryor & Casto, 2017). Reptilian species represented in the current issue are the green anole (*Anolis carolinensis*), the gopher tortoise (*Gopherus polyphemus*), and the snapping turtle (*Chelydra serpentina*) (Beck, Thompson, & Hopkins, 2017; Goessling et al., 2017; Tylan & Langkilde, 2017). Finally, one mammalian species is also represented, the polar bear (*Ursus maritimus*) (Neuman-Lee et al., 2017). The paper by Brace et al. took a meta-analytic comparative approach to studying immunity across taxonomic groups.

3 | METHODOLOGICAL APPROACHES

Similar to the taxonomic diversity among study organisms, technical approaches to conduct ecoimmunological research also vary considerably. Some techniques are more generalizable to assess constitutive or innate immunity, while others are more specialized and species-specific approaches to measure acquired immunological responses. Constitutive immune measures of bactericidal ability assess the blood's ability to kill foreign bacteria via an integrative immune response can be accomplished using essentially any blood, hemolymph, or secretive sample and has been used in a number of different species. Comparing the effects of freezing and repeated freeze–thaw cycles on plasma in this commonly used ecoimmunological test, between hatchling and adult snapping turtles, Beck et al. (2017) found that samples could be frozen for periods of time prior to running the assay, the assay is robust to at least one bout of thawing, but that the assay should be validated for individual species. Phytohemagglutinin (PHA) is a mitogen that can be used in virtually any species to simulate a proinflammatory response that can be measured via swelling of a particular area or tissue (Bowers et al., 2017). Although this assay is most commonly used in birds, Tylan and Langkilde (2017) present results for a validation of PHA use in the green anole. A comparison of different formulations reveals that while PHA does activate the immune system of the green anole, different cell types are preferentially activated by PHA-L versus PHA-P, providing a cautionary tale about carefully selecting immune reagents (Tylan & Langkilde, 2017). Manipulations of parasite load to assess interactions with immune system can be accomplished using pesticide treatment of environment including nests in avian species (Pryor & Casto, 2017).

Researchers can also focus more specifically on certain aspects of an immune response, using for example macrophage phagocytosis activity tests the functionality of macrophages (Kelly, MacGillivray, Hobson, MacDougall-Shackleton, & MacDougall-Shackleton, 2017). Specialized approaches are also available in a number of species, including assessing acquired immunoglobulin Y titers in birds (Kelly et al., 2017). Specific antibody responses to lipopolysaccharide (LPS), a mitogen used to mimic bacterial infection, were assessed in zebra finches (Grindstaff & Merrill, 2017).

4 | THEORETICAL APPROACHES

With the use of this wide array of ecoimmunological tools, key ecological and evolutionary questions can be addressed, thereby incorporating ecoimmunology into important theoretical frameworks. One major theme that has arisen within the field is understanding how immunity affects life history trade-offs. Brace et al. (2017) employed a phylogenetic meta-regression to test the idea that immune responses are costly and, given finite energy, must inherently trade off with other costly processes including growth and reproduction. Their analysis reveals that animals generally incur costs of immune activation, but small species that are relatively long-lived incur the largest costs (Brace et al., 2017). Looking more specifically within a species, European starling nestlings from nests infected with mites showed reduced bactericidal ability during periods of rapid somatic growth (Pryor & Casto, 2017). There are also interactions between reproductive age and offspring quality, whereby maternal and paternal ages have both differential and interactive effects on offspring immunoresponsiveness in house wrens (Bowers et al., 2017). Lastly, snapping turtles show age-related differences in immunity, where adult bactericidal capacity was greater than that of hatchlings (Beck et al., 2017).

Understanding how changing environments and external stressors impact immunity is also emerging as a common theme within ecoimmunology. The paper by Czerwinski and Sadd (2017) examined the effects of environmental pesticides on immune function in honey bees. Their study showed that exposures to the neonicotinoid pesticide, imidacloprid, altered immunity, and that exposure to the pesticide followed by an immune challenge significantly decreased survival, suggesting critical health consequences for pollinators facing multiple stressors (Czerwinski & Sadd, 2017). However, early life exposure to elevated corticosterone did not affect the immune response of zebra finches as assessed by an LPS challenge or by bactericidal capacity (Grindstaff & Merrill, 2017).

Understanding how environmental context and life history shapes immunological profiles is another common question. Kelly et al. (2017) demonstrated that song sparrows shift from innate to more acquired immune defenses when transitioning between life history stages of migration to breeding. Comparing seasonal responses in hemocyte numbers, phenoloxidase activity, humoral antimicrobial activity, melanization response, and the ability to survive fungal infections in three species of insects that have different overwintering strategies reveals that there are no generalizable patterns of immunity with changes in season (Ferguson & Sinclair, 2017). How the immune responses of different insects will react to changing environmental conditions remains an open question, as it is clear that one strategy does not fit all. Along these same lines, the paper by Goessling, Koler, Overman, Hiltbold, Guyer, and Mendonça (2017) evaluated the direct effects of rapid temperature change on immunity in gopher tortoises and showed that during summer, but not winter, rapid temperature reduction caused a series of changes in immunity. Their findings demonstrate that rapid temperature changes constrain immunity in ectothermic vertebrates, which has implications for global climate change (Goessling et al., 2017). Two of the studies in this special issue fall into this final theme but are focused on species of conservation concern (golden eagles and polar bears) and illustrate the utility of ecoimmunological approaches in conservation. MacColl et al. (2017) examined how *Leucocytozoon* parasite presence and body condition affected immune defenses in golden eagle populations. While body condition and age did not affect immune defenses, eagles with *Leucocytozoon* infections had higher concentrations of circulating complement proteins but not elevated opsonizing proteins for all microbes, suggesting that some eagles elevate immune defenses because they are exposed to more parasites (MacColl et al., 2017). Similarly, Neuman-Lee et al. (2017) demonstrated important links between the immune system and other physiological systems over time to better understand the health status of polar bears across demographic stages. Understanding natural variations in physiology and immunity over time lay the groundwork for interpreting responses to changing environments and climates.

5 | CONCLUSIONS

As the papers within this special issue demonstrate, a basic, integrative, and comparative approach to studying the immune system will allow us to develop a common theoretical framework for understanding interactions among environmental, physiological, and behavioral factors and their impact on health and disease within a larger ecological and evolutionary context. While current research directions are even broader taxonomically, technically, and ecologically than what is presented in this special issue on ecoimmunology, we think that this array of papers effectively demonstrates at least some of the integrative approaches now underway in ecoimmunology. Whether you are an established researcher, or just starting to investigate ecoimmunology, it is clear that this is an exciting time to be a part of this rapidly growing and ever-changing field.

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