

# Lifetime achievements in avian physiology

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# Lifetime achievements in avian physiology

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## Table of contents

- 04 **Editorial: Lifetime achievements in avian physiology**  
Colin G. Scanes and Sandra G. Velleman
- 07 **Sexual dimorphism for juvenile body weight in chickens divergently selected for 8-week body weight**  
Paul B. Siegel and Christa F. Honaker
- 14 **General commentary: sexual dimorphism for juvenile body weight in lines of chickens selected for 8-week body weight**  
Colin G. Scanes
- 18 **A career reflection**  
Sandra G. Velleman
- 22 **The journey of a lifetime: reflections on my career**  
Zehava Uni
- 27 **Growth hormone: lessons from chickens**  
Colin G. Scanes
- 31 **Sometimes it's good to be lucky: blood flow, glutathione, oxidative stress, and mitochondria**  
Walter Gay Bottje
- 35 **A university career in basic and applied avian immunology: important contributions of chicken models for autoimmune diseases**  
Gisela F. Erf
- 40 **Met-enkephalin and other opioid peptides in the stress response of chickens: lessons from laboratory animals and livestock**  
Krystyna Pierzchała-Koziec and Colin G. Scanes
- 44 **A career reflection: lifetime achievements in avian neuroanatomy and physiology**  
Wayne J. Kuenzel



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# Editorial: Lifetime achievements in avian physiology

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## KEYWORDS

growth hormone, intestinal development, met-enkephalin, mitochondria,  
neuroendocrine, satellite cells, sexual dimorphism, stress

## Editorial on the Research Topic Lifetime achievements in avian physiology

Lifetime Achievements in Avian Physiology topic provides a tantalizing account of achievements and philosophy of a series of senior avian physiologists. These papers represent only a fraction of the giants in research in avian physiology, specifically the physiology of chickens and other poultry species. The senior researchers are considered in alphabetical order of their last names.

Walter Bottje has had an illustrative research career. He states his passion as “physiology was really what floated my boat”. His research career in avian physiology began with a series of studies on heat stress in broiler chickens. Among his achievements include the following:

- Relationships between celiac blood flow and prostaglandins
- Oxidative stress/glutathione (GSH)/Reactive oxygen species (ROS)
- The functioning of mitochondria in muscle and how this affects feed efficiency
- Mitochondrial dysfunction including defects in the electron transport mechanism

and what he describes as “the gene and gene product landscape associated with feed efficiency”.

Erf has had a distinguished research career in basic and applied avian physiology. Among her research achievements in poultry included the following:

- The role of maternally derived immunoglobulins
- Relationships between genetics and stressors on the immune system
- Improving poultry health by immunomodulators.

Wayne Kuezel spent sabbaticals at the Roslin Institute (Scotland), Justus Liebig University Giessen (Germany) and Nanjing Agricultural University (China). During these, he gained from immersive collaboration catalyzing his overall research career going from strength to strength. Among the stellar contributions of Wayne Kuezel are the following:

- The development of a stereotaxis atlas for the chicken’s brain.
- The distribution of gonadotropin releasing hormone (GnRH) containing neurons and fibers in the avian brain.

- Advances in our understanding the neuroendocrine basis of stresses such as feed deprivation and restraint in chickens.

Krystyna Pierzchała-Koziec has had an outstanding research career. Her achievements have been in four, somewhat overlapping, areas:

- Stress physiology in chickens and livestock
- The physiology of Met-enkephalin
- Hormonal and neuroendocrine control of metabolism
- Fostering world-class basic and applied research in Poland and throughout Europe.

Scanes was drawn to avian physiology by two wonderful mentors: the late Professor John Phillips and Professor Sir Brian Follett in the UK. His research has included a prolonged focus on growth hormone (GH). His paper discusses GH effects in chickens on growth, lipid metabolism, reproduction, neural development and angiogenesis together with the control of GH release. He also introduces a series of questions that have not been addressed.

Production of chicken meat has expanded greatly over the last 50 years. According to FAOSTAT, production was 7.56 Mt (megatonne) in 1961, increasing to 15.9 Mt in 1974, 56.9 Mt in 1999 and 123.8 Mt in 2024. These dramatic increases can be attributed to genetics (growth being moderately heritable), nutrition, poultry health and management. We were delighted that Siegel agreed to contribute to this topic. He is the “father of poultry genetics”. He chose to focus on one aspect of his long and on-going research career, namely; sexual dimorphism in body weight in chickens. When this is considered on a proportional manner, there is continuing sexual dimorphism in chickens selected for growth (high body weight and low at eight weeks old) over 67 generations. This work and the physiology of sexual dimorphism in birds is also discussed in a commentary by Scanes.

Uni has an outstanding record of achievement in avian physiology. Her research can be classified as comprehensive and impactful.

- Development of the gastro-intestinal tract of chickens
- *In ovo* feeding in chickens and how *in ovo* feeding influences the proliferation, differentiation and maturation of epithelial cells in the small intestine
- The molecular basis of taste.

In 1955, U.S. Air Force Major General Frederick C. Blesse stated “No Guts, No glory”. This adage became one of Zehava Uni’s principles for a successful researcher. She also included the importance of resilience to adversity, flexibility and following “your true passion”.

Sandra Velleman’s interest in science was fostered from a very young age by her mother. One teacher recognized her research skills at a time of life when she was not even sure what a research scientist was. We are fortunate that she went on to an exemplary research career. Throughout her career, Sandy Velleman’s guiding predisposition was that extracellular matrix is a critical important component in non-connective tissues including muscle despite the then paradigm that extracellular matrix was not. She took the “risk”

to challenge the prevailing paradigm. Her laboratory was the first to demonstrate that satellite cells produce extracellular matrix proteoglycans using chicken breast muscle satellite cells. Velleman has a series of other land-mark achievements, namely, the following: 1. satellite cells are heterogeneous; 2. muscle development of muscle and consequently meat is influenced by extrinsic conditions (temperature and nutrition) and 3. maternal inheritance of aspects of muscle morphology.

There are some common themes from the papers and the distinguished avian physiologists. These include the following:

- The importance of mentors, collaborators and others providing the stimulus for research direction and the development of research programs.
- The importance of passion and willingness to challenge prevailing paradigms and/or develop a focuses research program(s).
- Collaborators and collaboration play a pivot role in research in avian physiology.

A common theme is the role of mentors. Examples of the sway of mentors include the late Paul Harrison (University of Illinois) for Walter Bottje and both Robert Etches and Robert Marsh for Gisela Erf. Turning to collaboration, the partnership between Sandy Velleman and Douglas McFarland was very fruitful building on the strengths of both researchers. Another example of close, successful and ongoing collaboration is that between Pierzchała-Koziec and Scanes on stress and opioid peptides. Bottje highlights the effect of a single discussion with Robert Wideman. Research lives have been changed by people and environments. It is interesting to note that three of the contributions come from the University of Arkansas, Center of Excellence in Poultry Science.

There are two quotations that provide insight into to the role of luck in research “Give me lucky generals” and what is a pertinent rejoinder “I am a great believer in luck, and I find the harder I work, the more I have of it”; these being attributed, albeit falsely or at least without supporting evidence, to respectively to Napoleon Bonaparte (1769-1821) and Thomas Jefferson (1743 - 1826). We are left with the statement from Louis Pasteur stated that “In the fields of observation chance favors only the prepared mind” in 1854 (Leonard, 2013).

## Author contributions

CS: Conceptualization, Writing – original draft, Writing – review & editing. SV: Conceptualization, Writing – review & editing.

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# Sexual dimorphism for juvenile body weight in chickens divergently selected for 8-week body weight

Paul B. Siegel\* and Christa F. Honaker

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There is a dearth of literature on the genetics of sexual dimorphism for juvenile body weight in meat-type chickens given its biological and economic relevance. Herein, we report the sexual dimorphism for 4- and 8-week body weights in White Plymouth Rock chicken lines that have undergone 67 generations of selection. Fluctuations in the degree of dimorphism occurred across generations, with greater dimorphism and less variation at 8 weeks than 4 weeks. Over the 67 generations, there was a significant decrease in the degree of dimorphism in the high line, with no changes in the low line. It is very difficult to genetically modify sexual dimorphism in a particular population using the currently available conventional tools, and nature possesses homeostatic mechanisms that maintain stasis in a population.

## KEYWORDS

chicken, body weight, selection, dimorphism, homeostasis

## Introduction

The weight of an organism at any point in its life can be considered a function of its genetic and environmental histories. Sexual dimorphism for body weight varies among gallinaceous birds, with male birds being heavier than female birds (e.g., chickens) or female birds being heavier than male birds (e.g., Japanese quail). In both cases, the degree of dimorphism at a specific age differs depending on the developmental and physiological aspects at the time of comparison. Furthermore, Rensch's rule for sexual dimorphism for body weight in wild birds has been compromised in the case of the domestic chicken (Remeš and Székely, 2010).

Chickens were domesticated during the Neolithic period and have been amenable to artificial selection for various traits, including those focusing on sport, show, ceremony, and foods (Smith and Daniel, 1975). Chicken meat as food was primarily a result of traits selected for other purposes until the past century, when specialized breeding programs were designed for rapid juvenile growth (Siegel, 2014, 2023). This development was genetically facilitated by the availability of foundation stocks (Hanke et al., 1974), short generation intervals, and moderate heritability for juvenile body weights. Crosses between breeds and lines within the breeds allowed the breeders to protect their commercial products. The number of days to market weight has reduced dramatically (Havenstein et al., 2003; Zuidhof et al., 2014), and the age at market weight is currently measured in days instead of weeks. Because of sexual dimorphism in juvenile body weights, male and female birds attain their market weights at different ages; hence, sex-separate rearing is not uncommon and has become more popular. High-speed imaging and artificial intelligence tools have allowed

autosexing of chicks at hatching through differences in the lengths of the primary and covert wing feathers, thereby replacing tedious human labor. Specific matings are needed, which are the result of sex-linked genetic effects (Chambers et al., 1994). Correlated responses, including increased feed intake (Carney et al., 2022), are associated with rapid juvenile growth and heavier body weights at younger ages. To address the potential cardiac, skeletal, and metabolic issues associated with excessive feed intake in the body weights of the breeders (adults), feeding programs to achieve the target body weights are readily available in management manuals provided by commercial distributors for their particular stocks.

Although the heritabilities for juvenile body weight in chickens can date back to several decades, as seen in the 176 summarized cases (Siegel, 1962), reports on the inheritance of sexual dimorphism *per se* are sparse. Sexual dimorphism for body weight in chickens can be viewed as the absolute or proportional differences between male and female birds. Thus, while the former may increase or decrease, the latter can remain constant or change. The inheritance of differences between the sexes for a common trait is confounded by multiple factors. Merritt (1966) and Mignon-Grasteau et al. (1998) provided valuable data and insights into the genetics involved as well as low heritability. Subsequently, Adedibu and Ayorinde (2011) reported the genetic differences in male to female body weight ratios at 4 and 8 weeks in one stock but only at 8 weeks in another stock. Maniatis et al. (2013) reported a genetic correlation of 0.91 for body weight between the sexes at 35 days, with heritabilities of 0.04 for the body weight differences and ratios. Although these results allow inference of little genetic variation for sexual dimorphism for juvenile body weights, differences among various breeds are well documented (American Poultry Association, 1947).

Starting from a common founder population of White Plymouth Rock (WPR) chickens, we developed two lines by divergent selection for a single trait, namely, body weight at 8 weeks (56 days) of age. After 67 generations of divergent selection, the two lines differed by more than 10-fold without any overlap in the body weight at selection age. Herein, we report the sexual dimorphisms for body weights at 4 and 8 weeks of age across the 67 selected generations as well as the founder population of these two lines.

## Materials and methods

### Animal use and care

All procedures and protocols used in this study as of 1997 have been approved by the Institutional Animal Care and Use Committee at Virginia Tech. Prior to 1997, the chickens were treated in a similar manner despite the university not having stated guidelines and protocols.

### Genetic lines

In 1957, a total of 15 male birds and 87 female birds from seven moderately inbred lines of early feathering WPR chickens were mated to produce a pedigreed population. This population provided the base for a selection experiment to produce two pedigreed lines,

where one was selected for high body weight (HW) and the other for low body weight (LW) at 8 weeks post-hatching (Siegel, 1962; Dunnington and Siegel, 1996; Dunnington et al., 2013; Jambui et al., 2017). Although the selection of the parents to produce subsequent segregating generations was based on the body weights of the male and female chickens at 8 weeks of age, there were restrictions to avoid strict truncation. At hatching, caution was taken not to overrepresent progeny from a sire and from dams within a sire. Where possible, full- and half-sib matings were avoided when selecting parents for the subsequent generations. Over the 67 generations reported herein, adjustments were made to the breeding population. Within each line, the number of sires was increased from 8 to 12 at the fifth generation. Then, we increased these numbers to 14 sires and 56 dams in the twenty-sixth generation. Throughout the study, each sire was assigned four dams. The numbers of effective parents in these lines have been reported earlier (Marquez et al., 2010; Harrison et al., 2023).

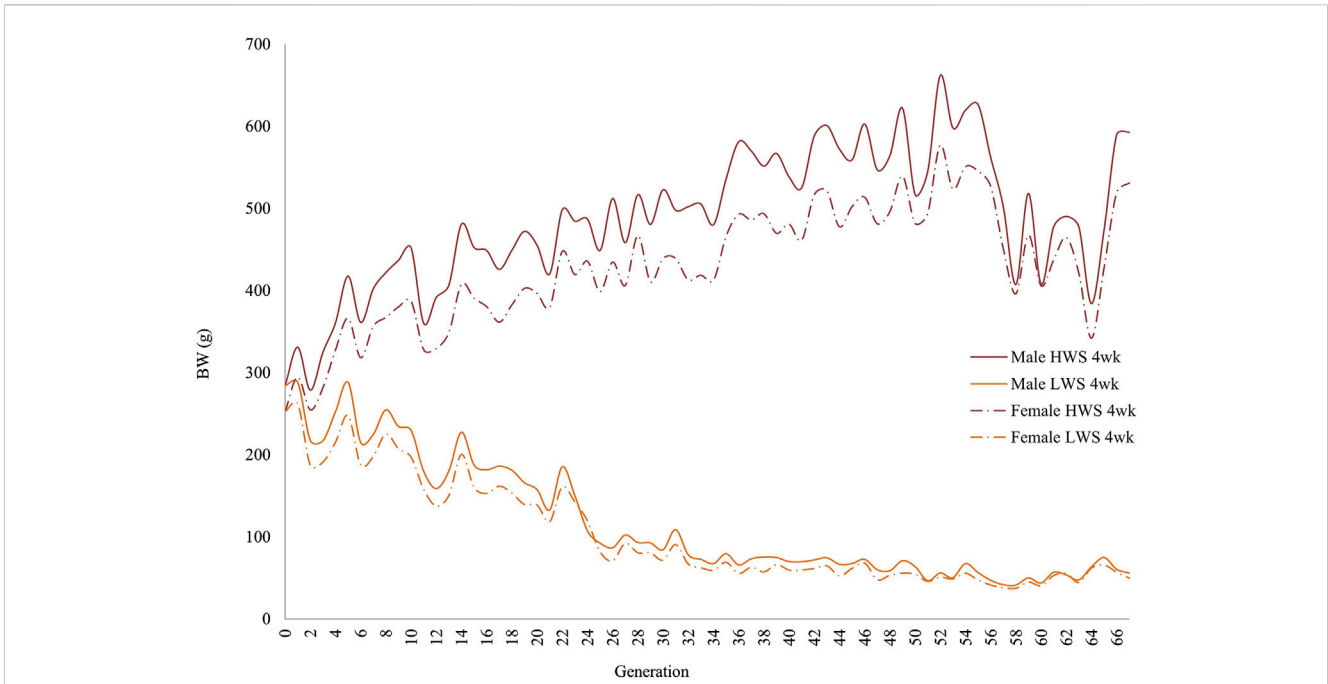
### Husbandry

The incubation and grow-out facilities were the same across all generations. Thus, there is some redundancy here with prior works (Dunnington and Siegel, 1996; Jambui et al., 2017). One generation was produced each calendar year, with the hatch date being the first Tuesday in March. There was also a second “insurance” hatch 2 weeks later. In some generations, chickens from the second hatch were used to reproduce the next generation. On day 22 of incubation, the chicks were removed from the hatcher and wing-banded for pedigree. Starting from the seventeenth generation, the chicks were vaccinated for Marek’s disease after wing-banding. Brooding was conducted in the same building every year, and the only exception to this was in generations 54–63 where the LW chicks were brooded in battery cages until 2–4 weeks of age before being placed in the floor pens.

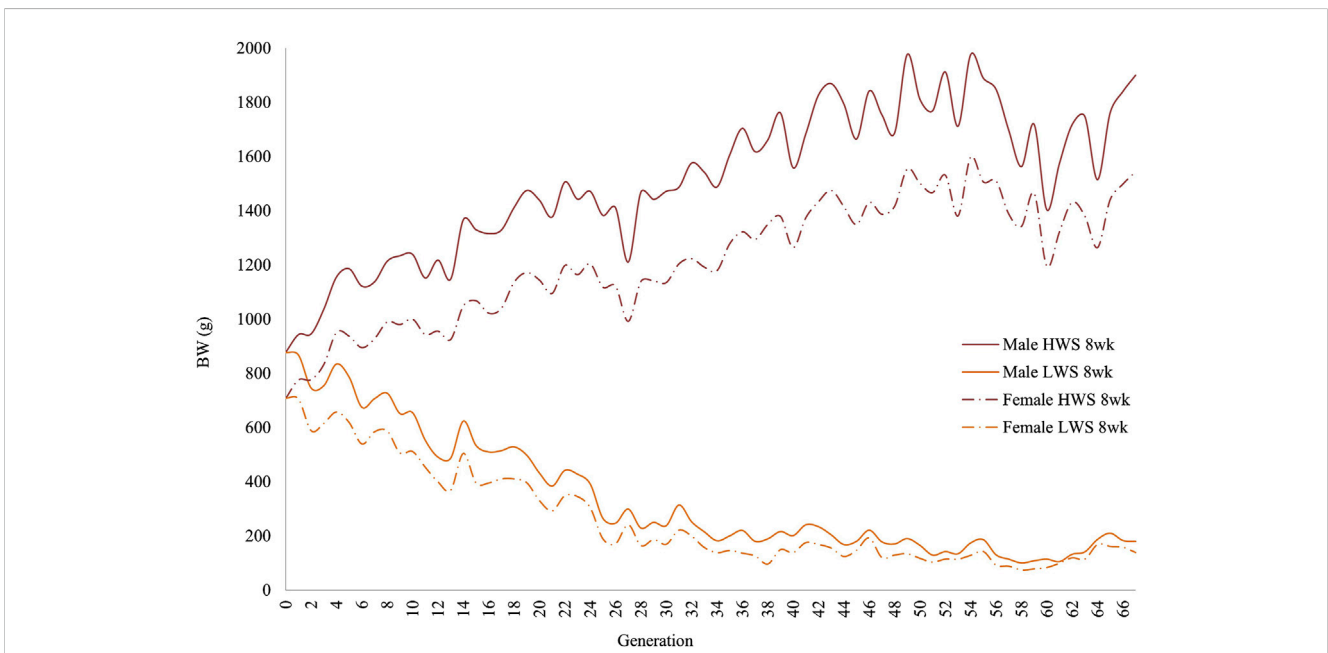
The lighting was continuous, with the litter being wood shavings on a concrete floor; the brooding was hot air supplemented with heat lamps. Water and an antibiotic-free mash diet containing a coccidiostat were allowed *ad libitum* throughout the study period. The diet was formulated to consist of 20% crude protein (CP) with a metabolizable energy (ME) of 2,685 kcal/kg. These values may have varied slightly from generation to generation owing to ingredient availability. Because of feed mill closing in the year 2022, we had to adjust the diet to 21% CP and 2,650 kcal/kg of ME.

### Traits measured and statistical analyses

In each generation, the individual body weights (g) were obtained at 4 and 8 weeks of age. Then, we calculated the means, standard deviations, and ratios (%) of female to male birds (lower the value, greater is the dimorphism) for each of the line-generation groups. Because the parental generation was a combination of several lines, it was analyzed separately from the two selected lines. Correlations between the means and generations were calculated for each line along with the regressions of means on the generations. For short-term associations, the generations were divided into six generational periods (2–12, 13–23, 24–34, 35–45,



**FIGURE 1**  
Generational mean body weights of the male and female chickens in the high (HWS) and low (LWS) body weight selected lines at 4 weeks of age.



**FIGURE 2**  
Generational mean body weights of the males and females in the high (HWS) and low (LWS) body weight selected lines at the 8-week selection age.

46–56, and 57–67) and overall (1–67) for the correlation and regression analyses. The percentages were converted to arcsine of their square-root values for analysis. Although the subdivisions of the time trends indicate multiple uses of the same data (period within overall and overall), they provide short- and long-term insights.

## Results

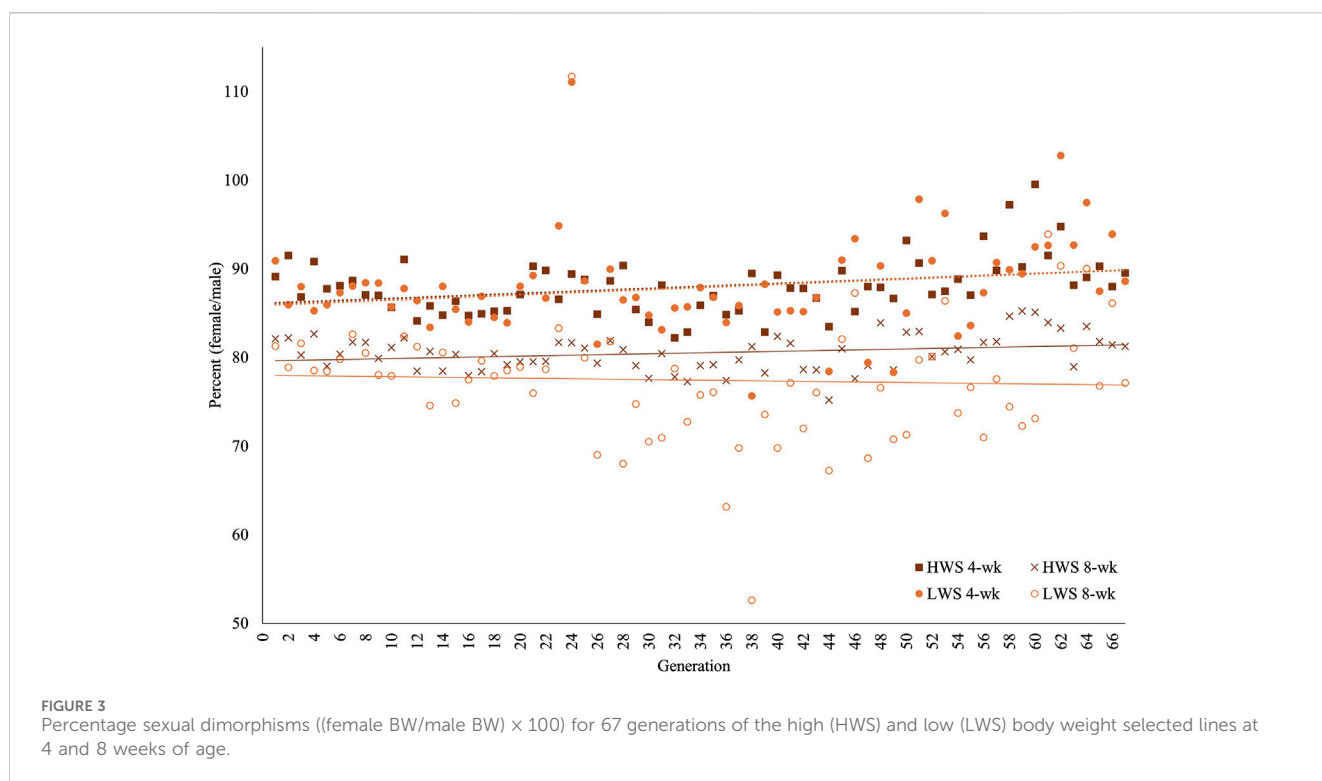
In both selected lines, the male chickens were consistently heavier than the female chickens at 4 and 8 weeks of age (Figures 1, 2). At 4 weeks, although the generational pattern was consistent for all generations of HW chickens, the degree of

TABLE 1 Sexual dimorphisms (female BW/male BW expressed as a percentage  $\pm$  SD<sup>a</sup>) by generational interval and overall at 4 and 8 weeks of age for the high (HW) and low (LW) body weight lines<sup>b</sup>.

Generation	4 weeks		8 weeks	
	HW	LW	HW	LW
F <sub>2</sub> –F <sub>12</sub>	88.04 $\pm$ 2.32	87.02 $\pm$ 1.18	80.88 $\pm$ 1.38	79.99 $\pm$ 1.76
F <sub>13</sub> –F <sub>23</sub>	86.44 $\pm$ 1.95	86.81 $\pm$ 3.30	79.61 $\pm$ 1.11	78.23 $\pm$ 2.53
F <sub>24</sub> –F <sub>34</sub>	86.42 $\pm$ 2.80	88.31 $\pm$ 7.92	79.66 $\pm$ 1.65	77.63 $\pm$ 12.17
F <sub>35</sub> –F <sub>45</sub>	86.75 $\pm$ 2.40	84.75 $\pm$ 4.29	79.38 $\pm$ 2.09	70.86 $\pm$ 7.97
F <sub>46</sub> –F <sub>56</sub>	88.70 $\pm$ 2.71	87.71 $\pm$ 6.59	80.73 $\pm$ 1.98	76.56 $\pm$ 6.30
F <sub>57</sub> –F <sub>67</sub>	91.63 $\pm$ 3.83	92.55 $\pm$ 4.39	82.81 $\pm$ 1.95	81.16 $\pm$ 7.66
F <sub>1</sub> –F <sub>67</sub>	88.01 $\pm$ 3.19	87.91 $\pm$ 5.42	80.53 $\pm$ 2.03	77.46 $\pm$ 7.71

<sup>a</sup>Standard deviation (SD) is for each analyzed generational interval.

<sup>b</sup>Parental (P<sub>0</sub>) generation dimorphisms were 88.9% and 80.8% at 4 and 8 weeks, respectively.



difference varied. For LW chickens, although the dimorphism followed the same pattern (males > females), some generations had slight differences between the male and female chickens. By 8 weeks, the magnitudes of dimorphism were more accentuated, with the male and female chickens consistently reflecting the within-generation environments.

On a relative basis (with lower percentage indicating greater dimorphism), the greater dimorphism in the founder populations at 8 weeks (80.8%) than 4 weeks (88.9%) continued throughout the 67 generations in both HW and LW chickens (Table 1; Figure 3). When viewed across the 67 generations, there were generations when the relative sexual dimorphism for body weight appeared to increase or decrease. This “self-correction” pattern was observed at

both ages, with the variation being greater in LW than HW chickens and more evident in the later than earlier generations (Table 1). The magnitude of variation in the HW chickens was consistently greater at 4 weeks than 8 weeks. In the LW chickens, the variation at 8 weeks was greater than that at 4 weeks, except for the F<sub>13</sub>–F<sub>23</sub> and F<sub>46</sub>–F<sub>56</sub> periods.

The same data were used in both the correlation and regression analyses because the evidence was unclear for cause–effect associations; the results obtained from these analyses were also similar. At 4 weeks, the regressions for both lines across all generations were essentially superimposed, while they were different at 8 weeks (Figure 3). Quantifications of these graphic patterns are provided in Tables 2, 3 for 4 and 8 weeks of age,

**TABLE 2** Correlations and regressions<sup>a</sup> of the percentage sexual dimorphisms (female BW/male BW) by generational interval and overall at 4 weeks of age for the high (HW) and low (LW) body weight lines.

Generation	Correlation		Regression	
	HW	LW	HW	LW
F <sub>2</sub> -F <sub>12</sub>	-0.49	0.23	-0.35 ± 0.20	0.08 ± 0.12
F <sub>13</sub> -F <sub>23</sub>	0.63*	0.63*	0.37 ± 0.15*	0.62 ± 0.26*
F <sub>24</sub> -F <sub>34</sub>	-0.61*	-0.50	-0.52 ± 0.22*	-1.19 ± 0.69
F <sub>35</sub> -F <sub>45</sub>	0.18	0.12	0.13 ± 0.24	0.16 ± 0.43
F <sub>46</sub> -F <sub>56</sub>	0.41	0.02	0.34 ± 0.25	0.04 ± 0.66
F <sub>57</sub> -F <sub>67</sub>	-0.49	0.07	-0.57 ± 0.34	0.09 ± 0.44
F <sub>1</sub> -F <sub>67</sub>	0.34**	0.21	0.06 ± 0.02**	0.06 ± 0.03*

<sup>a</sup>Statistically significant at  $p \leq 0.05$ .

\*\*Statistically significant at  $p \leq 0.01$ .

<sup>a</sup>Standard error of regression is for each analyzed generational interval.

**TABLE 3** Correlations and regressions<sup>a</sup> of the percentage sexual dimorphisms (female BW/male BW) by generational interval and overall at 8 weeks of age for the high (HW) and low (LW) body weight lines.

Generation	Correlation		Regression	
	HW	LW	HW	LW
F <sub>2</sub> -F <sub>12</sub>	-0.27	0.22	-0.11 ± 0.13	0.12 ± 0.17
F <sub>13</sub> -F <sub>23</sub>	0.29	0.49	0.10 ± 0.11	0.37 ± 0.22
F <sub>24</sub> -F <sub>34</sub>	-0.71*	-0.49	-0.35 ± 0.12*	-1.80 ± 1.07
F <sub>35</sub> -F <sub>45</sub>	-0.07	0.41	-0.05 ± 0.21	0.98 ± 0.73
F <sub>46</sub> -F <sub>56</sub>	0.23	-0.09	0.14 ± 0.19	-0.16 ± 0.63
F <sub>57</sub> -F <sub>67</sub>	-0.53	0.31	-0.31 ± 0.17	0.72 ± 0.73
F <sub>1</sub> -F <sub>67</sub>	0.25*	-0.05	0.03 ± 0.01*	-0.02 ± 0.05

<sup>a</sup>Statistically significant at  $p \leq 0.05$ .

<sup>a</sup>Standard error of regression is for each analyzed generational interval.

respectively. At 4 weeks, there were generational periods wherein the dimorphism increased or decreased significantly only during the first half of this long-term selection experiment (Table 2). Although the generational interval differences were evident in both lines at 8 weeks, the patterns between them were different (Table 3). Overall, there was a significant reduction in dimorphism in the HW group but not in the LW chickens. Moreover, with the exception of the F<sub>2</sub>-F<sub>12</sub> period, the standard errors of the regressions were one order of magnitude greater in the LW than HW chickens. These contrasting results between the two lines and ages are also seen in Figure 1.

## Discussion

The body weight of an organism at any point in time is a function of its genetic and nongenetic factors as well as past and present interactions. In multigenerational studies such as the one reported herein, epigenetic issues may also be relevant. The process

across generations is dynamic, and social issues can be a factor when both male and female chickens are involved; however, these were precluded by our reproductive design. The chronological and physiological ages may differ, and these were documented early for the HW and LW lines (Katanbaf et al., 1988); prior to and since then, we have been aware of this dichotomy, as evidenced in the developmental stages for numerous traits (Washburn and Siegel, 1963; Siegel and Dunnington, 1985, 1987; Zelenka et al., 1988; Jambui et al., 2017). Thus, studying the inheritance of sexual dimorphism for body weight in chickens is a complex process.

As noted in the introduction, there is a vast amount of literature on the heritabilities for juvenile body weights for male and female chickens. Although these values are population specific, they may be similar (such as 0.28 for male and 0.29 for female chickens at 35 days) (Maniatis et al., 2013) or dissimilar (0.28 for male and 0.43 for female chickens at 8 weeks of age) (Mignon-Grasteau et al., 1998). The realized heritabilities at selection age for the first four generations of our experiment (male: female) were 0.23:0.21, 0.33:0.32, 0.35:0.27, and 0.31:0.28, respectively, with a small but consistent pattern and an unweighted mean of 0.30:0.27 (Siegel, 1962). These estimates are consistent with molecular analyses that showed that the 8-week body weights in these lines are influenced by many genes, each with small effects (Lillie et al., 2018). However, these findings do not address dimorphism *per se*, as such estimates involve two sets of individuals (males and females). The fact that the published heritability estimates of dimorphism *per se* of 0.08 (Mignon-Grasteau et al., 1998) and 0.04 (Maniatis et al., 2013) for juvenile body weights were low is not surprising, nor is the fact that the genetic correlation for body weight between the sexes was 0.91 (Maniatis et al., 2013). As noted by Merritt (1966), the magnitude of difference in heritabilities for male and female chickens is based on the contributions of the sire versus those of the dam per the sex chromosome, i.e., the sire is homogametic and dam is heterogametic. This means that the sex-linked genes are paired in male but not female progeny. Hence, the genetics of the sex chromosome is especially relevant when considering the inheritance of sexual dimorphism, particularly when comparisons involve populations selected in opposite directions from a common founder (such as the Virginia high and low weight lines). This is especially relevant when the genes at certain loci are at different frequencies and may be lost over time. Moreover, as the lines became more diverse over generations, the maternal and linkage effects may have become more relevant to the complexity of the differences in the 4- and 8-week body weights.

The Virginia lines are the WPR chickens, which is a meat-type breed (Hanke et al., 1974) first recognized by the American Standard of Perfection in 1888 (American Poultry Association, 1947). The WPR breed is a composite of the Cochin, Light Brahma, Black Minorca, Black Java, Langshan, and Dominique breeds (American Poultry Association, 1947; Guo et al., 2019). An analysis of the genealogy of the Virginia lines (Guo et al., 2019) showed that the overall proportions of autosomal contributions from the contributing breeds were similar. These contributions (HW:LW) were Cochins (30:32), Dominique (33:30), Black Java (26:27), Langshan (7:4), Light Brahma (4:7), and Black Minorca (0:0). However, when viewed at the individual chromosome level, there were major differences; this was evidenced by the contributions of the founder WPR breeds toward the sex chromosomes. For the W chromosome, the contributions came from just two of the founders,

i.e., 49% Black Java and 51% Cochin, whose sexual dimorphism for juvenile body weights were 81% and 78%, respectively. In contrast, the percentage contributions to the Z chromosome (HW:LW) were from the Dominique (46:52), Black Java (28:21), Cochin (10:13), Light Brahma (11:9), Black Minorca (4:3), and Langshan (1:2) breeds, whose contributions to the dimorphism of juvenile body weights were 67%, 81%, 78%, 80%, 87%, and 81%, respectively (American Poultry Association, 1947). The changes in the contributions of these breeds toward the sex chromosomes occurred over many generations and were likely responsible for the cross-generational fluctuations that ultimately resulted in two and five of the original breeds contributing to the sex chromosomes.

Over the course of the 67 generations of selection for the high and low 8-week body weights, dynamic changes were noted to occur at the molecular and phenotypic levels for the males and females, with reductions in relative dimorphism at 4 and 8 weeks with selection for the HW line but not the LW line. Although the relative contributions from the founder WPR breeds were similar in both lines, there were large differences in the contributing stocks between the HW and LW lines in terms of the sex chromosomes. Across multiple generations, homeostatic mechanisms will often come into play, and the degree of dimorphism at a fixed age will be population-specific. It will be very difficult to genetically modify sexual dimorphism within a particular population using the conventional tools available at present. In breeding programs where the final product involves several closed populations, combining abilities may differ among the evaluated populations. The long-term divergent selection for 8-week body weight in the present study revealed the dynamic biological complexity of a trait that is ironically easy to measure.

## Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors without undue reservation.

## Ethics statement

The animal study, as of 1997, was approved by the Institutional Animal Care and Use Committee at Virginia Tech. Prior to 1997, the chickens were treated in a similar manner despite the university not having stated guidelines and protocols. The study was conducted in accordance with all local legislation and institutional requirements.

## References

- Adedibu, I. I., and Ayorinde, K. L. (2011). Sexual dimorphism in predicting body weight of two broiler strains. *Niger. J. Anim. Sci.* 13 (1), 20–31.
- American Poultry Association. (1947). *The American Standard of Perfection*. Daventry: American Poultry Association, Inc.
- Carney, V. L., Anthony, N. B., Robinson, F. E., Reimer, B. L., Korver, D. R., Zuidhof, M. J., et al. (2022). Evolution of maternal feed restriction practices over 60 years of selection for broiler productivity. *Poult. Sci.* 101 (10), 101957. doi:10.1016/j.psj.2022.101957
- Chambers, J. R., Smith, E. J., Dunnington, E. A., and Siegel, P. B. (1994). Sex-linked feathering ( $K, k+$ ) in chickens: a review. *Poult. Sci. Rev.* 5, 97–116.
- Dunnington, E. A., Honaker, C. F., McGilliard, M., and Siegel, P. B. (2013). Phenotypic responses of chickens to long-term, bidirectional selection for juvenile body weight -- historical perspective. *Poult. Sci.* 92 (7), 1724–1734. doi:10.3382/ps.2013-03069
- Dunnington, E. A., and Siegel, P. B. (1996). Long-term divergent selection for eight-week body weight in White Plymouth Rock chickens. *Poult. Sci.* 75, 1168–1179. doi:10.3382/ps.0751168
- Guo, Y., Lillie, M., Zan, Y., Beranger, J., Martin, A., Honaker, C. F., et al. (2019). A genomic inference of the White Plymouth Rock genealogy. *Poult. Sci.* 98 (11), 5272–5280. doi:10.3382/ps/pez411
- Hanke, O. A., Skinner, J. L., and Florea, J. W. (1974). *American poultry history, 1823-1973, an anthology overview of 150 years*. Madison: American Printing and Publishing, Inc, 1823–1973.
- Harrison, S. J., Siegel, P. B., Honaker, C. F., and Lewis, R. M. (2023). Population dynamics of a long-term selection experiment in White Plymouth Rock chickens selected for low or high body weight. *Poult. Sci.* 102 (5), 102575. doi:10.1016/j.psj.2023.102575

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PS: conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, supervision, validation, visualization, writing–original draft, and writing–review and editing. CH: data curation, formal analysis, investigation, methodology, validation, and writing–review and editing.

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- Havenstein, G. B., Ferket, P. R., and Qureshi, M. A. (2003). Growth, livability, and feed conversion of 1957 versus 2001 broilers when fed representative 1957 and 2001 broiler diets. *Poult. Sci.* 82 (10), 1500–1508. doi:10.1093/ps/82.10.1500
- Jambui, M., Honaker, C. F., and Siegel, P. B. (2017). Correlated responses to long-term divergent selection for 8-week body weight in female White Plymouth Rock chickens: sexual maturity. *Poult. Sci.* 96, 3844–3851. doi:10.3382/ps/pex224
- Katanbaf, M. N., Siegel, P. B., and Dunnington, E. A. (1988). Organ growth of selected lines of chickens and their F<sub>1</sub> crosses to a common body weight or age. *Theor. Appl. Genet.* 76 (4), 540–544. doi:10.1007/BF00260904
- Lillie, M., Sheng, Z. Y., Honaker, C. F., Andersson, L., Siegel, P. B., and Carlborg, Ö. (2018). Genomic signatures of 60 years of bidirectional selection for 8-week body weight in chickens. *Poult. Sci.* 97 (3), 781–790. doi:10.3382/ps/pex383
- Maniatis, G., Demiris, N., Kranis, A., Banos, G., and Kominakis, A. (2013). Genetic analysis of sexual dimorphism of body weight in broilers. *J. Appl. Genet.* 54 (1), 61–70. doi:10.1007/s13353-012-0116-y
- Marquez, G. C., Siegel, P. B., and Lewis, R. M. (2010). Genetic diversity and population structure in lines of chickens divergently selected for high and low 8-week body weight. *Poult. Sci.* 89, 2580–2588. doi:10.3382/ps.2010-01034
- Merritt, E. S. (1966). Estimates by sex of genetic parameters for body weight and skeletal dimensions in a random bred strain of meat type fowl. *Poult. Sci.* 45 (1), 118–125. doi:10.3382/ps.0450118
- Mignon-Grasteau, S., Beaumont, C., Poivey, J.-P., and de Rochambeau, H. (1998). Estimation of the genetic parameters of sexual dimorphism of body weight in 'label' chickens and Muscovy ducks. *Genet. Sel. Evol.* 30 (5), 481–491. doi:10.1186/1297-9686-30-5-481
- Remeš, V., and Székely, T. (2010). Domestic chickens defy Rensch's rule: sexual size dimorphism in chicken breeds. *J. Evol. Biol.* 23 (12), 2754–2759. doi:10.1111/j.1420-9101.2010.02126.x
- Siegel, P. B. (1962). Selection for body weight at eight weeks of age. *Poult. Sci.* 41 (3), 954–962. doi:10.3382/ps.0410954
- Siegel, P. B. (2014). Evolution of the modern broiler and feed efficiency. *Annu. Rev. Anim. Biosci.* 2, 375–385. doi:10.1146/annurev-animal-022513-114132
- Siegel, P. B. (2023). Broiler genetics and the future outlook. *Front. Physiol.* 14, 1150620. doi:10.3389/fphys.2023.1150620
- Siegel, P. B., and Dunnington, E. A. (1985). "Reproductive complications associated with selection for broiler growth," in *Poultry breeding and genetics*. Editors W. G. Hill, J. M. Manson, and D. Hewitt (Harlow, Essex, UK: Longman Group Ltd.), 59–72.
- Siegel, P. B., and Dunnington, E. A. (1987). Selection for growth in chickens. *Crit. Rev. Poult. Biol.* 1, 1–24.
- Smith, P., and Daniel, C. (1975). *The chicken book*. Boston: Little and Brown Co.
- Washburn, K. W., and Siegel, P. B. (1963). Influence of thiouracil on chickens selected for high and low body weights. *Poult. Sci.* 42, 161–169. doi:10.3382/ps.0420161
- Zelenka, D. J., Dunnington, E. A., Cherry, J. A., and Siegel, P. B. (1988). Anorexia and sexual maturity in female white rock chickens. I. Increasing the feed intake maturity in female white rock chickens. I. Increasing the feed intake. *Behav. Genet.* 18 (3), 383–387. doi:10.1007/BF01260938
- Zuidhof, M. J., Carney, V. L., Korver, D. R., and Robinson, F. E. (2014). Growth, efficiency, and yield of commercial broilers from 1957, 1978, and 2005. *Poult. Sci.* 93 (12), 2970–2982. doi:10.3382/ps.2014-04291



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# General commentary: sexual dimorphism for juvenile body weight in lines of chickens selected for 8-week body weight

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## KEYWORDS

sexual dimorphism, chicken, selection, growth, siegel 1

## 1 Introduction

This contribution is to recognize the scientific contribution of Paul Siegel and explore the report from [Siegel and Honaker \(2025\)](#) on sexual dimorphism of chicken. The present discussion explores the putative physiological mechanisms for the consistency of sexual dimorphism in growth rate across 67 generations. Paul Siegel has been conducting research on chicken growth and its genetic control for over 60 years. He is one of the people who established that the growth rate of chickens is highly heritable with the heritability of growth calculated as 0.39 from a study by [Siegel \(1962\)](#) and 0.41 from 176 reports as 0.41 ([Siegel, 1962](#)). Recently, he published a paper on the effects of selection for growth over 67 generations (one generation per year) focusing on the effects on sexually dimorphism in growth ([Siegel and Honaker, 2025](#)). Birds were selected for either high growth or slow growth (specifically body weight at 8 weeks old). Breeding employed 4 dams for each sire with matings of full- and half-sibs being avoided. Sexually dimorphism of growth was stable over 67 generations selected for growth. This indicates that there is a strong selection constraint for sexually dimorphism of growth and/or that it is a canalized genetic response. Sexually dimorphism of growth was also markedly greater (2.17-fold in the high growth line and 2.51-fold in the slow growth line) at 8-weeks old compared to 4-weeks old ([Table 1](#)).

Experimentally, growth is measured as either weight or height/length at one or several time points or the delta increase in weight or height/length (average daily gain or ADG) or expressed as parameters in an equation for growth such as the Gompertz equation. In livestock and poultry growth is most frequently expressed as weight or weight gain. In contrast, human growth is assessed as height (e.g., [Gasser et al., 2009](#)). While studies in reptiles employ length; the latter being the distance between snout–vent length in reptiles (e.g., [Cox and John-Alder, 2007](#)). [Siegel and Honaker \(2025\)](#) employed body weight at 8 weeks old as their parameters of growth.

While growth is a change in weight or height/length, a confounding conceptual issue is that there can be sexual dimorphism in mature weight or height/length at sexual maturity or when epiphyseal plates fuse. It is noted that either adult males or females can be larger even in closely related species. For instance, there is opposite sexual adult size dimorphism in lizards (*Sceloporus virgatus*: male < female; *Sceloporus jarrovi*: male > females) ([Cox and John-Alder, 2007](#)).

TABLE 1 Comparison of sexual dimorphism in 4- and 8-week-old chickens selected for 8-week-old body weight for 67 generations (calculated from data in Siegel and Honaker, 2025).

	Sexual dimorphism in growth (males minus females) as % of males	
	4 weeks-old	8-weeks old
Parental generation	11.1	19.1
<b>Generations F<sub>57</sub>-F<sub>67</sub></b>		
High growth line	8.4	18.2
Low growth line	7.5	18.8

## 2 Sexual dimorphism and growth

It is reasonable to assume that there has been tremendous selection pressure for animals to have the optimal size/weight and growth profile (delta size per unit time) for a specific environment. The corollary is that there will be optimal size/weight together with growth for the food available and other environmental considerations such as predators, temperature, and water availability.

In humans, sex differences in height are only small until puberty (reviewed: Gasser et al., 2009). Similarly, there is greater sexual dimorphism in body weight at 8- compared to 4-weeks of age (Table 1) (Siegel and Honaker, 2025).

## 3 Genetic basis of sexual dimorphism and growth

Sexual dimorphism of growth may have a simple genetic basis. In eutherian mammals, females have two X chromosomes and, consequently, two sets of genes. While one X chromosome is inactivated, some genes escape inactivation and there can be gene dosing (reviewed; Moeser et al., 2022). In birds having ZZ (males) and ZW (females), there is dosage with the Z chromosome gene, Z chromosome gene Doublesex and Mab-3-Related Transcription factor 1 (DMRT1) (Ioannidis et al., 2021; Li et al., 2025; reviewed: Zhang et al., 2023).

## 4 Physiological bases of sexual dimorphism and growth

### 4.1 Sex steroids

It is frequently assumed that the overall mechanism for sexual dimorphism in growth are sex steroids. Sex steroids promote growth in cattle. Castration reduces growth rate in cattle (e.g., Lee et al., 1990; Marti et al., 2013; Li et al., 2022). Moreover,

castration depresses circulating concentrations of growth hormone and thyroid hormones and is followed by shifts in microbial fermentation (Li et al., 2022; Shi et al., 2024). Implanting a mixture of androgens and estrogens (trenbolone acetate and estradiol 17 $\beta$ ) in increases growth (average daily gain) in steers while reducing protein turnover and the insulin response to glucose (e.g., Ferguson et al., 2023).

There are markedly differences between the effects of androgens on growth in chickens (negative) and turkeys (positive). Growth is either unaffected or tended to be increased by castration in chickens (Fennell and Scanes, 1992a; Chen et al., 2006; Symeon et al., 2010). It is cautioned that body weight gain reflects the aggregate of growth of multiple tissues some or all of which exhibit sexual dimorphism but of different magnitudes and different directions. For instance, while weights of adipose tissue were increased following castration and decreased by androgen replacement, there was no effect of castration on breast muscle but decreases with androgen at physiological concentrations (Fennell and Scanes, 1992a). Moreover, testosterone depressed ADG with the effect overcome by a peripheral androgen blocker (Fennell et al., 1996). Similarly, in female-larger species of reptiles, testosterone reduces growth but increase growth in male - larger species (Duncan et al., 2020). In turkeys, growth and muscle development are enhanced by exogenous androgens (Fennell and Scanes, 1992b) and castration tends to decrease growth and muscle weight (Pierson et al., 1981; Burke and Edwards, 1994).

### 4.2 Hypothalamo-pituitary (growth hormone)-insulin-like growth factor axis

Another underlying assumption is the sexual dimorphism is related to growth hormone-insulin-like growth factor. There are sexually dimorphic patterns for growth hormone secretion, for instance, in humans (e.g., Jessup et al., 2003), rats (e.g., Chowen et al., 1996) and chickens where castration is followed by feminization of GH secretion (Pampori and Shapiro, 1994). The physiological mechanism for SSD involves IGF-1. For instance, castration increases hepatic IGF-1 expression in male *Sceloporus undulatus* while testosterone having no effect (Cox and John-Alder, 2007).

### 4.3 Hypothalamo-pituitary-adrenocortical (HPA) axis

The HPA axis has been related to sexual dimorphism of growth with SNPs in *chrh1* that are associated with rates of growth in yellow catfish (Wang et al., 2024). Moreover, there is sexual dimorphism in the effects of corticosteroid-binding globulin (CBG) on hepatic functioning (Toews et al., 2022).

#### 4.3.1 Immune and gastro-intestinal functioning

The extent to which sexual dimorphism is secondary to other sexual differences such as immune or gastro-intestinal is unclear (reviewed; Moeser et al., 2022). For example, there tends to be a larger immune response to *E. coli* or sheep red blood cells in young

chickens receiving estradiol with this being blocked by estrogen receptor antagonist (Leiner et al., 1996).

## 5 Discussion

It would be predicted there would be drift in sexual dimorphism over the 67 generations, this was not the case (Table 1) (Siegel and Honaker, 2025). And would suggest that growth and sexual dimorphism are tightly linked. It is speculated that expression of DMRT1 may be, at least partially, responsible for the sexual dimorphism of growth in chickens. What is not known is whether genetic female chickens (ZW) expressing male levels of DMRT1 will grow at male rates or that males with higher levels of DMRT1 expression grow at superior rates. These might be accomplished by selection for DMRT1 expression early in embryonic development or via transgenic approaches.

## Author contributions

CS: Writing – original draft, Investigation, Resources, Writing – review and editing, Data curation, Project administration, Visualization, Methodology, Supervision, Conceptualization, Validation.

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## References

- Burke, W. H., and Edwards, H. M. (1994). Effect of early castration on body weight, muscle growth, and bone characteristics of male Nicholas strain turkeys. *Poult. Sci.* 73, 457–463. doi:10.3382/ps.0730457
- Chen, K. L., Hsieh, C. Y., and Chiou, P. W. S. (2006). Caponization effects on growth performance and lipid metabolism in taiwan country chicken cockerels nchu.edu.tw. *J. Anim. Sci.* 19, 438–443. doi:10.5713/ajas.2006.438
- Chowen, J. A., García-Segura, L. M., González-Parra, S., and Argente, J. (1996). Sex steroid effects on the development and functioning of the growth hormone axis. *Cell. Mol. Neurobiol.* 16, 297–310. doi:10.1007/3333333333333333BF02088097
- Cox, R. M., and John-Alder, H. B. (2007). Growing apart together: the development of contrasting sexual size dimorphisms in sympatric *Sceloporus* lizards. *Herpetol.* 63, 245–257. doi:10.1655/0018-0831(2007)63[245:gatto]2.0.co;2
- Duncan, C. A., Cohick, W. S., and John-Alder, H. B. (2020). Testosterone reduces growth and hepatic IGF-1 mRNA in a female-larger lizard, *Sceloporus undulatus*: evidence of an evolutionary reversal in growth regulation. *Integr. Org. Biol.* 2, obaa036. doi:10.1093/iob/obaa036
- Fennell, M. J., Radecki, S. V., Proudman, J. A., and Scanes, C. G. (1996). The suppressive effects of testosterone on growth in young chickens appears to be mediated via a peripheral androgen receptor; studies of the anti-androgen ICI 176,334. *Poult. Sci.* 75, 763–766. doi:10.3382/ps.0750763
- Fennell, M. J., and Scanes, C. G. (1992a). Inhibition of growth in chickens by testosterone, 5 $\alpha$ -dihydrotestosterone and 19-nortestosterone. *Poult. Sci.* 71, 357–366. doi:10.3382/ps.0710357
- Fennell, M. J., and Scanes, C. G. (1992b). Effects of androgen (testosterone, 5 $\alpha$ -dihydrotestosterone, 19-nortestosterone) administration on growth in turkeys. *Poult. Sci.* 71, 539–547. doi:10.3382/ps.0710539
- Ferguson, T. D., Loos, C. M. M., Vanzant, E. S., Urschel, K. L., Klotz, J. L., and McLeod, K. R. (2023). Impact of ergot alkaloid and steroidal implant on whole-body protein

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turnover and expression of mTOR pathway proteins in muscle of cattle. *Front. Vet. Sci.* 10, 1104361. doi:10.3389/fvets.2023.1104361

Gasser, T., Sheehy, A., Molinari, L., and Largo, R. H. (2009). Sex dimorphism in growth. *Ann. Hum. Biol.* 27, 187–197. doi:10.1080/030144600282299

Ioannidis, J., Taylor, G., Zhao, D., Liu, L., Idoko-Akoh, A., Gong, D., et al. (2021). Primary sex determination in birds depends on DMRT1 dosage, but gonadal sex does not determine adult secondary sex characteristics. *Proc. Natl. Acad. Sci. U. S. A.* 118, e2020909118. doi:10.1073/pnas.2020909118

Jessup, S. K., Dimaraki, E. V., Symons, K. V., and Barkan, A. L. (2003). Sexual dimorphism of growth hormone (GH) regulation in humans: endogenous GH-releasing hormone maintains basal GH in women but not in men. *J. Clin. Endocrinol. Metab.* 88, 4776–4780. doi:10.1210/jc.2003-030246

Lee, C. Y., Henricks, D. M., Skelley, G. C., and Grimes, L. W. (1990). Growth and hormonal response of intact and castrate male cattle to trenbolone acetate and estradiol. *J. Anim. Sci.* 68, 2682–2689. doi:10.2527/1990.6892682x

Leitner, G., Landsman, T., Blum, O., Zaltsmann, N., and Heller, E. D. (1996). Effects of gonadal steroids and their antagonists on the humoral immune response of immune-selected broiler chicks. *Poult. Sci.* 75, 1373–1382. doi:10.3382/ps.0751373

Li, J., Zhang, X., Wang, X., Wang, Z., Li, X., Zheng, J., et al. (2025). Single-nucleus transcriptional and chromatin accessible profiles reveal critical cell types and molecular architecture underlying chicken sex determination. *J. Adv. Res.* 70, 29–43. doi:10.1016/j.jare.2024.05.007

Li, Z., Shi, J., Lei, Y., Wu, J., Zhang, R., Zhang, X., et al. (2022). Castration alters the cecal microbiota and inhibits growth in Holstein cattle. *J. Anim. Sci.* 100, skac367. doi:10.1093/jas/skac367

Marti, S., Realini, C. E., Bach, A., Pérez-Juan, M., and Devant, M. (2013). Effect of castration and slaughter age on performance, carcass, and meat quality traits of Holstein calves fed a high-concentrate diet. *J. Anim. Sci.* 91, 1129–1140. doi:10.2527/jas.2012-5717

- Moeser, A. J., Roney, A., Fardisi, M., and Thelen, K. (2022). Biological sex: an understudied factor driving disease susceptibility in pigs. *J. Anim. Sci.* 100, skac146. doi:10.1093/jas/skac146
- Pampori, N. A., and Shapiro, B. H. (1994). Testicular regulation of sexual dimorphisms in the ultradian profiles of circulating growth hormone in the chicken. *Eur. J. Endocrinol.* 131, 313–318. doi:10.1530/eje.0.1310313
- Pierson, F. W., Hester, P. Y., and Wilson, E. K. (1981). The effect of caponization and dietary 17 alpha-methyltestosterone on the incidence of leg abnormalities in turkeys. *Poult. Sci.* 60, 2144–2149. doi:10.3382/ps.0602144
- Shi, J., Li, Z., Jia, L., Ma, Y., Huang, Y., He, P., et al. (2024). Castration alters the ileum microbiota of Holstein bulls and promotes beef flavor compounds. *BMC Genomics* 25, 426. doi:10.1186/s12864-024-10272-8
- Siegel, P. B. (1962). Selection for body weight at eight weeks of age. *Poult. Sci.* 41, 954–962. doi:10.3382/ps.0410954
- Siegel, P. B., and Honaker, C. F. (2025). Sexual dimorphism for juvenile body weight in chickens divergently selected for 8-week body weight. *Front. Physiol.* 15, 1534334. doi:10.3389/fphys.2024.1534334
- Symeon, G. K., Mantis, F., Bizelis, I., Kominakis, A., and Rogdakis, E. (2010). Effects of caponization on growth performance, carcass composition, and meat quality of medium growth broilers. *Poult. Sci.* 89, 1481–1489. doi:10.3382/ps.2009-00411
- Toews, J. N. C., Philippe, T. J., Hill, L. A., Dordevic, M., Miguez-Crespo, A., Homer, N. Z. M., et al. (2022). Corticosteroid-binding globulin (SERPINA6) establishes postpubertal sex differences in rat adrenal development. *Endocrinology* 163, bqac152. doi:10.1210/endo/bqac152
- Wang, Y., Guo, W., Gaorui Gong, G., Huang, P., and Mei, J. (2024). Phenotypic and genetic analysis of sexual dimorphism in growth, feed intake and feed conversion efficiency in yellow catfish. *Aquaculture* 586, 740767. doi:10.1016/j.aquaculture.2024.740767
- Zhang, X., Li, J., Chen, S., Yang, N., and Zheng, J. (2023). Overview of avian sex reversal. *Int. J. Mol. Sci.* 24, 8284. doi:10.3390/ijms24098284



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# A career reflection

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## KEYWORDS

chickens, growth selection, heterogeneity, muscle, satellite cells, turkeys

## Introduction

Being asked to write an opinion paper for the Frontiers in Avian Physiology Lifetime Achievements Topic is an honor. While considering this paper and what research area to focus on, I began reflecting on my career as a scientist, which commenced over 40 years ago. I reflected on all the mountains and detours that had to be overcome and the opportunities along the way. With the current challenging times for pursuing scientific research, I decided to provide a career perspective outlining my scientific journey instead of writing an opinion paper on a specific research topic.

My interest in science started as a young girl growing up outside of Boston. When I was 6 years old, I proudly announced to my mother that I was going to be a veterinarian. I had always been drawn to animals and was passionate about biological science. My mother helped fuel these interests by maintaining a membership at the Museum of Science in Boston. Every Saturday, I would attend science classes followed by a visit to their library to select books for us to read together during the week. I still remember the instructor's name and some of the demonstrations carried out to illustrate scientific concepts. The time spent at the Museum of Science helped build my scientific passion. In school, I was placed in the honors science curriculum and took 10th-grade biology in the ninth grade. I was so fortunate to have a teacher who recognized my research skills. One day, she told me I was not going to be a veterinarian but a research scientist. I did not even know what a research scientist did, and to be honest, I was crushed. She signed my yearbook, saying, "My budding scientist." At that time, I thought I would prove her wrong by becoming a veterinarian. She saw something in me that I did not, and I am forever grateful to her for planting the seed of a research scientist in my mind.

My undergraduate studies could be summarized as follows: I obtained my BA degree with distinction in Biology from Boston University in 1981. This statement would severely underrepresent this transformative period of my life. I was fortunate to take Cell Biology with a new assistant professor, Dr. Robert E. Hausman. I loved the Cell Biology course and was excited to attend lectures and learn as much as possible. One day, I finally mustered the courage to attend Dr. Hausman's office hours and ask if I could switch advisors to him. The meeting changed my life. In addition to him becoming my advisor, he asked if I would like to work in his laboratory during the summer to help set it up. At the end of the summer, Dr. Hausman asked if I would like to apply for the research honors program. As in ninth grade, someone saw something in me that I did not recognize. My undergraduate research was on prostaglandin E1 during embryonic muscle development, resulting in my first peer-reviewed research publication in Biophysical Biochemical Research Communication in 1981 (Hausman and Velleman, 1981). More importantly, my lifelong interest in the cellular communication mechanisms that lead to tissue and organ formation was formed. Opportunities often present themselves as minor steps in your life but can result in a new life direction. I am not sure where my life would be if I had not gone

to Dr. Hausman's office hours. My life certainly would have been different, and that is all I know.

To further pursue cellular communication, my interest evolved into the new area of how the extrinsic environment outside the cell, the extracellular matrix, affected cellular behavior. I pursued my doctoral studies with Dr. Paul F. Goetinck at the University of Connecticut, focusing on the role of the extracellular matrix environment in avian limb development. After completing my doctorate in 1986, I was eager to learn emerging molecular biology techniques to study human diseases involving the extracellular matrix. To achieve this goal, I was accepted as a National Institutes of Health postdoctoral trainee at the University of Pennsylvania Medical School's Connective Tissue Research Institute. During my doctoral studies, I had thought that I wanted to leave academia and pursue osteoarthritis research in industry. Gaining molecular biology skills was essential. However, I realized that working with humans, especially children presenting with various connective tissue disorders, was very different from working with research animals. It troubled me to witness children with severe connective tissue disorders, such as osteogenesis imperfecta. After much deliberation, I realized I did not have the emotional makeup for the career I had thought would be my future direction and needed to find a new path. Another opportunity then presented itself—a hidden, life-changing pathway for me. At the University of Connecticut, an NIH program project grant to the Health Center, and they needed someone to lead the animal component of the research. It was explained to me with much chagrin that I would be in the Animal Science Department, which was a part of the College of Agricultural Sciences. My previous research had used an avian model, but I was always part of a biology department, not one focused on domestic animal research. I accepted the postdoctoral position, which included the option to develop my own research program for the future.

After 2 years in the postdoctoral position at the University of Connecticut, I was promoted to a non-tenure-track assistant professor of Animal Science, focused on developing a new research program in avian muscle growth mechanisms. At a biotechnology meeting held at the University of Connecticut, I met Dr. Douglas McFarland from South Dakota State University, who presented his research on avian breast muscle adult myoblasts, or satellite cells. These are the cells responsible for the regeneration and growth of muscle. I asked Dr. McFarland if he thought satellite cells could be regulated by the extracellular matrix. At that time, the extracellular matrix had only been identified in connective tissue, and muscle was not a connective tissue. My instinct was that the extracellular matrix might be an important component in non-connective tissues. I took a big risk, but Dr. McFarland was excited about collaborating with me on this. Hence, another life-changing opportunity arose through attending a meeting and asking a question. In 1998, I published our research results demonstrating that avian breast muscle satellite cells produce their own extracellular matrix (Velleman, 1998). This was a groundbreaking finding that completely challenged the current dogma. We now know that the extracellular matrix is present in all tissues and organs, regulating biological homeostasis and growth, maintaining structural organization, and supporting regeneration. My message here is to hold onto your beliefs, even if established findings oppose them; you may be contributing significant new knowledge.

In 1995, I transitioned into a tenure-track assistant professorship in the Department of Animal Sciences at The Ohio State University. I was promoted through the ranks, and in 2022, I received the honorific title of Distinguished Professor of Food, Agricultural, and Environmental Sciences in Animal Sciences. In 2024, I retired and became a professor emeritus in the Department of Animal Sciences. During my tenure at both the University of Connecticut and The Ohio State University, the greatest joy has been impacting the lives of those I trained. My goal was to provide opportunities to others, similar to those that made such a huge difference in my life trajectory. My undergraduate and graduate students and postdoctoral researchers represent my legacy.

During my career, I published over 215 peer reviewed research publications, 8 book chapters, and have co-edited 8 books. My career was accompanied with disappointments too. You must stay strong during these periods of doubt to achieve your goals. Of my discoveries, the following are the ones which I deem most important.

## Satellite cells produce their own extracellular matrix extrinsic environment

The extracellular matrix includes collagens, proteoglycans, and non-collagenous glycoproteins and was believed to be produced by only connective tissue cells that are important in the structural support of tissues such as bone and cartilage. Non-connective tissues, such as muscle, were not thought to produce extracellular matrix proteins. In 1998 (Velleman, 1998), my laboratory was the first to show that breast muscle satellite cells synthesized extracellular matrix heparan sulfate proteoglycans. Heparan sulfate proteoglycans are a group of extracellular matrix macromolecules linking muscle cells to their extrinsic environment and regulating growth through fibroblast growth factor 2 signal transduction. This was one of the first demonstrations of an extracellular matrix protein being synthesized by a non-connective-tissue cell type and having a function beyond just structural support. Subsequent studies through the years focused on two families of heparan sulfate proteoglycans, syndecans and glypicans, and how they differentially regulate breast muscle cell proliferation and differentiation.

## Heterogeneity of satellite cells

Muscle growth in poultry occurs through the formation of myofibers or hyperplasia of myoblasts, with myoblasts fusing to form multinucleated myotubes that mature into muscle fibers and muscle fiber bundles. After hatching, all muscle growth is from satellite cells donating their nuclei to existing muscle fibers, resulting in the enlargement of myofibers through hypertrophy. Although commonly thought of as a homogenous single-cell population, satellite cells are composed of multiple populations with differing proliferation and differentiation in poultry. The research we conducted has shown that growth selection in poultry has altered the types of satellite cells present in the breast muscle and their biological activity (Velleman, 2022; Xu et al., 2023; Xu

and Velleman, 2023). In broilers, satellite cell proliferation and differentiation have decreased with growth selection, whereas the opposite has occurred in meat-type turkeys (Xu and Velleman, 2023). Decreased satellite cell proliferation and differentiation, especially in broilers, may be associated with muscle fiber degenerative myopathies such as wooden breast. The satellite cell is the cell type responsible for the repair and regeneration of myofibers, which is likely suppressed with decreased satellite cell biological activity.

## Effects of post-hatch extrinsic conditions (temperature and nutrition) on muscle development and meat quality

Feed restrictions are used by the industry, and newly hatched chicks and poults can be exposed to hot and cold temperatures during handling and transportation. In addition to a potential to reduce the final breast muscle weight, these extrinsic stimuli immediately after hatching can also change the expression of muscle-specific genes and cause the conversion of the satellite cells to an adipogenic cell fate, increasing fat within the breast muscle (Velleman et al., 2010; Velleman et al., 2014a; Velleman et al., 2014b). Xu et al. (2022) showed that proliferating satellite cells are more sensitive to temperature than differentiating satellite cells in the expression of adipogenic genes. Immediately after hatching, satellite cells rapidly proliferate, increasing their responsiveness. Selection for growth in turkeys has increased the thermal sensitivity of satellite cells. When satellite cells exhibit their highest mitotic activity immediately after hatching, with increased proliferation, they are capable of expressing adipogenic genes, which may significantly affect the composition and morphological structure of the breast muscle. A key finding from my research is that administering feed restrictions during the first week post-hatch leads to increased intramuscular lipid accumulation in the market-age breast muscle. However, if a feed restriction is applied during the second week post-hatch, after the period of maximal satellite cell activity, increased intramuscular fat accumulation is eliminated in the market-age breast muscle.

## Maternal inheritance of breast muscle morphology in turkeys

Commercial turkeys are produced by crossing a sire line usually selected for greater muscling and growth. During studies of muscle development in several line crosses, it was observed that the breast muscle morphology of the offspring crosses was always the same as that of the female parent around market age (Velleman and Nestor, 2004). These findings indicated maternal inheritance of breast muscle morphological structure. This was one of the first observations of maternal inheritance influencing a trait of economic importance in a domestic animal.

The most appropriate way to summarize my career is one of others recognizing talent in me and providing opportunities. For those early in their career, always remain open to new paths. A new path might not be presented as a dramatic modification but perhaps as something subtle in nature. As a professional, I have tried to make a difference in the lives of my students by presenting them with new chances and adding novel information to the knowledge database. In the future, I hope others will continue pursue satellite cell heterogeneity coupled with differential expression of extracellular matrix genes as this is a key element in both the growth of muscle and onset of myopathies.

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## References

- Hausman, R. E., and Velleman, S. G. (1981). Prostaglandin E1 receptors on chicken embryo myoblasts. *Biochem. Biophys. Res. Comm.* 103, 212–219.
- Velleman, S. G. (1998). The role of the extracellular matrix in muscle development. *Basic Appl. Myol.* 8, 94.
- Velleman, S. G., and Nestor, K. E. (2004). Inheritance of breast muscle morphology in turkeys at sixteen weeks of age. *Poult. Sci.* 83, 1060–1066. doi:10.1093/ps/83.7.1060
- Velleman, S. G., Nestor, K. E., Coy, C. S., Harford, I., and Anthony, N. B. (2010). Effect of posthatch feed restriction on broiler breast muscle development and muscle transcriptional regulatory factor gene and heparan sulfate proteoglycan expression. *Int. J. Poult. Sci.* 9, 417–425. doi:10.3923/ijps.2010.417.425
- Velleman, S. G., Coy, C. S., and Emmerson, D. A. (2014a). Effect of the timing of posthatch feed restrictions on broiler breast muscle development and muscle transcriptional regulatory factor gene expression. *Poult. Sci.* 93, 1484–1494. doi:10.3382/ps.2013-03813
- Velleman, S. G., Coy, C. S., and Emmerson, D. A. (2014b). Effect of the timing of posthatch feed restrictions on the deposition of fat during broiler breast muscle development. *Poult. Sci.* 93, 2622–2627. doi:10.3382/ps.2014-04206
- Velleman, S. G. (2022). Why breast muscle satellite cell heterogeneity is an issue of importance for the poultry industry: an opinion paper. *Front. Physiol.* 13, 987883. doi:10.3389/fphys.2022.987883
- Xu, J., and Velleman, S. G. (2023). Effects of thermal stress and mechanistic target of rapamycin and wingless-type mouse mammary tumor virus integration site family pathways on the proliferation and differentiation of satellite cells derived from the breast muscle of different chicken lines. *Poult. Sci.* 102, 102608. doi:10.1016/j.psj.2023.102608
- Xu, J., Strasburg, G. M., Reed, K. M., and Velleman, S. G. (2022). Thermal stress affects proliferation and differentiation of Turkey satellite cells through the mTOR/S6K pathway in a growth-dependent manner. *PLoS One* 17 (1), e0262576. doi:10.1371/journal.pone.0262576
- Xu, J., Strasburg, G. M., Reed, K. M., Bello, N. M., and Velleman, S. G. (2023). Differential effects of temperature and mTOR and Wnt-planar cell polarity pathways on syndecan-4 and CD44 expression in growth-selected Turkey satellite cell populations. *PLoS ONE* 18 (2), e0281350. doi:10.1371/journal.pone.0281350



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# The journey of a lifetime: reflections on my career

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## KEYWORDS

poultry (chicken), intestinal development and function, early feeding, in ovo feeding, taste receptor, energy dynamics before hatch, yolk sac tissue

## Introduction

When I was invited to write a reflection on my scientific career, I felt both honoured and deeply moved. This invitation prompted me to look back at more than 35 years of research and teaching, at the Faculty of Agriculture of the Hebrew University, from a broader perspective. It has been a journey that began with my early days as a young PhD student, continued through my postdoctoral work at Cornell University Veterinary School, and evolved into my roles as a Senior Lecturer, Associate Professor, Full Professor, and currently, as Professor Emeritus and Vice President of the World's Poultry Science Association (WPSA).

These 4 decades of scientific and professional activity have brought me enormous satisfaction, curiosity, and challenges, shaping my identity as a scientist, mentor, colleague, and individual. I have navigated this journey alongside my beloved family, which includes my three children and my life partner.

This reflection is not merely a summary of my academic achievements or contributions to poultry science. It is also a story of meeting poultry students and researchers from various countries, in many conferences, sessions and discussions, sharing mutual enthusiasm to answer research questions and try to solve problems in poultry science. On a side-note, I also hope this story will inspire young female scientists who consider to become an independent researcher and establishing their own laboratories.

Looking back, I recognize that a career in science and research has been the best choice I could have made. Curiosity has continually fuelled my drive to ask new questions, to seek meaningful answers, and what I like best - to transform findings and knowledge into practice. Guiding graduate students and watching them grow into independent researchers has been among the most rewarding aspects of my career.

My research collaborations with poultry scientists worldwide, from United States (mainly North Carolina and Virginia), Brazil, China, Australia, Italy, France, Germany, Poland, and Canada, have broadened my horizons both scientifically and personally. The international knowledge exchanges, whether through joint experiments, laboratory visits, or global conferences, have enriched my perspective and strengthened my belief in the power of global poultry research collaboration. Representing the Hebrew University of Jerusalem to the international research community has always filled me with pride.

## Lessons for young scientists

What advices can I offer to young scientists? My career has taught me few lessons:

- No Guts, No glory

Years ago, I hanged on my office wall, a poster that states, “No guts, No glory”. This statement expressed what I felt during my first years as an independent researcher in the university. I liked the dual meaning of gut/guts (...as I investigated the gut physiology). But obviously, the actual meaning of this statement, is that in order to succeed-you need an inner drive, curiosity, courage, and a touch of adventure.

- Be resilience to difficulties

Reflecting on my personal journey I realize that my determination to become a good researcher is deeply rooted in my family history. Both my parents were the sole survivors of large families which were murdered during the Holocaust. Their survival story was a model for me and implanted in me a sense of duty and responsibility to honour their resilience and strength.

- Follow the direction that sparks your true passion

I extremely enjoyed my biology undergraduate studies as a student at Haifa university. The curriculum combined zoology and botany, regularly conducted in the field, with hands-on learning experiences several times a week. From those days, I learned a life lesson: Follow the path that truly motivates and fulfills you intellectually. You should do what you really love and find meaningful. This principle has guided me ever since, and I share it with all my students.

- Stay flexible to meet research demands and embrace changes in your career journey

My M. Sc. and Ph.D. at the Hebrew University, Faculty of Agriculture, was focused on molecular genetic markers for disease resistance in poultry (under the supervision of Prof. D. Heller and Prof. A. Cahaner). Later, during a postdoctoral fellowship at Cornell Veterinary School (in Prof. Ton Schat laboratory), I expanded my understanding of the avian immune cells and tissue culture. Upon returning to Israel, I was looking for a a tenure-track position in the university. At that time the only available position, in the Animal Science Department, was in the area of poultry nutrition. In those days, the poultry nutrition research was primarily focused on feed ingredients and dietary optimization, with the intestinal system examined mainly through pathology or anatomy. So, I decided to be flexible and integrate my cellular and molecular expertise into poultry nutrition research area.

It was the right decision! Publications that came out from my lab were the first to describe cellular and molecular aspects of intestinal development in poultry. This includes characterizing epithelial cell types: defining chicken enterocytes before and after hatch; studying the proliferation and differentiation patterns of intestinal crypt and villus cells, identifying goblet cells and mucin production; sequencing nutrient transporters in the chicken gut; examined

gene expression before and after hatch, and in various early or late nutrition and various environmental conditions; showing the microvilli development and elongation on the apical membrane of the chicken enterocyte cells and also study the effect of early or late feeding (24 h–36 h post hatch) on intestinal cellular dynamics.

- Apply your findings in practice

My Research findings were widely cited and opened new research directions in poultry nutrition. But most importantly, they led to a simple and practical conclusion: there is an opportunity to jumpstart the intestinal maturation and functionality in poultry. Application of this conclusion resulted in “in ovo feeding and early feeding” strategies, currently applied by several industrial companies.

## My research themes

Through my career I had several research themes and interests. Among them are: The pre- and post-hatch morphological, molecular and functional changes, of the duodenum, jejunum and ileum; The In ovo feeding (feeding the embryo before hatch) and early nutrition interventions; Examine the role of yolk nutrients and yolk sac tissue function during incubation period; Stimulus of feed, specific nutrients (e.g., minerals, vitamin D3) on digestive system development and on bone properties; Identify digestive and absorptive limitations and develop nutritional or management strategies to overcome them; Microflora/microbiome: modulating the gut microbiota in early life; Taste perception in chickens.

More recent work includes energy dynamics in the embryo from mid-incubation until placement, the hatching muscle and breast muscle, use of AI in muscle histology, and early detection of muscle myopathies in poultry. Additional evidences, using new research techniques shows that early feeding promotes intestinal maturation by shifting the ratios of specialized epithelial cells subpopulations.

The following are some key themes from my life-time career which I am honored to present in more details.

## Developmental physiology of the avian digestive system

More than 15 papers were published between 1996 and 2003 summarizing the findings of M. Sc. and PhD students from my lab (Uni et al., 1996; Uni et al. 1998a; Uni et al. 1998b; Uni et al. 1999; Uni et al. 2000; Uni et al., 2023a). Publications characterized localization of enterocyte cells, their turnover at early age, ontogeny of intestinal enzymes, transporters, goblet cells, villi and microvilli structure during the transition from yolk nutrition to exogenous feeding. Also the critical time windows for intestinal maturation and for nutrient absorption was defined as well as the adaptation of gut tissues to nutritional and environmental signals (Geyra et al., 2001a; Geyra et al., 2001b; Gal-Garber et al., 2003; Uni et al., 2000; Uni et al. 2001; Uni et al. 2023b).

The impact of this new body of knowledge provided the conceptual and practical foundation for nutritional management of newly hatched chicks in the poultry industry and led to the idea of early and in ovo feeding (Uni and Ferket, 2004).

## Early nutrition and in ovo feeding

The research identifies key factors limiting the development and survival of pre-hatch broiler embryos and hatchlings, including nutrient availability in the egg, digestive capacity, and reliance on yolk reserves pre and post-hatch. These constraints contribute to poor chick quality and early mortality. Approaches such as early feeding (providing feed immediately post-hatch) and in ovo feeding (nutrient administration before hatch) can mitigate these issues. Combining both methods hold significant potential to improve early growth, feed efficiency, and overall bird performance, especially given to the rapid growth rates of modern broilers.

Introducing and promoting the concept of in ovo feeding, a terminology which refer to nutrient supplementation directly to the embryo amniotic fluid before hatching, was done hand by hand with a great colleague and partner - Prof. Peter Ferket from North Carolina State University. Together we patented the idea (Uni and Ferket, 2003; US Patent No. 6,592,878) and developed few in ovo feeding solutions which are suitable for enriching the amniotic fluid of the embryo 3 days before hatch, during transfer time at the hatchery (Uni et al., 2005; Foye et al., 2007). The pioneering experiments were done with Embrex Inovoject machine who developed the technology for mass injection and for targeting the amniotic fluid of the broiler embryo at E18. Experiments with specific nutrients/minerals and vitamins were preformed successfully. For example, in ovo feeding with zinc-methionine lead to changes in chicken intestinal zinc exporter mRNA expression and to small intestinal functionality (Tako et al., 2005). A formula that contained also carbohydrates improves energy status of late-term chicken embryos and promote hatchability (Uni, et al., 2005; Foye et al., 2007). Exploring in ovo delivery of carbohydrates, amino acids, minerals, and bioactive compounds (see reviews by Kadam et al., 2013; Peebles., 2018; Das et al., 2021) linked early feeding to improved and accelerated intestinal and muscular development (Kornasio et al., 2011), growth, feed efficiency, immune function, and even bone mineralization. For example,; Eggs injected in ovo at E17 with a solution containing minerals, vitamins (including vitamin D3), and carbohydrates produced chicks with improved bone mechanical properties, cortical and trabecular structure, and mineralization at various stages compared to controls. Notably, enhancements were seen pre-hatch and during early post-hatch days, with lasting improvements in bone architecture and mineralization at later stages (d 28 and 54). The results indicate that embryonic nutrition can positively influence both early and long-term skeletal development in broilers (Yair et al., 2013; Yair et al., 2015).

Research from the last 5 years focused on the dynamic changes in the subpopulations of intestinal cells. Using RNAscope methodology we were able to show that nutritional stimulation by in-ovo feeding modulates cellular proliferation, differentiation and maturation in the small intestinal epithelium of pre-post hatch chick by shifting the ratios of specialized epithelial cells (Reicher et al., 2020; Reicher et al., 2022a; Reicher et al., 2022b).

In ovo feeding is now widely used in poultry science. Our publications transformed the understanding of how prenatal nutrition can shape lifetime performance in poultry, influencing both academic research and industrial feeding strategies (Noy and Uni, 2010). An excellent review publication by Oliveira G. et al.

(2023) provides a bibliographical mapping of research related to in ovo injection practice and shows the global research from various laboratories using more than 100 different substances and ingredients delivered in ovo. I was glad to see the names of the three most frequently cited authors: Uni (573 citations), Ferket (376 citations) and Peebles (260 citations).

In ovo feeding has taken a great step forward due to the attention of the poultry industry as a practice that can strengthen and leverage poultry production systems.

## The yolk and the yolk sac tissue

The exploration of the chicken embryo nutrition lead to investigation of the yolk - The major source of nutrients for the embryo during the 21 days of incubation. The yolk is composed of nutrient-rich content and surrounded by a tissue (yolk sac tissue = YST) derived from the embryo's midgut. Our findings pointed towards limitations in yolk mineral (P, Fe, Zn, Cu, and Mn) and fat availability and in their utilization by embryo during incubation (Uni et al., 2012). Content and uptake of minerals in the yolk of broiler embryos during incubation and effect of nutrient enrichment - by in ovo feeding - were studied (Yair and Uni, 2011; Yair et al., 2015) and exhibit positive, long term effects of elevating mineral reserves in the yolk on bone structure, composition, and mechanical properties.

YST functionality was examined by gene expression from E 13 to day of hatch, revealing its dynamic roles in embryonic development (Yadgary et al., 2014). Over 3,500 genes changed expression during this period, reflecting shifts in YST function. Early on, the YST showed high erythropoietic (blood-forming) activity, while later it upregulated genes for lipid digestion, transport, and metabolism. The YST also produced plasma proteins typically made by the liver. Toward hatch, epithelial cell degradation was observed. When we asked the question if incubation temperature has an effect on YST development and functionality, we found that even a variation of less than 2 Celsius (from the optimal incubation temperature) led to impaired functionality. Both "cold" (36.3 °C), and "hot" (39.3 °C) incubation temperatures altered YST gene expression and reduced yolk utilization, impairing yolk utilization and potentially hatchling quality (Dayan et al., 2020). These results demonstrate that non-optimal incubation temperatures disrupt YST metabolic gene regulation. Overall, the YST functions as a multifunctional organ, which function temporarily substituting for the intestine, liver, and bone marrow to support the embryo until hatching (Wang and Uni 2023).

## Taste perception: taste receptors in the chicken intestine

Since curiosity is one of the main characters needed for a researcher, we continued asking questions about the chicken intestine. The question about taste perception in broiler chicken is an important one as it may have an effect on appetite and on feeding behavior. In one of our studies taste receptor genes were identified in the gastrointestinal tract (GIT) of embryonic and post-hatch chickens. Bitter (ggTas2r1, ggTas2r2, ggTas2r7) and umami

(ggTas1r1, ggTas1r3) receptors and their signalling proteins were expressed in the gut, suggesting that chickens use taste pathways in the gastrointestinal tract to sense nutrients and regulate digestion. We used a two-choice test to determine taste detection thresholds in chickens and found that chickens were as sensitive to bitterness as mammals but less sensitive to sweet and umami tastes (Cheled-Shoval et al., 2015; Cheled-Shoval et al., 2002).

## Further research activities

Other current research activities in my lab are: efforts for elucidated growth, energy dynamics, metabolic disorders in fast-growing broilers, energy partitioning in the pre-post hatch period and subsequently, in ovo feeding of guanidinoacetate (GAA) supplementation, a precursor for creatine production (an organic compound that facilitates recycling of ATP, primarily in muscle and brain tissue). We also study muscle myopathies (e.g., spaghetti meat, woody breast) and their nutritional determinants, including energy dynamics in developing muscle, and the introducing of AI-assisted histological analysis for early detection of breast muscle tissue abnormalities. (Dayan et al., 2023a; Dayan et al., 2023b; Dayan et al., 2023c).

The impact of this research is via bridging molecular physiology through precision livestock management, offering innovative approaches to meat quality and food loss reduction.

## My career reflection in numbers

- Academic Standing: Full Professor, Department of Animal Sciences, Faculty of Agriculture, Hebrew University of Jerusalem. Personally, I see this as an achievement since the percentage of female full professors in the Israeli academy is relatively low, less than 17% in 2020. This is in comparison to other western countries, like the USA (35%), France (32%) England (31%) and Germany (29%). The fact that representation of women decreases significantly at higher academic ranks - with the percentage of female full professors being lower than the overall percentage of women in senior faculty positions - is a worldwide issue.
- Publications: During my career I published over 100 peer-reviewed publications, 4 book chapters, 14,000+ citations/All these is reflected in h-index 61. <https://scholar.google.co.il/citations?hl=iw&user=162oYyUAAAAJ>
- Ranking: Ranked among the top Animal Science researchers in Israel and globally. Ranked as number 1 in the list of 100 most cited papers published in poultry science 1945 to 2020 (Taylor Jr, 2021); In 2022 I was placed in the top 0.02% percentage rank for life time achievements in poultry by scholarGPS in the animal science discipline.
- Scientific Influence: Mentor to many MSc and PhD students, most of them are active and involve in academia and industry. Frequent collaborator with universities and industry (among them North Carolina State University, Wageningen University, Virginia Tech, Embrex, Evonik, Zinpro). Speaker and organizer in global poultry and animal nutrition symposia.

Vice-President of the World Poultry Science Association (WPSA)

In summary, by integrating cellular and molecular knowledge into applied poultry nutrition, we demonstrated that scientific insight could lead to practical advances for the industry. The new body of knowledge led to a revolution in poultry nutrition. The understanding that intestinal functionality can be affected during a specific window time of “pre-post hatch period” had a pivotal effect on global chicken performance.

I wish to thank my mentors along my career: Avigdor Cahaner, Dan Heller, Sue Lamont, Ton Schat, Paul Siegel, Peter Ferket, Catherine Ricks and Erik Wong. All of them were an inspiration to my academic and research life.

My scientific path has been shaped by curiosity, perseverance, and a passion for connecting ideas, people, and generations. I feel immense gratitude for having contributed to poultry science, to the progress of my students, and to the worldwide community of poultry researchers.

## Author contributions

ZU: Writing – review and editing, Writing – original draft.

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## References

- Cheled-Shoval, S. L., Druyan, S., and Uni, Z. (2015). Bitter, sweet and umami taste receptors and downstream signaling effectors: expression in embryonic and growing chicken gastrointestinal tract. *Poult. Sci.* 94 (8), 1928–1941. doi:10.3382/ps/pev152
- Cheled-Shoval, S. L. C., Uni, Z., and Scanes, C. G. (2022). "Taste in birds," in *Sturkie's avian physiology* (: Academic Press), 205–222.
- Das, R., Mishra, P., and Jha, R. (2021). In ovo feeding as a tool for improving performance and gut health of poultry: a review. *Front. Veterinary Sci.* 8, 754246. doi:10.3389/fvets.2021.754246
- Dayan, J., Reicher, N., Melkman-Zehavi, T., and Uni, Z. (2020). Incubation temperature affects yolk utilization through changes in expression of yolk sac tissue functional genes. *Poult. Sci.* 99 (11), 6128–6138. doi:10.1016/j.psj.2020.07.037
- Dayan, J., Melkman-Zehavi, T., Reicher, N., Braun, U., Inhuber, V., Mabeesh, S. J., et al. (2023a). Supply and demand of creatine and glycogen in broiler chicken embryos. *Front. Physiology* 14, 1079638. doi:10.3389/fphys.2023.1079638
- Dayan, J., Melkman-Zehavi, T., Goldman, N., Soglia, F., Zampiga, M., Petracci, M., et al. (2023b). In-ovo feeding with creatine monohydrate: implications for chicken energy reserves and breast muscle development during the pre-post hatching period. *Front. Physiology* 14, 1296342. doi:10.3389/fphys.2023.1296342
- Dayan, J., Goldman, N., Waiger, D., Melkman-Zehavi, T., Halevy, O., and Uni, Z. (2023c). A deep learning-based automated image analysis for histological evaluation of broiler pectoral muscle. *Poult. Sci.* 102 (8), 102792. doi:10.1016/j.psj.2023.102792
- Foye, O. T., Ferket, P. R., and Uni, Z. (2007). The effects of in ovo feeding arginine,  $\beta$ -hydroxy- $\beta$ -methyl-butylate, and protein on jejunal digestive and absorptive activity in embryonic and neonatal Turkey poults. *Poult. Sci.* 86 (11), 2343–2349. doi:10.3382/ps.2007-00110
- Gal-Garber, O., Mabeesh, S., Sklan, D., and Uni, Z. (2003). Nutrient transport in the small intestine:  $\text{Na}^+$ ,  $\text{K}^+$ -ATPase expression and activity in the small intestine of the chicken as influenced by dietary sodium. *Poult. Sci.* 82 (7), 1127–1133. doi:10.1093/ps/82.7.1127
- Geyra, A., Uni, Z., and Sklan, D. (2001a). Enterocyte dynamics and mucosal development in the posthatch chick. *Poult. Sci.* 80 (6), 776–782. doi:10.1093/ps/80.6.776
- Geyra, A., Uni, Z., and Sklan, D. (2001b). The effect of fasting at different ages on growth and tissue dynamics in the small intestine of the young chick. *Br. J. Nutr.* 86 (1), 53–61. doi:10.1079/bjn2001368
- Kadam, M. M., Barekain, M. R., K Bhanja, S., and Iji, P. A. (2013). Prospects of in ovo feeding and nutrient supplementation for poultry: the science and commercial applications—A review. *J. Sci. Food Agric.* 93 (15), 3654–3661. doi:10.1002/jsfa.6301
- Kornasio, R., Halevy, O., Kedar, O., and Uni, Z. (2011). Effect of in ovo feeding and its interaction with timing of first feed on glycogen reserves, muscle growth, and body weight. *Poult. Sci.* 90 (7), 1467–1477. doi:10.3382/ps.2010-01080
- Noy, Y., and Uni, Z. (2010). Early nutritional strategies. *World's Poult. Sci. J.* 66 (4), 639–646. doi:10.1017/s0043933910000620
- Oliveira, G., McManus, C., Salgado, C., and dos Santos, V. (2023). Bibliographical mapping of research into the relationship between in ovo injection practice and hatchability in poultry. *Veterinary Sci.* 10, 296–304. doi:10.3390/vetsci10040296
- Peebles, E. D. (2018). In ovo applications in poultry: a review. *Poult. Sci.* 97 (7), 2322–2338. doi:10.3382/ps/pey081
- Reicher, N., Melkman-Zehavi, T., Dayan, J., and Uni, Z. (2020). It's all about timing: early feeding promotes intestinal maturation by shifting the ratios of specialized epithelial cells in chicks. *Front. Physiology* 11. doi:10.3389/fphys.2020.596457
- Reicher, N., Melkman-Zehavi, T., Dayan, J., and Uni, Z. (2022a). Intra-amniotic administration of l-glutamine promotes intestinal maturation and enteroendocrine stimulation in chick embryos. *Sci. Rep.* 12 (1), 2645. doi:10.1038/s41598-022-06440-z
- Reicher, N., Melkman-Zehavi, T., Dayan, J., Wong, E. A., and Uni, Z. (2022b). Nutritional stimulation by in-ovo feeding modulates cellular proliferation and differentiation in the small intestinal epithelium of chicks. *Anim. Nutr.* 8, 91–101. doi:10.1016/j.aninu.2021.06.010
- Tako, E., Ferket, P. R., and Uni, Z. (2005). Changes in chicken intestinal zinc exporter mRNA expression and small intestinal functionality following intra-amniotic zinc-methionine administration. *J. Nutr. Biochem.* 16 (6), 339–346. doi:10.1016/j.jnutbio.2005.01.002
- Taylor Jr, R. L. (2021). The 100 most cited Poultry Science papers. *Poult. Sci.* 100 (7), 101256. doi:10.1016/j.psj.2021.101256
- Uni, Z., and Ferket, P. R. (2003). *Enhancement of development of oviparous species by in ovo feeding U.S. Patent*. U.S. Patent and Trademark Office.
- Uni, Z., and Ferket, R. P. (2004). Methods for early nutrition and their potential. *World's Poult. Sci. J.* 60 (1), 101–111. doi:10.1079/wps20049
- Uni, Z., Noy, Y., and Sklan, D. (1996). Development of the small intestine in heavy and light strain chicks before and after hatching. *Br. Poult. Sci.* 37 (1), 63–71. doi:10.1080/00071669608417837
- Uni, Z., Ganot, S., and Sklan, D. (1998a). Posthatch development of mucosal function in the broiler small intestine. *Poult. Sci.* 77 (1), 75–82. doi:10.1093/ps/77.1.75
- Uni, Z., Platin, R., and Sklan, D. (1998b). Cell proliferation in chicken intestinal epithelium occurs both in the crypt and along the villus. *J. Comp. Physiology B* 168 (4), 241–247. doi:10.1007/s003600050142
- Uni, Z., Noy, Y., and Sklan, D. (1999). Posthatch development of small intestinal function in the poult. *Poult. Sci.* 78 (2), 215–222. doi:10.1093/ps/78.2.215
- Uni, Z., Geyra, A., Ben-Hur, H., and Sklan, D. (2000). Small intestinal development in the young chick: crypt formation and enterocyte proliferation and migration. *Br. Poult. Sci.* 41 (5), 544–551. doi:10.1080/00071660020009054
- Uni, Z., Gal-Garber, O., Geyra, A., Sklan, D., and Yahav, S. (2001). Changes in growth and function of chick small intestine epithelium due to early thermal conditioning. *Poult. Sci.* 80 (4), 438–445. doi:10.1093/ps/80.4.438
- Uni, Z., Tako, E., Gal-Garber, O., and Sklan, D. (2003a). Morphological, molecular, and functional changes in the chicken small intestine of the late-term embryo. *Poult. Sci.* 82 (11), 1747–1754. doi:10.1093/ps/82.11.1747
- Uni, Z., Smirnov, A., and Sklan, D. (2003b). Pre- and posthatch development of goblet cells in the broiler small intestine: effect of delayed access to feed. *Poult. Sci.* 82 (2), 320–327. doi:10.1093/ps/82.2.320
- Uni, Z., Ferket, P. R., Tako, E., and Kedar, O. (2005). In ovo feeding improves energy status of late-term chicken embryos. *Poult. Sci.* 84 (5), 764–770. doi:10.1093/ps/84.5.764
- Uni, Z., Yadgary, L., and Yair, R. (2012). Nutritional limitations during poultry embryonic development. *J. Appl. Poult. Res.* 21 (1), 175–184. doi:10.3382/japr.2011-00478
- Wong, E. A., and Uni, Z. (2021). Centennial Review: the chicken yolk sac is a multifunctional organ. *Poult. Sci.* 100 (3), 100821. doi:10.1016/j.psj.2020.11.004
- Yadgary, L., Wong, E. A., and Uni, Z. (2014). Temporal transcriptome analysis of the chicken embryo yolk sac. *BMC Genomics* 15 (1), 690. doi:10.1186/1471-2164-15-690
- Yair, R., and Uni, Z. (2011). Content and uptake of minerals in the yolk of broiler embryos during incubation and effect of nutrient enrichment. *Poult. Sci.* 90 (7), 1523–1531. doi:10.3382/ps.2010-01283
- Yair, R., Shahar, R., and Uni, Z. (2013). Prenatal nutritional manipulation by in ovo enrichment influences bone structure, composition, and mechanical properties. *J. Animal Sci.* 91 (6), 2784–2793. doi:10.2527/jas.2012-5548
- Yair, R., Shahar, R., and Uni, Z. (2015). In ovo feeding with minerals and vitamin D3 improves bone properties in hatchlings and mature broilers. *Poult. Sci.* 94 (11), 2695–2707. doi:10.3382/ps/pev252



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# Growth hormone: lessons from chickens

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## KEYWORDS

growth hormone, chicken, stress, lipolysis, growth

## Introduction

In chickens, the anterior pituitary gland produces the same palette of hormones seen across the vertebrates:

- Adrenocorticotrophic hormone (ACTH) and  $\beta$ -endorphin
- Follicle-stimulating hormone (FSH)
- Growth hormone (GH)
- Luteinizing hormone (LH)
- Prolactin
- Thyrotropin (TSH)
- Neuropeptides, e.g.,
  - Met-enkephalin
  - Relaxin 3 (Lv et al., 2022)

This discussion focuses on contributions of the author and his collaborators with comments on what is still not known.

## Control of GH release and synthesis

Chicken somatotrophs respond to GH-releasing hormone (GHRH) and some neuropeptides. Intra-cellular concentrations of calcium ions in somatotrophs are increased by GHRH, thyrotropin-releasing hormone (TRH) (3/4 of somatotrophs), pituitary adenylate cyclase-activating peptide (85% of somatotrophs), leptin (51%), gonadotropin-releasing hormone (GnRH) (40%), and ghrelin (21%) (Scanes et al., 2007). Table 1 summarizes the neuropeptides that influence the release of GH (reviewed: Scanes, 2022). Some neuropeptides affect the release of more than one hormone. For instance, neuropeptide W decreases the secretion of GH, prolactin, and ACTH in chickens (Bu et al., 2016; Liu et al., 2022). What are still unknown are the following:

- Why there are multiple stimulatory and inhibitory factors?
- How pituitary cells influence the functioning of others?
- What the role of folliculostellate cells is?

These produce growth factors/hormones including annexin 1, fibroblast growth factor 2 (FGF2), leptin, and vascular endothelial growth factor (VEGF), and these presumably exert paracrine effects (Zhang et al., 2021).

**TABLE 1** Summary of the hypothalamic releasing hormones/neuropeptides influencing the secretion of GH (based on discussions in Scanes, 2022).

Releasing hormone/neuropeptide	GH
GHRH	+
GnRH	+?
Ghrelin	+
Leptin	+
NPW	–
PACAP	+
SRIF	–
TRH	+

+ indicates increase; – indicates decrease.

## GH isoforms

There are multiple forms of GH in the chicken pituitary gland:

- Monomer (40%)
- Glycosylated (16%)
- Dimer (14%)
- 15–16 kDa sub-monomeric isoform (16%) (Luna et al., 2005)

The sub-monomeric isoform of GH predominates in immune tissues (Luna et al., 2005) and retinal ganglion cells in chickens (Baudet et al., 2003).

## GH and growth

The hypothalamo-pituitary GH–insulin-like growth factor-1 (IGF-1) axis exists in chickens and other birds. GH increases growth in hypophysectomized young chickens (King and Scanes, 1986). Growth is reduced in sex-linked dwarf chickens with a mutation(s) in the GH receptor gene (Burnside et al., 1991). Plasma concentrations of IGF-1 are reduced in hypophysectomized young chickens and restored by GH treatment (Huybrechts et al., 1985). GH increases IGF-1 release from chick hepatocytes (Houston and O'Neill, 1991) and in adult chickens (Radecki et al., 1997). The mechanism for GH's effect on growth is mediated via Janus kinase (JAK)-2 (Zhou et al., 2005). Studies addressing the question as to whether GH increases growth in intact broilers are at best equivocal (Leung et al., 1986; Vasilatos-Younken et al., 1988; Cogburn et al., 1989; Scanes et al., 1990).

## GH and thyroid hormones

GH decreases hepatic deiodination of triiodothyronine ( $T_3$ ) in young chickens (Darras et al., 1992) with optimal

circulating concentrations of  $T_3$  essential for growth. GH-receptor-deficient dwarf chickens have reduced plasma concentrations of  $T_3$  (Scanes et al., 1983).

## GH and lipolysis

Mammalian and avian GH stimulates *in vitro* lipolysis (glycerol release from adipose tissue explants) (Campbell and Scanes, 1985) and inhibits glucagon-induced lipolysis (Campbell and Scanes, 1987). A GH antagonist prevents GH's effect on lipolysis *per se* but unexpectedly retains full activity in suppressing glucagon-induced lipolysis (Campbell et al., 1993). Moreover, reptilian, amphibian, and fish GH lacks lipolytic activity but inhibits glucagon-induced lipolysis (Campbell et al., 1991). What are not known are the following:

- Are the effects of GH physiologically relevant?
- Are these direct effects on adipocytes, or are these effects mediated through other cell types present in adipose tissue, such as endothelial cells and macrophages, followed by paracrine effects of cytokines or other neuropeptides?

The lipolytic effect is probably mediated through JAK-2 based on studies in mice (Shi et al., 2014). However, the mechanism for anti-lipolytic effects is yet to be determined.

## GH and reproduction

Administration of GH to laying hens increases shell thickness (Donoghue et al., 1990); this may be due to effects on the oviduct. This observation was followed by reports of oviductal and ovarian effects of GH. For instance, GH increases progesterone release from large yellow follicles (Hrabia et al., 2014a). GH decreases mucosal apoptosis in the oviduct but increases the expression of a specific gene (Hrabia et al., 2014b; Socha et al., 2017). Moreover, GH is present in the testes and ovary of chickens (Luna et al., 2014). There are associations between GH polymorphisms and egg production (Su et al., 2014).

## Stress and GH

Stress affects GH levels in post-hatch chickens. Plasma concentrations of GH were depressed following challenge with ACTH (Davison et al., 1980). Plasma concentrations of GH are also decreased by epinephrine (Harvey and Scanes, 1978) and morphine (Harvey and Scanes, 1987). Heat stress did not affect plasma concentrations of GH in young chickens but depressed hepatic expression of the GHR (Uyanga et al., 2022). Corticosterone induces somatotrophs in chick embryos (e.g., Bossis and Porter, 2000). Plasma concentrations of GH are increased by nutritional deprivation such as withholding feed or feeding a protein-deficient diet (Buonomo et al., 1982); the latter being presumed to be due to dietary stress depressing negative feedback for  $T_3$  and IGF-1.

## GH and the brain

Both GH- and prolactin-containing neurons are present within avian brains (Ramesh et al., 2000). Chick embryo retinal ganglion cells express GH (reviewed: Harvey et al., 2003; Harvey et al., 2012). Moreover, GH exerts a neuroprotective role in reducing apoptosis of retinal ganglion cells (Sanders et al., 2005). *In vitro*, GH depresses apoptosis and expression of caspase-3 and apoptosis-inducing factor-1 in neural retina explants from chick embryos (Harvey et al., 2006). Apoptosis in retinal ganglion cells is increased by antisera to GH *in ovo*, supporting a role for locally produced GH in regulating retinal apoptosis (Sanders et al., 2005). In an avian model for ischemic stroke, GH exerts a neuroprotective effect on cultured chick embryo hippocampal cells exposed to oxygen–glucose deprivation (Olivares-Hernández et al., 2021). Moreover, GH influences neurite development in the inner ear with increases in extension and branching of neurites in chick embryos (Gabielpillai et al., 2018). Information on the underlying mechanism(s) for neuronal effects of GH is lacking.

## GH and angiogenesis

Chick embryo chorioallantoic membranes (CAMs) are useful for examining the effects of hormones and growth factors on angiogenesis. Clapp et al. (1993) reported that “the 16-kilodalton N-terminal fragment of human prolactin is a potent inhibitor of angiogenesis” using chick embryo CAMs. In contrast, the formation of blood vessels was stimulated by either an anterior pituitary tissue or GH (Gould et al., 1995). The signal transduction mechanism for these effects remains unclear.

## Author contributions

CS: Conceptualization, Formal Analysis, Project administration, Supervision, Writing – original draft, Writing – review and editing.

## References

- Baudet, M.-L., Sanders, E. J., and Harvey, S. (2003). Retinal growth hormone in the chick embryo. *Endocrinology* 144, 5459–5468. doi:10.1210/en.2003-0651
- Bossis, I., and Porter, T. E. (2000). Ontogeny of corticosterone-inducible growth hormone-secreting cells during chick embryonic development. *Endocrinology* 141, 2683–2690. doi:10.1210/endo.141.7.7554
- Bu, G., Lin, D., Cui, L., Huang, L., Lv, C., Huang, S., et al. (2016). Characterization of neuropeptide B (NPB), neuropeptide W (NPW), and their receptors in chickens: evidence for NPW being a novel inhibitor of pituitary GH and prolactin secretion. *Endocrinology* 157, 3562–3576. doi:10.1210/en.2016-1141
- Buonomo, F. C., Griminger, P., and Scanes, C. G. (1982). Effects of gradation in protein-calorie restriction on the hypothalamic-pituitary-gonadal axis in young domestic fowl. *Poult. Sci.* 61, 800–803. doi:10.3382/ps.0610800
- Burnside, J., Liou, S. S., and Cogburn, L. A. (1991). Molecular cloning of the chicken growth hormone receptor complementary deoxyribonucleic acid: mutation of the gene in sex-linked dwarf chickens. *Endocrinology* 128, 3183–3192. doi:10.1210/endo-128-6-3183
- Campbell, R. M., and Scanes, C. G. (1985). Lipolytic activity of purified pituitary and bacterially derived growth hormone on chicken adipose tissue *in vitro*. *Proc. Soc. Exp. Biol. Med.* 180, 513–517. doi:10.3181/00379727-180-42210
- Campbell, R. M., and Scanes, C. G. (1987). Growth hormone inhibition of glucagon and cAMP-induced lipolysis by chicken adipose tissue *in vitro*. *Proc. Soc. Exp. Biol. Med.* 184, 456–460. doi:10.3181/00379727-184-42500
- Campbell, R. M., Kawauchi, H., Lewis, U. J., Papkoff, H., and Scanes, C. G. (1991). Comparison of lipolytic and antilipolytic activities of lower vertebrate growth hormones on chicken adipose tissue *in vitro*. *Proc. Soc. Exp. Biol. Med.* 197, 409–415. doi:10.3181/00379727-197-43275
- Campbell, R. M., Chen, W. Y., Wiehl, P., Kelder, B., Kopchick, J. J., and Scanes, C. G. (1993). A growth hormone (GH) analog that antagonizes the lipolytic effect but retains full insulin-like (antilipolytic) activity of GH. *Proc. Soc. Exp. Biol. Med.* 203, 311–316. doi:10.3181/00379727-203-43604
- Clapp, C., Martial, J. A., Guzman, R. C., Rentier-Delure, F., and Weiner, R. I. (1993). The 16-kilodalton N-terminal fragment of human prolactin is a potent inhibitor of angiogenesis. *Endocrinology* 133, 1292–1299. doi:10.1210/endo.133.3.7689950
- Cogburn, L. A., Liou, S. S., Rand, A. L., and McMurtry, J. P. (1989). Growth, metabolic and endocrine responses of broiler cockerels given a daily subcutaneous injection of natural or biosynthetic chicken growth hormone. *J. Nutr.* 119, 1213–1222. doi:10.1093/jn/119.8.1213

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- Darras, V. M., Berghman, L. R., Vanderpooten, A., and Kühn, E. R. (1992). Growth hormone acutely decreases type III iodothyronine deiodinase in chicken liver. *FEBS Lett.* 310, 5–8. doi:10.1016/0014-5793(92)81133-7
- Davison, T. F., Scanes, C. G., Harvey, S., and Flack, I. H. (1980). The effect of an injection of corticotrophin on plasma concentrations of corticosterone, growth hormone and prolactin in two strains of domestic fowl. *Br. Poult. Sci.* 21, 287–293. doi:10.1080/00071668008416671
- Donoghue, D. J., Campbell, R. M., and Scanes, C. G. (1990). Effect of biosynthetic chicken growth hormone on egg production in white leghorn hens. *Poult. Sci.* 69, 1818–1821. doi:10.3382/ps.0691818
- Gabrielpillai, J., Geissler, C., Stock, B., Stöver, T., and Diensthuber, M. (2018). Growth hormone promotes neurite growth of spiral ganglion neurons. *NeuroReport* 29, 637–642. doi:10.1097/WNR.0000000000001011
- Gould, J., Aramburo, C., Capdevielle, M., and Scanes, C. G. (1995). Angiogenic activity of anterior pituitary tissue and growth hormone on the chick embryo chorio-allantoic membrane: a novel action of GH. *Life Sci.* 56, 587–594. doi:10.1016/0024-3205(94)00491-a
- Harvey, S., and Scanes, C. G. (1978). Effect of adrenaline and adrenergic active drugs on growth hormone secretion in immature cockerels. *Experientia* 34, 1096–1097. doi:10.1007/BF01915371
- Harvey, S., and Scanes, C. G. (1987). Opiate inhibition of growth hormone secretion in young chickens. *Gen. Comp. Endocrinol.* 65, 34–39. doi:10.1016/0016-6480(87)90219-x
- Harvey, S., Kakebeeke, M., Murphy, A. E., and Sanders, E. J. (2003). Growth hormone in the nervous system: autocrine or paracrine roles in retinal function? *Can. J. Physiol. Pharmacol.* 81, 371–384. doi:10.1139/y03-034
- Harvey, S., Baudet, M.-L., and Sanders, E. J. (2006). Growth hormone and cell survival in the neural retina: caspase dependence and independence. *NeuroReport* 17, 1715–1718. doi:10.1097/01.wnr.0000239952.22578.90
- Harvey, S., Lin, W., Gitterman, D., El-Abry, N., Qiang, W., and Sanders, E. J. (2012). Release of retinal growth hormone in the chick embryo: local regulation? *Gen. Comp. Endocrinol.* 176, 361–366. doi:10.1016/j.ygcen.2012.01.021
- Houston, B., and O'Neill, I. E. (1991). Insulin and growth hormone act synergistically to stimulate insulin-like growth factor-I production by cultured chicken hepatocytes. *J. Endocrinol.* 128, 389–393. doi:10.1677/joe.0.1280389
- Hrabia, A., Sechman, A., and Rzasca, J. (2014a). Effect of growth hormone on basal and LH-stimulated steroid secretion by chicken yellow ovarian follicles. An *in vitro* study. *Folia. Biol. (Krakow)* 62, 313–319. doi:10.3409/fb62\_4.313
- Hrabia, A., Leśniak-Walentyn, A., Sechman, A., and Gertler, A. (2014b). Chicken oviduct—the target tissue for growth hormone action: effect on cell proliferation and apoptosis and on the gene expression of some oviduct-specific proteins. *Cell Tissue Res.* 357, 363–372. doi:10.1007/s00441-014-1860-6
- Huybrechts, L. M., King, D. B., Lauterio, T. J., Marsh, J., and Scanes, C. G. (1985). Plasma concentrations of somatomedin-C in hypophysectomized, dwarf and intact growing domestic fowl as determined by heterologous radioimmunoassay. *J. Endocrinol.* 104, 233–239. doi:10.1677/joe.0.1040233
- King, D. B., and Scanes, C. G. (1986). Effect of mammalian growth hormone and prolactin on the growth of hypophysectomized chickens. *Proc. Soc. Exp. Biol. Med.* 182, 201–207. doi:10.3181/00379727-182-42328
- Leung, F. C., Taylor, J. E., Wien, S., and Van Iderstine, A. (1986). Purified chicken growth hormone (GH) and a human pancreatic GH-releasing hormone increase body weight gain in chickens. *Endocrinology* 118, 1961–1965. doi:10.1210/endo-118-5-1961
- Liu, M., Bu, G., Wan, Y., Zhang, J., Mo, C., Li, J., et al. (2022). Evidence for neuropeptide W acting as a physiological corticotropin-releasing inhibitory factor in male chickens. *Endocrinology* 163, bqac073. doi:10.1210/endo/bqac073
- Luna, M., Martínez-Moreno, C. G., Ahumada-Solórzano, M. S., Harvey, S., Carranza, M., and Aramburo, C. (2014). Extrapituitary growth hormone in the chicken reproductive system. *Gen. Comp. Endocrinol.* 203, 60–68. doi:10.1016/j.ygcen.2014.02.021
- Luna, M., Barraza, N., Berumen, L., Carranza, M., Pedernera, E., Harvey, S., et al. (2005). Heterogeneity of growth hormone immunoreactivity in lymphoid tissues and changes during ontogeny in domestic fowl. *Gen. Comp. Endocrinol.* 144, 28–37. doi:10.1016/j.ygcen.2005.04.007
- Lv, C., Zheng, H., Jiang, B., Ren, Q., Zhang, J., Zhang, X., et al. (2022). Characterization of relaxin 3 and its receptors in chicken: evidence for relaxin 3 acting as a novel pituitary hormone. *Front. Physiol.* 13, 1010851. doi:10.3389/fphys.2022.1010851
- Olivares-Hernández, J. D., Balderas-Márquez, J. E., Carranza, M., Luna, M., Martínez-Moreno, C. G., and Aramburo, C. (2021). Growth hormone (GH) enhances endogenous mechanisms of neuroprotection and neuroplasticity after oxygen and glucose deprivation injury (ogd) and reoxygenation (ogd/r) in chicken hippocampal cell cultures. *Neural Plast.* 2021, 9990166. doi:10.1155/2021/9990166
- Radecki, S. V., McCann-Levorse, L., Agarwal, S. K., Burnside, J., Proudman, J. A., and Scanes, C. G. (1997). Chronic administration of growth hormone (GH) to adult chickens exerts marked effects on circulating concentrations of insulin-like growth factor-I (IGF-I), IGF binding proteins, hepatic GH regulated gene I, and hepatic GH receptor mRNA. *Endocrine* 6, 117–124. doi:10.1007/BF02738954
- Ramesh, R., Kuenzel, W. J., Buntin, J. D., and Proudman, J. A. (2000). Identification of growth-hormone- and prolactin-containing neurons within the avian brain. *Cell Tissue Res.* 299, 371–383. doi:10.1007/s004419900104
- Sanders, E. J., Parker, E., Aramburo, C., and Harvey, S. (2005). Retinal growth hormone is an anti-apoptotic factor in embryonic retinal ganglion cell differentiation. *Exp. Eye Res.* 81, 551–560. doi:10.1016/j.exer.2005.03.013
- Scanes, C. G., Marsh, J., Decuyper, E., and Rudas, P. (1983). Abnormalities in the plasma concentration of thyroxine, triiodothyronine and growth hormone in sex-linked dwarf and autosomal dwarf white leghorn domestic fowl (*Gallus domesticus*). *J. Endocrinol.* 97, 127–135. doi:10.1677/joe.0.0970127
- Scanes, C. G., Peterla, T. A., Kantor, S., and Ricks, C. A. (1990). *In vivo* effects of biosynthetic chicken growth hormone on broiler-strain chickens. *Growth, Dev. Aging* 54, 95–106.
- Scanes, C. G., Glavaski-Joksimovic, A., Johannsen, S. A., Jefinija, S., and Anderson, L. L. (2007). Subpopulations of somatotropes with differing intracellular calcium concentration responses to secretagogues. *Neuroendocrinol.* 85, 221–231. doi:10.1159/000102968
- Scanes, C. G. (2022). “Pituitary gland,” in *Sturkie's Avian Physiology 7th edition*. Editors C. G. Scanes, and S. Dridi (New York: Academic Press), 759–814.
- Shi, S. Y., Luk, C. T., Brunt, J. J., Sivasubramaniyam, T., Lu, S. Y., Schroer, S. A., et al. (2014). Adipocyte-specific deficiency of janus kinase (JAK) 2 in mice impairs lipolysis and increases body weight, and leads to insulin resistance with ageing. *Diabetologia* 57, 1016–1026. doi:10.1007/s00125-014-3185-0
- Socha, J. K., Sechman, A., Mika, M., and Hrabia, A. (2017). Effect of growth hormone on steroid concentrations and mRNA expression of their receptor, and selected egg-specific protein genes in the chicken oviduct during pause in laying induced by fasting. *Domest. Anim. Endocrinol.* 61, 1–10. doi:10.1016/j.domaniend.2017.05.001
- Su, Y. J., Shu, J. T., Zhang, M., Zhang, X. Y., Shan, Y. J., Li, G. H., et al. (2014). Association of chicken growth hormone polymorphisms with egg production. *Genet. Mol. Res.* 13, 4893–4903. doi:10.4238/2014.July.4.3
- Uyanga, V. A., Zhao, J., Wang, X., Jiao, H., Onagbesan, O. M., and Lin, H. (2022). Dietary L-citrulline modulates the growth performance, amino acid profile, and the growth hormone/insulin-like growth factor axis in broilers exposed to high temperature. *Front. Physiol.* 13, 937443. doi:10.3389/fphys.2022.937443
- Vasilatos-Younken, R., Cravener, T. L., Cogburn, L. A., Mast, M. G., and Wellenreiter, R. H. (1988). Effect of pattern of administration on the response to exogenous pituitary-derived chicken growth hormone by broiler-strain pullets. *Gen. Comp. Endocrinol.* 71, 268–283. doi:10.1016/0016-6480(88)90255-9
- Zhang, J., Lv, C., Mo, C., Liu, M., Wan, Y., Li, J., et al. (2021). Single-cell RNA sequencing analysis of chicken anterior pituitary: a bird's-eye view on vertebrate pituitary. *Front. Physiol.* 12, 562817. doi:10.3389/fphys.2021.562817
- Zhou, Y., Wang, X., Hadley, J., Corey, S. J., and Vasilatos-Younken, R. (2005). Regulation of JAK2 protein expression by chronic, pulsatile GH administration *in vivo*: a possible mechanism for ligand enhancement of signal transduction. *Gen. Comp. Endocrinol.* 144, 128–139. doi:10.1016/j.ygcen.2005.05.001



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# Sometimes it's good to be lucky: blood flow, glutathione, oxidative stress, and mitochondria

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## 1 Luck begins

Much of the success I have had can be attributed to a good share of luck. I came out of high school interest in science – I'm not sure what I liked about it but I just wanted to learn more. I went to Eastern Illinois University (EIU) in a Pre-Professional route majoring in Zoology. I chose EIU because I wanted to swim competitively and not for any academic reason. I knew the Ray Padovan who had coached me in age-group swimming one summer. I lucked out because EIU had a strong biology program that helped me in graduate school and beyond. After my first semester, Padovan told me I would receive a tuition scholarship through the Athletic Department based on my GPA (not for my phenomenal swimming ability). I came out of Eastern with a BS in Zoology that included 5 physiology courses and a minor in Chemistry. Physiology was really what floated my boat but it took me awhile to get back to it. During my MS in ruminant nutrition, at Southern Illinois University (Carbondale, IL) because of a snowstorm, Amtrak Railroad and Interstate 57 were closed. If the snowstorm had not shut everything down, I would never have met my wife, Sari. This was a huge stroke of luck!

After the MS, I went to the University of Illinois for a PhD. After going through two labs (ruminant nutrition and rumen microbiology), I finally got back to my real interest in physiology with Dr. Paul Harrison (PCH). I would not recommend this path for graduate students as it added a couple years to my PhD program. I worked on heat stress physiology in broilers and ended up with 5 publications (Bottje W. G. and Harrison P. C., 1985; Bottje W. G. and Harrison P. C., 1985; Bottje W. G. and Harrison P. C., 1986; Bottje W. G. and Harrison P. C., 1986; Bottje and Harrison, 1987). However, the nearly 2-year delay was lucky because I ended up doing a post-doc that ultimately led to an NIH grant a couple years later. I interviewed at the University of New Hampshire but (luckily) I was not hired for that position. One thing that I lacked was post-doc experience.

When I put my PhD committee together, the 'normal' number of committee members was 5. I added a sixth member, Dr. Ken Holmes, in the Dept. of Veterinary Biosciences (U of I). Dr. Holmes had developed a new method of measuring blood flow in tissue called a thermal pulse decay (TPD) system. I was lucky enough to have been hired into his lab as a post-doc to work on further development and validation of the TPD system (see Arkin et al., 1986). The TPD method could measure time course changes in blood flow (tissue perfusion) at 3 min intervals in 6 areas in a single organ or multiple organs over several hours. Placement of probes in the renal cortex and medulla, enabled us to take repeated measurements in these regions of the kidney – something that had never been done before.

## 2 Contributions to science

### 2.1 Getting started

While working in Dr. Holmes' lab, Dr. Hassan (in an adjacent lab), came in 1 day and mentioned that while working with a chemical that rapidly depletes hepatic glutathione (GSH)<sup>1</sup> levels, he noticed that the rat's ears turned red. He said, "I think there are changes in blood flow happening – you should see if it affects liver blood flow". We conducted a set of studies on rats that revealed an inverse relationship between hepatic blood flow and tissue GSH. This study eventually led to an NIH grant.

I took a chance and gave my interview seminar for the Dept. Animal Science (University of Arkansas, UA) on the GSH and liver blood flow study in rats (even though the position was for an Environmental Physiologist in poultry). I was hired and started at the UA, Division of Agriculture in July of 1985. That fall, I attended the American Physiology Society (APS) fall meeting (Niagra Falls, CN) and presented a poster on the apparent inverse relationship between GSH and liver blood flow. Two people stopped by my poster that had a huge impact on me. The first one was Dr. Aubrey Taylor who was President of APS who thought the research was interesting and novel and encouraged me to pursue this rigorously. I submitted the GSH-liver blood flow manuscript one more time and got it accepted in *Biochemical Pharmacology* (Bottje et al., 1986). The second person I met was Dr. Bob Wideman (at Pennsylvania State University) who was interested in the TPD method and how it might be used for studying blood flow mechanisms in the avian kidney. We ended up doing a series of studies a few years later using his one lobe avian kidney model. That was a very good piece of luck for me.

In early 1986, I gave a seminar for the Chemistry Department at UA the liver blood flow and GSH interrelationship. After the seminar, Dr. Collis Geren (Dept. Chair and later the Dean of the Graduate School) offered to help me package an NIH grant which was extremely fortunate because I had not written a grant proposal before – another piece of luck. Dr. Geren was world renown for his fundamental work in spider venom toxicity. Dr. Geren was also one of those people who looks out for the general good of the community and never self-serving. In 1987, the grant was ranked in the top 5% and fully funded by NIEHS. Starting off as an Assistant Professor with a 5 years large federal grant was extremely lucky. I was able to hire a couple of post doc and graduate students without relying on departmental funds.

### 2.2 Antioxidants, oxidative stress, blood flow and prostaglandins

To our knowledge, the inverse relationship between GSH and hepatic blood *in vivo* (Bottje et al., 1986) was the first time this was reported. Subsequently, we later reported that indomethacin, an inhibitor of prostaglandin synthase, attenuated both the increase in celiac blood flow in broilers (Beers et al., 1990) and hepatic blood flow and elevations in 6-keto PGF<sub>1a</sub> (prostacyclin) in rabbits

(Bottje et al., 1991) and swine (Bottje et al., 1992). There were also inverse relationships between GSH levels and prostaglandin synthesis in renal medullary homogenates (Nejad and Bottje, 1992). The increased blood flow in tissues following toxic insult could contribute to tissue damage as well as help in tissue repair and recovery.

### 2.3 Interorgan circulation of glutathione

A fundamental study by Anderson et al. (1980) described interorgan circulation of GSH that entailed synthesis in the liver followed by export into the general circulation and taken up by extrahepatic tissues. In that study, blood samples were taken at a single time point; ~20 from a systemic artery and hepatic portal vein (representing afferent sources of blood entering the liver) with only 4 samples obtained from the hepatic vein which is difficult to reach due to its location next to the diaphragm within the thoracic cavity. Birds, however, do not have a diaphragm, thus it was possible to obtain repeated blood samples from the hepatic vein. This was facilitated with a hooked needle that Bob Wideman used in his avian kidney studies. In the study by Wang et al. (1998), interorgan circulation of GSH was clearly confirmed and was documented in the avian liver for the first time. This technique also enabled assessment effects of a stress hormone (norepinephrine) that stimulated GSH release from the liver (Song et al., 2000) and hepatic extraction of circulating amino acids and impact of methionine infusion across the hepatic vasculature (Song et al., 2001).

### 2.4 Oxidative stress, mitochondria, and pulmonary hypertension syndrome (PHS)

At the fall physiology meeting in 1986, Bob Wideman mentioned a new problem in the poultry industry that he had seen at altitude and was now showing up at sea level; ascites (PHS). I visited his lab after the meeting and he showed me evidence of lung damage in day old chicks. The GSH-oxidative stress studies associated with the NIEHS studies led to an interest in determining if oxidative stress was associated with PHS and presented in report by Enkvetchakul et al. (1993) and later to a study investigating Vit E and PHS (Bottje et al., 1995). This research also sparked an interest in mitochondrial function and biochemistry as mitochondria are a major site of endogenous oxidative stress. Site-specific defects in the electron transport chain that would contribute to higher oxidative stress were identified in liver (Cawthon et al., 1999), lung (Iqbal et al., 2001), and heart (Tang et al., 2002) obtained from broilers with PHS.

### 2.5 Mitochondria and feed efficiency

Interest in mitochondria continued with studies that revealed evidence of a link between muscle mitochondrial function and feed efficiency (FE). In a series of studies, evidence of mitochondrial dysfunction and/or biochemistry, including site-specific defects in electron transport, in tissues obtained from broilers expressing a low FE phenotype were identified in muscle (Bottje et al., 2002; 2009; Iqbal et al., 2001), duodenum (Ojano-Dirain et al., 2004; Ojano-Dirain et al., 2007), liver (Iqbal et al., 2001), lymphocytes

<sup>1</sup> Glutathione is an endogenous antioxidant found at mM levels in most cells. It plays vital roles in numerous redox reactions in the cell.

(Lassiter et al., 2006), and heart muscle (Tinsley et al., 2010). Differences in proton leak kinetics were also determined in muscle mitochondria between high and low FE groups (Bottje et al., 2009).

## 2.6 Global gene expression and feed efficiency

Because mitochondrial ROS initiate signal transduction, we conducted global gene and protein expression analysis to understand the gene and gene product landscape associated with feed efficiency (Kong et al., 2011; 2016; Bottje et al., 2012, Bottje et al., 2017a; Bottje et al., 2017b). Interesting aspects of the story were that mitochondria in high FE animals appeared to have enriched ribosomal machinery and protein translation compared to muscle from low FE phenotype (Bottje et al., 2017b). Based on the global expression studies, further insight into fundamental mechanisms revealed that high FE birds exhibited enrichment of intracellular degradation pathways of autophagy and proteosomes (Piekarski-Welscher et al., 2018). This suggests that high FE animals may either repair proteins quicker or turnover damaged proteins to a greater extent than low FE. The myostatin signaling pathway was shown to play a role in the phenotypic expression of FE also (Lassiter et al., 2018). Using an analytical method of regulatory impact factor (RIF) analysis (Hudson et al., 2009; 2012; Reverter et al., 2010) identified progesterone as having a major influence on the phenotypic expression of FE (Bottje et al., 2017a). This led to work that clearly identified the presence of several hormone receptors including progesterone on avian mitochondria (Lassiter et al., 2018).

## 2.7 Water efficiency

Since 2019, I have been lucky to serve as project director (PD) on a USDA NIFA Sustainable Agriculture Systems project<sup>2</sup>. The “catalysts” for this were Dr.s Dridi (UA) and Lei (Cornell University) coerced me into being the PD. One sub-aim on this project was headed up by Dr. Sara Orłowski (UA) who successfully selected broilers for low water conversion ratio (LWCR, water efficient) and high water conversion ratio (HWCR, water inefficient) from a modern random bred (MRB) base broiler population<sup>3</sup> (Hiltz et al., 2021). A series of studies have been conducted to assess the effect that divergent selection has had on gene and/or protein expression in the hypothalamus, kidney, intestines, immune systems, and meat quality (see Aloui et al., 2024; Lassiter et al., 2024; Lassiter et al., 2025; Orłowski et al., 2024; Santamaria et al., 2025). While selection for feed conversion ratio (FCR) has a positive impact on water, selection for WCR has resulted in even further improvements in water use efficiency. These studies hopefully will provide a way to help the poultry industry down the road as water scarcity becomes even more prevalent in the face of hotter temperatures over longer periods of time.

<sup>2</sup> USDA NIFA SAS 2019-69012-29905. Empowering the US Broiler Industry for Transformation and Sustainability.

<sup>3</sup> The modern random bred (MRB) line was established in 2016 and represented a composite of commercial broiler lines at that time.

## 3 Summary

Have I been lucky? Absolutely! Many events have put me in the right place at the right time. I have been fortunate to have had great graduate students, post-docs and collaborators. I was part of the development of a Center that brought in some of the best faculty in poultry science. I also want to acknowledge contributions by Dr. Kentu Lassiter who has been working in the lab since he was an undergraduate student. Finally, I've also been extremely lucky to have received funding throughout my career through various Federal agencies, State, and industry sources.

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## References

- Aloui, L., Greene, E. S., Tabler, T., Lassiter, K., Bottje, W. G., Orłowski, S., et al. (2024). Effect of heat stress on hypothalamic expression profile of water homeostasis genes in low- and high-water efficient chicken lines. *Phys. Reports* 12 (5), e15972. doi:10.14814/phy2.15972
- Anderson, M. E., Bridges, R. J., and Meister, A. (1980). Direct evidence for interorgan transport of glutathione and that the non-filtration renal mechanism for glutathione utilization involves  $\gamma$ -glutamyl transpeptidase. *BBRC* 96, 848–852. doi:10.1016/0006-291X(80)91433-3
- Arkin, H., Holmes, K. R., Chen, M. M., and Bottje, W. G. (1986). Thermal pulse decay (TPD) method for the simultaneous measurement of local thermal conductivity and blood perfusion: a theoretical analysis. *J. Biomech. Eng.* 108, 204–214. doi:10.1115/1.3138604
- Beers, K. W., Nejad, H., and Bottje, W. G. (1990). Indomethacin attenuates celiac blood flow hyperemia following glutathione depletion. *Biochem. Pharm.* 40, 2331–2335. doi:10.1016/0006-2952(90)90730-9
- Bottje, W. G., and Harrison, P. C. (1985a). The effect of tap water, carbonated water, sodium bicarbonate and calcium chloride on blood acid-base balance in cockerels subjected to heat stress. *Poult. Sci.* 64, 107–113. doi:10.3382/ps.0640107
- Bottje, W. G., and Harrison, P. C. (1985b). Effect of carbonated water on growth of cockerels subjected to constant and cyclic heat stress temperatures. *Poult. Sci.* 64, 1285–1292. doi:10.3382/ps.0641285
- Bottje, W. G., and Harrison, P. C. (1986a). The effect of heat stress and hypercapnia on postprandial intestinal hyperemia in domestic cockerels. *Poult. Sci.* 65, 1607–1614.
- Bottje, W. G., and Harrison, P. C. (1986b). Alpha-adrenergic regulation of celiac blood flow and plasma catecholamine response during acute heat stress in fed cockerels. *Poult. Sci.* 65, 1598–1606. doi:10.3382/ps.0651598
- Bottje, W. G., and Harrison, P. C. (1987). Celiac cyclic blood flow pattern response to feeding and heat stress exposure. *Poult. Sci.* 66, 2039–2042. doi:10.3382/ps.0662039
- Bottje, W. G., Enkvetchakul, B., Moore, R., and McNew, R. (1995). Effect of  $\alpha$ -tocopherol on antioxidants, peroxidation, and the incidence of pulmonary hypertension syndrome in domestic fowl. *Poult. Sci.* 74, 1356–1369.
- Bottje, W., Glahn, R., Beers, K., Nejad, H., Graupner, W., and Holmes, K. R. (1991). Indomethacin attenuation of hepatic perfusion and plasma 6-keto PGF<sub>1 $\alpha$</sub>  elevations following glutathione depletion in rabbits. *Biochim. Biophys. Acta* 1073, 168–176. doi:10.1016/0304-4165(91)90198-P
- Bottje, W., Glahn, R., Beers, K., Nejad, H., and Holmes, K. (1992). Effect of diethyl maleate on glutathione, blood pressure, hepatic and renal cortical perfusion and portal 6-ketoPGF<sub>1 $\alpha$</sub>  and TxB<sub>2</sub> in swine. *Comp. Biochem. Physiol.* 101C, 125–129. doi:10.1016/0742-8413(92)90209-P
- Bottje, W., Tang, Z., Iqbal, M., Cawthon, D., Okimoto, R., Wing, T., et al. (2002). Association of mitochondrial function with feed efficiency within a single genetic line of Male broilers. *Poult. Sci.* 81, 546–555. doi:10.1093/ps/81.4.546
- Bottje, W., Brand, M. D., Ojano-Dirain, C., Lassiter, K., Toyomizu, M., and Wing, T. (2009). Mitochondrial proton leak kinetics and relationship with feed efficiency within a single genetic line of Male broilers. *Poult. Sci.* 88, 1683–1693. doi:10.3382/ps.2009-00100
- Bottje, W. G., Kong, B., Song, J. J., Hargis, B. M., Lassiter, K., Wing, T., et al. (2012). Gene expression in breast muscle associated feed efficiency in a single male broiler line using a chicken 44k microarray II. Differentially expressed focus genes. *Poult. Sci.* 91, 2576–2587. doi:10.3382/ps.2012-02204
- Bottje, W. G., Kong, B., Reverter, A., Waardenberg, A. J., Lassiter, K., and Hudson, N. J. (2017a). Progesterone signaling in broiler skeletal muscle is associated with divergent feed efficiency. *BMC Syst. Biol.* 11, 29. doi:10.1186/s12918-017-0396-2
- Bottje, W. G., Lassiter, K., Piekarski-Welsher, A., Dridi, S., Gomez-Reverter, A., Hudson, N. J., et al. (2017b). Proteogenomics reveals enriched ribosome assembly and protein translation in *Pectoralis major* of high feed efficiency pedigree broiler males. *Front. Physiology* 8 (article 306), 1–11. doi:10.3389/fphys.2017.00306
- Cawthon, D., McNew, R., Beers, K. W., and Bottje, W. G. (1999). Evidence of mitochondrial dysfunction in broilers with pulmonary hypertension syndrome (Ascites): effect of t-butyl hydroperoxide on function, glutathione and related thiols. *Poult. Sci.* 78, 114–125. doi:10.1093/ps/78.1.114
- Enkvetchakul, B., Bottje, W., Anthony, N., Moore, R., and Huff, W. (1993). Compromised antioxidant status associated with ascites in broilers. *Poult. Sci.* 72, 2272–2280. doi:10.3382/ps.072272
- Hiltz, J. Z., Orłowski, S. K., Harrington, L. N., Maynard, C. W., Tabler, T., and Anthony, N. B. (2021). Applied research note: development of a novel low flow water monitoring system poultry/agriculture systems. *J. Appl. Poult. Res.* 30, 1–6. doi:10.1016/j.japr.2021.100151
- Hudson, N. J., Reverter, A., and Dalrymple, B. P. (2009). A differential wiring analysis of expression data correctly identifies the gene containing the causal mutation. *PLoS Comput. Biol.* 5 (5), e1000382. doi:10.1371/journal.pcbi.1000382
- Hudson, N. J., Dalrymple, B. P., and Reverter, A. (2012). Beyond differential expression: the quest for causal mutations and effector molecules. *BMC Genomics* 13, 356. doi:10.1186/1471-2164-13-356
- Iqbal, M., Cawthon, D., Wideman, R. F., Jr., and Bottje, W. G. (2001). Lung mitochondrial dysfunction in pulmonary hypertension syndrome. I. Site-specific defects in the electron transport chain. *Poult. Sci.* 80, 485–495. doi:10.1093/ps/80.4.485
- Kong, B.-W., Song, J. J., Lee, J. Y., Hargis, B. M., Wing, T., Lassiter, K., et al. (2011). Gene expression in breast muscle associated feed efficiency in a single male broiler line using a chicken 44k microarray. I. Top differentially expressed genes. *Poult. Sci.* 90, 2535–2547. doi:10.3382/ps.2011-01435
- Kong, B.-W., Lassiter, K., Piekarski, A., Reverter-Gomez, A., Hudson, N. J., and Bottje, W. G. (2016). Proteomics of breast muscle tissue associated with the phenotypic expression of feed efficiency within a pedigree male broiler line. I. Highlight on mitochondria. *PLoS* 11 (5), e0155679. doi:10.1371/journal.pone.0155679
- Lassiter, K., Iqbal, M., Pumford, N. R., Ojano-Dirain, C., Tinsley, N., Wing, T., et al. (2006). Differential expression of mitochondrial and extra-mitochondrial proteins in lymphocytes of low and high feed efficient male broilers. *Poult. Sci.* 85, 2251–2259. doi:10.1093/ps/85.12.2251
- Lassiter, K., Dridi, S., Greene, E. S., Kong, B., and Bottje, W. G. (2018). Identification of mitochondrial hormone receptors in avian muscle cells. *Poult. Sci.* 97, 2926–2933. doi:10.3382/ps/pey126
- Lassiter, K., Aloui, L., Greene, E. S., Maqaeada, M., Tabler, T., Dridi, S., et al. (2024). Water homeostasis gene expressed in the kidneys of broilers divergently selected for water conversion ratio. *Poult. Sci.* 104, 104560. doi:10.1016/j.psj.2024.104560
- Lassiter, K., Loujain, A., Green, E. S., Maqaeada, M., Schaeffer, K., Roach, B., et al. (2025). Intestinal gene expression in heat-stressed broilers selected for high water efficiency. *Front. Avian Physiol.*
- Nejad, H. H., and Bottje, W. G. (1992). Glutathione depletion and rabbit renal medulla prostacyclin and thromboxane: levels *in vivo* and following homogenate incubation *in vitro*. *Int. J. Biochem.* 24, 561–564. doi:10.1016/0020-711X(92)90327-W
- Ojano-Dirain, C., Iqbal, M., Cawthon, D., Swonger, S., Wing, T., Cooper, M., et al. (2004). Site-specific effects in electron transport in duodenal mitochondria is associated with low feed efficiency in broiler breeder males. *Poult. Sci.* 83, 1394–1403. doi:10.1093/ps/83.8.1394
- Ojano-Dirain, C., Tinsley, N. B., Wing, T., Cooper, M., and Bottje, W. (2007). Membrane potential and hydrogen peroxide production in duodenal mitochondria in broilers chickens (*Gallus gallus*) with low and high feed efficiency. *Comp. Biochem. Physiol.* 147, 934–941.
- Orłowski, S., Greene, E. S., Lassiter, K., Tabler, T., Bottje, W., and Dridi, S. (2024). Research note: carcass yield and meat quality in high- and low-water efficient broiler lines exposed to heat stress. *Poult. Sci.* 103 (9), 103921. doi:10.1016/j.psj.2024.103921
- Piekarski-Welsher, A., Greene, E., Lassiter, K., Kong, B. C., Dridi, S., and Bottje, W. (2018). Enrichment of autophagy and proteasome pathways in breast muscle of feed efficient pedigree male broiler. *Front. Physiol.* 26 (9), 1342. doi:10.3389/fphys.2018.01342
- Reverter, A., Hudson, N. J., Nagaraj, S. H., Perez-Enciso, M., and Dalrymple, B. P. (2010). Regulatory impact factors: unraveling the transcriptional regulation of complex traits from expression data. *Bioinformatics* 26 (7), 896–904. doi:10.1093/bioinformatics/btq051
- Santamaria, J. M., Beck, C. N., Orłowski, S. K., Maqueda, M., and Bottje, W. G. (2025). Selection for improved water efficiency in broiler breeder lines does not negatively impact immune response capabilities to Gram- and Gram+ bacterial components and a killed *Salmonella* enteritidis vaccine. *Vet. Sci.* 12, 279. doi:10.3390/vetsci12030279
- Song, Z., Cawthon, D., Beers, K., and Bottje, W. G. (2000). Hepatic and extra-hepatic stimulation of glutathione release by norepinephrine. *In Vivo. Poult. Sci.* 147 (4), 934–941. doi:10.1016/j.cbpa.2007.02.029
- Song, Z., Beers, K., Dibner, J. J., Vázquez-Añón, M., McNew, R., and Bottje, W. G. (2001). Hepatic extraction of plasma free amino acids and response to hepatic portal venous infusion of methionine sources in anesthetized SCWL males. *Comp. Biochem. Physiol. (B)* 130, 237–250. doi:10.1016/s1096-4959(01)00430-4
- Tang, Z., Iqbal, M., Cawthon, D., and Bottje, W. G. (2002). Heart and muscle mitochondrial dysfunction in pulmonary hypertension syndrome in broilers. *Gallus Domest. Comp. Biochem. Physiol.* 132, 527–540. doi:10.1016/s1095-6433(02)00005-3
- Tinsley, N., Iqbal, M., Pumford, N. R., Lassiter, K., Ojano-Dirain, C., Wing, T., et al. (2010). Investigation of mitochondrial protein expression and oxidation in heart muscle in low and high feed efficient male broilers in a single genetic line. *Poult. Sci.* 89, 349–352. doi:10.3382/ps.2009-00138
- Wang, S., Bottje, W. G., Cawthon, D., Evenson, C., Beers, K., and McNew, R. (1998). Hepatic export of glutathione and uptake of constituent amino acids, glutamate and cysteine in broilers *in vivo*. *Poult. Sci.* 77, 1556–1564. doi:10.1093/ps/77.10.1556



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# A university career in basic and applied avian immunology: important contributions of chicken models for autoimmune diseases

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## Introduction

It is an honor to be invited to contribute an opinion paper for the Frontiers in Avian Physiology Lifetime Achievements Topic and have the opportunity to share and reflect on my 38 year career in academia as a researcher, teacher, and mentor, and to bring awareness to the importance of genetic lines of chickens to unravel complex interactions of the immune system with other physiological systems.

## Educational and professional journey

I grew up in southwestern Germany. Having no clear plans after High School (Abitur), I spent the summer with family friends in New Brunswick, Canada. That summer turned into now 50 years in North America.

After 1 year studying science at the University of New Brunswick, I realized I needed to find real-life applications to my studies. Through friends, I learned about the Nova Scotia Agricultural College and the many science-based problem solving contributions one could make in agricultural sciences. After graduating with an Associate Degree in Animal Science from NSAC, I enrolled at the University of Guelph to complete the BS degree. One of my favorite classes was reproductive physiology taught by Dr. Robert Etches. During office hours, he encouraged me to pursue an MS degree under his tutelage working on understanding the ovulation cycle of the hen. I happily accepted and much enjoyed working with chickens and in the laboratory, using radioimmunoassays to establish hormone profiles leading to ovulation, learning endocrinology and reproductive physiology, as well as studying the literature, writing, and presenting and publishing our novel research findings (Lang et al., 1984a; Lang et al., 1984b). Moreover, I greatly value this opportunity and introduction to basic scientific research and its real-life application in an important production animal.

As I was nearing completion of the MS degree, I knew I wanted to pursue a PhD. An opportunity presented itself during a brief visit to Cornell University where I met Dr. James A. Marsh, Avian Immunologist, who was looking for a graduate student interested in working on neuro-endocrine-immune interactions in chickens. I had

no background in immunology, but the opportunity to combine my MS experience with a new scientific field piqued my interest. I applied and was accepted into Cornell's newly formed Inter-college Immunology PhD program under the tutelage of Dr. Marsh in the Department of Poultry Science, supported by a teaching assistantship in Biology. The learning and training environments in the Department of Poultry Science, the Immunology program, and the Biology Department were superb. The immunology program offered an introductory course that provided me a solid basis for the excellent, intensive graduate courses on various immunology topics. The most impactful course for me was immunophysiology which was taught by my mentor, Dr. Marsh. He introduced us to the many interactions between the immune system and other physiological systems, and to the eloquent experimental approaches used to demonstrate these interactions in avian models. He deeply instilled in me to view the immune system in the "whole animal" context and not as a system working independently of other physiological systems. This philosophy played a major role in my future research and teaching, as well as in my ability to collaborate with nutritionists, geneticists, physiologists, environmental scientists, veterinarians, and biomedical researchers on immunology projects.

For my dissertation, I studied thyroid-immune system interactions using chicken strains with hormonal abnormalities. Most experiments focused on the sex-linked recessive dwarf (SLD) strain in comparison to the normal growing Cornell K (K) strain control. The SLD-strain has near-normal thyroid activity but impaired peripheral conversion of thyroxine (T<sub>4</sub>) to triiodothyronine (T<sub>3</sub>) due to low peripheral 5'-monodeiodinase activity. The K and SLD strains were originally derived from the same populations and, importantly for comparative immune function studies, both strains were homozygous for B15 at the major histocompatibility complex--the main genetic region coding for immunoregulatory genes. Using the chorio-allantoic membrane (CAM) bioassay and the mixed lymphocyte response (MLR) culture assay to measure alloantigen-reactive lymphocyte responses, we found that this response was lower in the SLD-than the K-strain throughout a 20-month study. Dietary supplementation of T<sub>3</sub> increased plasma concentrations of T<sub>3</sub> in both strains but did not enhance the SLD strain's depressed alloantigen responses. On the other hand, using *in vitro* mitogen proliferation assays, the responses to the T cell mitogens phytohemagglutinin (PHA) and concanavalin A (Con A) were not different in SLD-compared to K-strain cockerels and increased with increasing dietary T<sub>3</sub> supplementation in both strains. However, the PHA:ConA ratio (PHA and Con A activate different T cell subsets) was lower in SLD-than in K-strain chickens at 6 and 12 week but increased to K-strain levels by 12 weeks with T<sub>3</sub> supplementation. Collectively, these findings support immune-modulating effects of T<sub>3</sub> on cell-mediated immune responses, whereby effects depended on the age of the chicken, the T cell population stimulated, and method of T cell activation, i.e., through the T cell receptor in the CAM and MLR assays versus mitogen receptors. I should mention that I developed all the assays for these studies, which was a challenge and often led to frustration, even to the point of considering a project change. But in the end, everything came together in a comprehensive dissertation and four peer-reviewed publications, as well as a book chapter co-authored

with Dr. Marsh (Erf et al., 1987; Erf and Marsh, 1987; Erf and Marsh, 1988; Erf and Marsh, 1989; Marsh and Erf, 1996).

Upon graduation, I accepted a tenure-track position as Assistant Professor (Immunology) in Biological Sciences at Smith College, a Liberal Arts College for women in Northampton, MA. Having discovered my passion for teaching at Cornell University and gained a well-rounded knowledge-base in immunology, I felt well prepared for this position. Despite the heavy teaching appointment, I was able to set up a research project on immune system development in congenitally hypothyroid mice (Erf, 1993), for which I received an NSF Research Opportunities for Women, Research Planning Grant. An invitation to collaborate from Dr. J. Robert Smyth, Jr, Poultry Geneticist at the University of Massachusetts, Amherst, provided a return to avian immunology. Dr. Smyth had developed a chicken model characterized by spontaneous, post-natal loss of pigment cells (melanocytes) in feathers and eyes, and suspected that the immune system played a role in the melanocyte loss. With his mentorship, I prepared and was awarded an NIH R15 grant to study the role of T cells in the loss of epidermal melanocytes in what is now known as the Smyth line chicken model for autoimmune vitiligo. With my team of outstanding undergraduate researcher we made great progress, defining T cell population profiles in growing feathers (site of epidermal pigment cells) before and throughout out progression of vitiligo in the same individual, which was possible due to the predictable disease expression and the minimally invasive access to the target tissue (Erf et al., 1995; Shrestha et al., 1997; Erf et al., 1997). This project reignited my passion for research, the chicken model, working with students in the laboratory and at the farm, attending professional meetings, and immersing myself in the research topic. However, I was spending more and more time at work, and realized I needed a better research-teaching and life-work balance, especially after the birth of our son.

At this time, I was made aware that the newly formed Department and Center of Excellence for Poultry Science at the University of Arkansas in Fayetteville, AR, was looking for an avian immunologist. I applied, hoping that 5 years of teaching experience and building a successful research program in immunology at an undergraduate institution would still make me competitive for this position. I got the job! and for the first few years felt like I was on sabbatical! It was a dream come true to work within a state-of-the-art research facility, in a large department focused on poultry science at all levels, with outstanding, supportive colleagues to learn from and collaborate with, and with opportunities to mentor both undergraduate and graduate student research. To meet my 20% teaching appointment, I developed a graduate level immunology lecture course, an intensive immunology laboratory course, and an undergraduate hands-on research course, which was funded by a USDA Higher Education Challenge grant. For my research I established breeding populations of the Smyth line vitiligo model, which consists of three MHC-matched lines, i.e.: 1) the vitiligo-susceptible, highly disease expressing Smyth line (65%–95% vitiligo incidence; varied low incidence of associated autoimmune diseases like uveitis, alopecia areata and hypothyroidism), 2) the vitiligo-susceptible but low expressing parental Massachusetts Brown line (0%–2% incidence), and 3) the Light-brown Leghorn, which serves as the non-susceptible, pigmentation control (Sreekumar et al., 1996; Wick et al., 2006; Erf, 2021). We received several federal grants for research on

autoimmune vitiligo and for other multifactorial diseases using chicken models, e.g., the Pulmonary Arterial Hypertension (ascites) Resistant and Susceptible lines (Pavlidis et al., 2007; Hamal et al., 2010a; Hamal et al., 2010b; Wideman et al., 2013). My efforts in immunology research and teaching were recognized through UA and national awards, as well as an Endowed Professorship in Avian Immunology from Tyson Foods, which enabled me to provide numerous experiential learning opportunities for undergraduates working with our animal models. These efforts greatly fostered the students' enthusiasm for learning and pursuing future careers in academia, veterinary and human medicine, and the Poultry and Allied Industry.

In 2015, we adopted the last remaining populations of UCD 200/206 chickens with autoimmune scleroderma/systemic sclerosis (UCD-SSc; a fibrotic disease of skin and organs with underlying vasculitis), as well as the Obese strain (OS) of chickens with Hashimoto's thyroiditis. Like the Smyth line autoimmune vitiligo model, the UCD-SSc and OS chickens made, and continue to make, important contributions to avian immunology and our understanding of the multifactorial nature of autoimmune and other postnatal diseases (Wick et al., 2006; Erf and Le Poole, 2019; Erf, 2021). For all avian autoimmune models, disease susceptibility was shown to be multigenic, resulting in aberrant target cell-, immune-, and/or endocrine-functions that may not result in disease without extrinsic and/or intrinsic environmental factors (Wick et al., 2006; Erf, 2021).

We also received grants from the Poultry and Allied Industry, including funding for studies on maternal antibodies (Hamal et al., 2006), the effects of nutrition, genetic selections, heat- and cold-stress, dietary immunomodulators on the immune system, as well as immune responses to vaccines and immunomodulatory effects of vaccine adjuvants (Bottje et al., 1997; Fritts et al., 2004; Konjufca et al., 2004; Wideman et al., 2004; Bowen et al., 2006; Rocchi et al., 2023; Santamaria et al., 2024; Beck et al., 2025). Through our research efforts, teaching immunology, mentoring students at all levels, and collaborations with colleagues in different fields, I never stopped learning--keeping up with the extensive and fast moving field of immunology, experimental techniques and approaches, and studying various animal, organ, and cellular systems.

## Contributions of Smyth line autoimmune vitiligo studies to avian immunology

Throughout the years, we established the Smyth line autoimmune vitiligo model as an excellent model for human autoimmune vitiligo and associated autoimmune diseases for biomedical and translational research. Additionally, by studying immune system development and function in healthy controls and disease-susceptible individuals, we contributed a lot of new knowledge and experimental approaches to avian immunology, especially regarding cellular immunity (Wang and Erf, 2003; Wang and Erf, 2004; Shi et al., 2012; Shi and Erf, 2012; Jang et al., 2014; Sorrick et al., 2022; Falcon et al., 2024).

One of the most impactful methods that originated when studying the evolving autoimmune response to epidermal

melanocytes in the pulp of growing feathers (GFs), is the GF-pulp bioassay. The GF-pulp is a column (e.g., 8–10 by 2–3 mm) of cutaneous tissue which consists of mostly inner dermis and an outer epidermal layer and is surrounded by the feather sheath. The GFs are loosely attached in the follicular cup, can be easily removed, regenerate, and yield sufficient pulp tissue for multiple *ex vivo* analyses. Simultaneous intradermal (i.d.) injection of a test-material (e.g., microbial components, antigens, vaccines, etc.) into multiple GFs of an individual, and subsequent periodic collection of GFs for laboratory analysis, allows for quantitative, qualitative, and temporal assessment of the *in vivo* cellular/tissue responses to the test-material. This is comparable to the periodic sampling of blood to measure humoral responses, except each GF constitutes a defined reaction site--hence, we often refer to it as an "*in vivo* test tube." This approach revealed differences in inflammatory responses to different microbial components, vaccine antigens, mitogens, bioactivities of nanomaterials, and adjuvants, and was shown to provide a unique platform to uncover effects of nutrition, environment, and genetic selection on cellular responses initiated in GF-pulps in chickens, and, more recently, in turkeys. Moreover, the combination of the GF bioassay with other minimally invasive procedures (e.g., blood sampling, mucosal swabs) to collect samples for *ex vivo* and *in vitro* laboratory analyses, yields insight into local and systemic immune responses to the i.d. injected test-material (Erf and Ramachandran, 2016; Sullivan and Erf, 2017; Erf et al., 2017; Erf et al., 2023; Rocchi et al., 2023; Byrne and Erf, 2024; Beck et al., 2025; Santamaria et al., 2025; Anderson et al., 2025). This approach greatly reduces the number of animals needed to study tissue/cellular responses over time from their initiation to resolution in the "whole animal" context.

Looking back, I am very excited and thankful to have had such a full-filling career in research and teaching and the opportunity to contribute to the advancement of avian immunology. I was fortunate to have access to the avian autoimmune disease models and highly value their contributions to my career, the professional development of many undergraduate and graduate students, and our understanding of avian immune system development and function in health and disease.

## Author contributions

GE: Writing – original draft, Writing – review and editing.

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The author(s) declared that generative AI was not used in the creation of this manuscript.

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## References

- Anderson, A. G., Beck, C. N., Santamaria, J. M., Lee, J. T., Adhikari, R. S. J., Rochell, S. J., et al. (2025). Influence of dietary arginine ratio on local and systemic inflammatory responses to lipopolysaccharide in broilers. *Poult. Sci.* 105, 106167. doi:10.1016/j.psj.2025.106167
- Beck, C. N., Santamaria, J. M., and Erf, G. F. (2025). Inflammatory and humoral immune responses to commercial autogenous *Salmonella* bacterin vaccines in Light-brown leghorn pullets: primary and secondary vaccine responses. *Vaccines* 13, 311. doi:10.3390/vaccines13030311
- Bottje, W. G., Erf, G. F., Bersi, T. K., Wang, S., Barnes, D., and Beers, K. W. (1997). Effect of dietary dl- $\alpha$ -tocopherol on tissue tocopherol and pulmonary hypertension syndrome (ascites) in broilers. *Poult. Sci.* 76, 1506–1512. doi:10.1093/ps/76.11.1506
- Bowen, O. T., Wideman, R. F., Anthony, N. B., and Erf, G. F. (2006). Variation in the pulmonary hypertensive responsiveness of broilers to lipopolysaccharide and innate variation in nitric oxide production by mononuclear cells. *Poult. Sci.* 85, 1349–1363. doi:10.1093/ps/85.8.1349
- Byrne, K. A., and Erf, G. F. (2024). The bacterial cell wall components lipopolysaccharide and peptidoglycan initiate divergent local tissue and systemic inflammatory response profiles in the chicken model. *Animals* 14, 3661. doi:10.2290/ani14243661
- Erf, G. F. (1993). Immune development in young-adult C.RF-hyt mice is affected by congenital and maternal hypothyroidism. *Proc. Soc. Exp. Biol. Med.* 204, 40–48. doi:10.3181/00379727-204-43632
- Erf, G. F., and Le Poole, I. C. (2019). “Animal models,” in *Vitiligo*. 2nd Edn, Editors M. Picardo, and A. Taieb (Springer, SPI Global), 205–223.
- Erf, G. F., and Marsh, J. A. (1987). Triiodothyronine affects mitogen responsiveness in sex-linked dwarf and cornell K strain chickens. *Dev. Comp. Immunol.* 11, 395–406. doi:10.1016/0145-305x(87)90083-8
- Erf, G. F., and Marsh, J. A. (1988). Triiodothyronine affects the phytohemagglutinin to concanavalin A proliferative response ratio in sex-linked dwarf chickens. *Proc. Soc. Exp. Biol. Med.* 189, 5–12. doi:10.3181/00379727-189-42772
- Erf, G. F., and Marsh, J. A. (1989). The effect of dietary triiodothyronine on mixed lymphocyte responsiveness in young male chickens. *Dev. Comp. Immunol.* 13, 177–186. doi:10.1016/0145-305x(89)90032-3
- Erf, G. F., and Ramachandran, I. R. (2016). The growing feather as a dermal test-site: comparison of leukocyte profiles during the response to *Mycobacterium butyricum* in growing feathers, wattles, and wing webs. *Poult. Sci.* 95, 2011–2022. doi:10.3382/ps/pew122
- Erf, G. F., Briles, W. E., and Marsh, J. A. (1987). Graft-versus-host response in sex-linked dwarf, autosomal dwarf and control K strain chickens. *Dev. Comp. Immunol.* 11, 769–779. doi:10.1016/0145-305x(87)90064-4
- Erf, G. F., Trejo-Skalli, A. V., and Smyth, J. R., Jr (1995). T cells in regenerating feathers of Smyth line chickens with vitiligo. *Clin. Immunol. Immunopathol.* 76, 120–126. doi:10.1006/clin.1995.1105
- Erf, G. F., Trejo-Skalli, A. V., Poulin, M., and Smyth, J. R., Jr (1997). Dermal lymphoid aggregates in autoimmune Smyth line chickens. *Vet. Immun. Immunopathol.* 58, 335–343. doi:10.1016/s0165-2427(97)00036-6
- Erf, G. F., Bersi, T. K., Wang, X., Sreekumar, G. P., and Smyth, J. R. (2001). Herpesvirus connection in the expression of autoimmune vitiligo in smyth line chickens. *Pigment. Cell. Res.* 14, 40–46. doi:10.1034/j.1600-0749.2001.140107.x
- Erf, G. F., Falcon, D. M., Sullivan, K. A., and Bourdo, S. E. (2017). T lymphocytes dominate local leukocyte infiltration in response to intradermal injection of functionalized graphene-based nanomaterial. *J. Appl. Toxicol.* 37, 1317–1324. doi:10.1002/jat.3492
- Erf, G. F. (2021). “Autoimmune diseases of poultry,” in *Avian immunology*. 3rd Edn, Editors K. A. Schat, T. Göbel, and L. Vervelde (San Diego, CA: Elsevier, Academic Press), 437–455.
- Erf, G. F., Kong, H. R., Falcon, D. M., and Byrne, K. A. (2023). Two-window approach to monitor and assess cellular and humoral immune responses in poultry. *Poultry* 2, 82–97. doi:10.3390/poultry2010009
- Falcon, D. M., Byrne, K. A., Sales, M. A., and Erf, G. F. (2024). Spontaneous immunological activities in the target tissue of vitiligo-prone smyth and vitiligo-susceptible brown lines of chicken. *Front. Immunol.* 15, 1386727. doi:10.3389/fimmu.2024.1386727
- Fritts, C. A., Erf, G. F., Bersi, T. K., and Waldroup, P. W. (2004). Effect of source and level of vitamin D on immune function in growing broilers. *J. Appl. Poult. Res.* 13, 263–273. doi:10.1093/japr/13.2.263
- Hamal, K., Burgess, S., Pevzner, I., and Erf, G. F. (2006). Maternal antibody transfer from dams to their egg-yolk, egg-white and chicks in two meat lines of chickens. *Poult. Sci.* 85, 1364–1372. doi:10.1093/ps/85.8.1364
- Hamal, K. R., Wideman, R. F., Anthony, N. B., and Erf, G. F. (2010a). Differential gene expression of pro-inflammatory chemokines and cytokines in lungs of ascites-resistant and -susceptible broiler chickens following intravenous cellulose microparticle injection. *Vet. Immunol. Immunopathol.* 133, 250–255. doi:10.1016/j.vetimm.2009.07.011
- Hamal, K. R., Wideman, R. F., Anthony, N. B., and Erf, G. F. (2010b). Differential expression of vasoactive mediators in microparticle challenged lungs of chickens that differ in susceptibility to pulmonary arterial hypertension. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* 298, R235–R242. doi:10.1152/ajpregu.00451.2009
- Jang, H. M., Erf, G. F., Rowland, K. C., and Kong, B.-W. (2014). Genome resequencing and bioinformatics analysis of SNP containing candidate genes in the autoimmune vitiligo Smyth line chicken model. *BMC Genomics* 15, 707. doi:10.1186/1471-2164-15-707
- Konjufca, V. K., Bersi, T. K., Bottje, W. G., and Erf, G. F. (2004). Influence of dietary vitamin E on phagocytic functions of macrophages in broilers. *Poult. Sci.* 83, 1530–1534. doi:10.1093/ps/83.9.1530
- Lang, G. F., Walton, J. W., and Etches, R. J. (1984a). The effect of aminoglutethimide on steroid secretion, ovulation and LH release in the hen. *Poult. Sci.* 63, 1861–1871. doi:10.3382/ps.0631861
- Lang, G. F., Etches, R. J., and Walton, J. S. (1984b). The effects of luteinizing hormone, progesterone, testosterone, estradiol and corticosterone on ovulation and luteinizing hormone release in hens treated with aminoglutethimide. *Biol. Reprod.* 30, 278–288. doi:10.1095/biolreprod30.2.278
- Marsh, J. A., and Erf, G. F. (1996). “Interactions between the thyroid and the immune system,” in *The physiology of immunity*. Editors J. A. Marsh, and M. D. Kendall (Boca Raton, Florida: CRC Press, Inc.), 221–235.
- Pavlidis, H. O., Balog, J. M., Stamps, L. K., Hughes, J. D., Jr, Huff, W. E., and Anthony, N. B. (2007). Divergent selection for ascites incidence in chickens. *Poult. Sci.* 86, 2517–2529. doi:10.3382/ps.2007-00134
- Rocchi, A. J., Santamaria, J. M., Beck, C. N., Sales, M. A., Hargis, B. M., Tellez-Isaia, G., et al. (2023). Immunosuppressive effects of cyclic, environmental heat-stress in broiler chickens: local and systemic inflammatory responses to intradermal injection of lipopolysaccharide. *Vet. Sci.* 11, 16. doi:10.3390/vetsci11010016
- Santamaria, J. M., Beck, C. N., and Erf, G. F. (2024). Local inflammatory and systemic antibody responses initiated by a first intradermal administration of autogenous *Salmonella*-killed vaccines and their components in pullets. *Vaccines* 12, 1159. doi:10.3390/vaccines12101159
- Santamaria, J. M., Beck, C. N., Orlowski, S. K., Maqueda, M., Bottje, W. G., and Erf, G. F. (2025). Selection for improved water efficiency in broiler breeder lines does not negatively impact immune response capabilities to Gram<sup>+</sup> and Gram<sup>+</sup> bacterial components and a killed-Salmonella vaccine. *Vet. Sci.* 12, 279. doi:10.3390/vetsci12030279
- Shi, E., and Erf, G. F. (2012). IFN- $\gamma$ , IL-21 and IL-10 co-expression in evolving autoimmune vitiligo lesions of Smyth line chickens. *J. Invest. Dermatol.* 132, 642–649. doi:10.1038/jid.2011.377

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- Shi, F., Kong, B.-W., Song, J. J., Lee, J. Y., Dienglewicz, R. L., and Erf, G. F. (2012). Understanding mechanisms of spontaneous autoimmune vitiligo development in the Smyth line chicken model by transcriptomic microarray analysis of evolving lesions. *BMC Immunol.* 13, 18. doi:10.1186/1471-2172-13-18
- Shresta, S., Smyth, J. R. Jr., and Erf, G. F. (1997). Profiles of pulp infiltrating lymphocytes at various times throughout feather regeneration in Smyth line chickens with vitiligo. *Autoimmunity* 25, 193–201. doi:10.3109/08916939708994728
- Sorricks, J., Huett, W., Byrne, K. A., and Erf, G. F. (2022). Autoimmune activities in choroids of visually impaired Smyth chickens with autoimmune vitiligo. *Front. Med.* 9, 846100. doi:10.3389/fmed.2022.846100
- Sreekumar, G. P., Erf, G. F., and Smyth, J. R. Jr. (1996). 5-Azacytidine treatment induces autoimmune vitiligo in the parental control strains of the Smyth line chicken model for autoimmune vitiligo. *Clin. Immunol. Immunopathol.* 81, 136–144. doi:10.1006/clin.1996.0169
- Sullivan, K. A., and Erf, G. F. (2017). CD4+ T cells dominate the leukocyte infiltrations response initiated by intra-dermal injection of phytohemagglutinin into growing feathers in chickens. *Poult. Sci.* 96, 3574–3580. doi:10.3382/ps/pex135
- Wang, X., and Erf, G. F. (2003). Melanocyte-specific cell mediated immune response in vitiliginous Smyth line chickens. *J. Autoimmun.* 21, 149–160. doi:10.1016/s0896-8411(03)00087-8
- Wang, X., and Erf, G. F. (2004). Apoptosis in feathers of smyth line chickens with autoimmune vitiligo. *J. Autoimmun.* 22, 21–30. doi:10.1016/j.jaut.2003.09.006
- Wick, G., Andersson, L., Hala, K., Gershwin, M. E., Selmi, C. F., Erf, G. F., et al. (2006). Avian models with spontaneous autoimmune diseases. *Adv. Immunol.* 92, 71–117. doi:10.1016/S0065-2776(06)92002-1
- Wideman, R. F., Chapman, M. E., Wang, W., and Erf, G. F. (2004). Immune modulation of the pulmonary hypertensive response to bacterial lipopolysaccharide (LPS, endotoxin) in broilers. *Poult. Sci.* 83, 624–637. doi:10.1093/ps/83.4.624
- Wideman, R. F., Rhoads, D. D., Erf, G. F., and Anthony, N. B. (2013). Pulmonary hypertension syndrome (PHS, ascites syndrome) in broilers: a review. *Poult. Sci.* 92, 64–83. doi:10.3382/ps.2012-02745

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# Met-enkephalin and other opioid peptides in the stress response of chickens: lessons from laboratory animals and livestock

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## 1 Introduction

Endogenous opioid peptides and their receptors are involved in the regulation of many physiological processes, including nociception, analgesia, respiration, cardiovascular and gastrointestinal system activity, as well as nervous, endocrine, and immune functions. Opioid peptides, forming the family of enkephalins, dynorphins, and endorphins, are synthesized as large peptides (precursors) named preproenkephalin, prodynorphin, and proopioidmelanocortin, respectively.

### 1.1 Genes encoding opioid peptides

Opioid peptides from all families are encoded by four genes:

- A. Proenkephalin (*PENK*) encodes a specific protein:
  - a. Met-enkephalin (YGGFM),
  - b. Leu-enkephalin (YGGFL),
  - c. Extended Met-enkephalin (YGGFMXX).
- B. Prodynorphin (*PDYN*) encodes the following:
  - a. Dynorphins A and B
  - b.  $\alpha$ - and  $\beta$ -neoendorphins.
- C. Proopioidmelanocortin (*POMC*) encodes  $\beta$  endorphin together with adrenocorticotrophic hormone (ACTH).
- D. Pronociceptin (*PNOG*) encodes nociceptin.

### 1.2 Opioid receptors

Opioid peptides belong to the G-protein-coupled receptor superfamily and act by binding to opioid receptors localized in the brain and peripheral tissues, specifically the following:

- A. Delta opioid receptors (DORs), binding Met- and Leu-enkephalin,
- B. Kappa opioid receptors (KORs), binding dynorphins A and B,
- C. Mu opioid receptors (MORs), binding  $\beta$ -endorphin,
- D. Recently, the nonopioid orphanin FQ/nociceptin (NOP) receptor was included; it binds nociceptin.

Opioid properties were broadly searched as important modulators of hypothalamic–pituitary–adrenal (HPA) axis activity, particularly during stress responses. Endorphin- and enkephalin-producing neurons are present in the paraventricular nucleus and the median eminence and modulate adrenocorticotrophic hormone (ACTH)-controlling neurons (Van'T Veer et al., 2012).

The present communication focuses on Met-enkephalin in chickens, the effect of stress on Met-enkephalin physiology, insights gained from laboratory animals and livestock, and open questions on opioid peptides.

## 2 Loci for Met-enkephalin synthesis and release

Met-enkephalin is found in multiple tissues of rats, including the anterior pituitary gland, neurointermediate lobe of the pituitary gland, adrenal gland, hypothalamus, heart, lung, spleen, liver, seminal vesicle, vas deferens, kidney, bladder detrusor, and duodenum, with the highest concentration in the neurointermediate lobe (Kolta et al., 1992). Similarly, in chickens, Met-enkephalin is synthesized in the hypothalamus, anterior pituitary gland, adrenal glands, duodenum, proventriculus, and crop (Scanes and Pierzchala-Koziec, 2024a; Scanes and Pierzchala-Koziec, 2024b).

## 3 Met-enkephalin and stress

Stress (imposition of mechanical restraint) in rats is followed rapidly by increases in plasma concentrations of native (pentapeptide) Met-enkephalin (Pierzchala and Van Loon, 1990). Concentrations of Met-enkephalin are also elevated in lambs isolated from other sheep, including dams (Pierzchala-Koziec et al., 2018; 2019). In chickens, both plasma concentrations of pentapeptide Met-enkephalin and PENK expression are elevated in young chickens subjected to restraint stress (Scanes et al., 2024). There are also effects of other stresses on plasma concentrations of pentapeptide Met-enkephalin and PENK expression. For instance, withholding water was accompanied by depressed concentrations of Met-enkephalin in both the anterior pituitary and adrenal glands, together with increased PENK expression in the same organs (Scanes and Pierzchala-Koziec, 2024a). Moreover, there are decreased plasma concentrations of Met-enkephalin in chickens deprived of feed (Scanes and Pierzchala-Koziec, 2024a). There is increasing evidence that Met-enkephalin plays a role in the immune system (Zhao et al., 2016; Tian et al., 2018; 2024; Wang et al., 2018). The relationships between Met-enkephalin and immune functioning in chickens remain unclear.

## 4 Control of pentapeptide Met-enkephalin release

The neurotransmitter acetylcholine plays an important role in regulating the release and synthesis of the native pentapeptide Met-enkephalin. The release of Met-enkephalin from the adrenal glands is under cholinergic control, as

evidenced by with the nicotinic agonist nicotine, which increases concentrations of both native Met- and Leu-enkephalin in the adrenal medulla and other tissues in rats (Van Loon et al., 1991; Pierzchala-Koziec and Van Loon, 1994). Moreover, *in vitro* Met-enkephalin release and PENK gene expression have been observed in the hypothalamus, anterior pituitary gland, adrenal glands, crop, proventriculus, and duodenum in chickens (Scanes et al., 2024; 2025). Intestinal explants, at least, exhibit shifts in both PENK gene expression and Met-enkephalin release in the presence of both nicotinic and muscarinic cholinergic antagonists (Scanes et al., 2025).

Opioids downregulate the Met-enkephalin system. The classical opioid morphine depresses plasma concentrations of Met-enkephalin and PENK expression in both the anterior pituitary and adrenal glands in young chickens (Scanes and Pierzchala-Koziec, 2024b). Moreover, the effects of restraint stress are attenuated by the administration of the opioid antagonist naltrexone (Scanes et al., 2024).

## 5 Total immuno-reactive Met-enkephalin in plasma and tissues

Stress in rats is followed rapidly by shifts in plasma concentrations of total Met-enkephalin (Pierzchala and Van Loon, 1990), with the latter being generated by enzymatic hydrolysis of plasma proteins. There are analogous changes in plasma concentrations of total Met-enkephalin in lambs isolated from their dams (Pierzchala-Koziec et al., 2018; 2019). It remains unclear what total Met-enkephalin signifies. Possible explanations include the following:

1. Proenkephalin or peptides larger than the pentapeptide Met-enkephalin that are derived from proenkephalin but lack immuno-reactivity in the native Met-enkephalin radioimmunoassay.
2. Met-enkephalin binding to proteins in the circulation and/or secretory granules.
3. A combination of possibilities 1 and 2.

Multiple peptides are derived from proenkephalin in the bovine and presumably chicken adrenal glands, including extended Met-enkephalin, Met-enkephalin [Arg<sup>6</sup> and Phe<sup>7</sup>] peptides B, E, F, and I, and BAM 22, 20, and 12 (Stern et al., 1979; 1981), with different activities (Figure 1).

## 6 Other opioid peptides and stress

To the best of our knowledge, there are no reports of Leu-enkephalin, dynorphins A and B together, and  $\alpha$ - and  $\beta$ -neendorphins in birds. There are few reports of dynorphins even in humans. Similarly, there is only a single report of circulating concentrations of  $\beta$  endorphin in chickens, in which the molecular forms of  $\beta$ -endorphin were examined (Hylka and Thommes, 1991). In addition, plasma concentrations of both ACTH and  $\beta$ -endorphin increase in response to stressors, such as exposure to ether or administration of lipopolysaccharide, in domestic geese (Barna et al., 1998).

Opioid peptides (bovine)	Structure	Guinea pig relative potency <sup>XA</sup>
Dynorphin <sub>1-13</sub>	YGGFLRRIRPKLK	100
Met-enkephalin	YGGFM	1.44
Leu-enkephalin	YGGFL	0.12
Peptide I	SPHLEDETKELQKRYGGFMRRVGRPEWWM DYQKRYGGFL	<0.052
Peptide F	YGGFMKKMDELYPLEVEEEEANGGEVLGKRYGGFM	0.17
Peptide B	FAEPLPSEEEGESYSKEVPEMEKRYGGFMRF	<0.26
Met-enkephalin [Arg <sup>6</sup> , Phe <sup>7</sup> ]	YGGFMRF	NA
Peptide E	YGGFMRRVGRPEWWM DYQKRYGGFL	54.2
Putative chicken equiv. to peptide B	YGGFMRRVGRPEWWM DYQKRYGGFL	NA
Des <sup>25</sup> Peptide E	YGGFMRRVGRPEWWM DYQKRYGGF	34.7
BAM 22	YGGFMRRVGRPEWWM DYQKRYG	40.0
BAM 20	YGGFMRRVGRPEWWM DYQKR	23.6
BAM 12	YGGFMRRVGRPE	3.35

FIGURE 1

Structure of selected opioid peptides isolated from cattle adrenal glands together with putative chicken homologs and biological activities in a presumed KOR assay. <sup>X</sup>Relative to dynorphin<sub>1-13</sub> as 100. <sup>A</sup>Calculated from IC<sub>50</sub>s from Goldstein et al., 1979; Kilpatrick et al., 1981. NA, not available [Key: pink–dibasic amino-acid residues, green–Met-enkephalin residues, blue–Leu-enkephalin residues, red–difference between chicken and bovine sequences).

## 7 Discussion and conclusions

The physiological relevance of circulating Met-enkephalin and other endogenous opioid peptides in birds remains poorly understood. To better document the physiology of Met-enkephalin acting as a hormone, studies on its circulating forms and their regulation are essential. Thus, during the past few years, we have measured immunoreactive Met-enkephalin in plasma and tissues to characterize the large circulating forms of peptidase-derivable Met-enkephalin and define, in hens, the physiological regulation of plasma responses of free Met-enkephalin (five amino acids) and the extended form of Met-enkephalin to psychological stress. Similar to rats (Pierzchala and Van Loon, 1990), restraint- or crowding-induced stress elicited biphasic responses of Met-enkephalin (Scanes et al., 2024; Scanes and Pierzchala-Koziec, 2024a).

Restraint stress in rats increased plasma native Met-enkephalin, which is in parallel with the increases in plasma epinephrine and norepinephrine. Thereafter, there was a divergence in the plasma concentrations of Met-enkephalin and catecholamines during the period of restraint stress. Plasma Met-enkephalin showed a biphasic response to 30 min of restraint: increasing at 1 and 30 min of stress; in contrast, catecholamines increased only at 1–3 min of restraint. It seems probable that the brief duration of the initial peak of plasma Met-enkephalin induced by restraint stress results from a central nervous system regulatory mechanism (interaction with the sympathetic nervous system) rather than from a limitation in Met-enkephalin pool size since the more severe stress of immobilization produced a prolonged elevation of plasma Met-enkephalin (Pierzchala-Koziec and Van Loon, 1994). In hens, depletion of peripheral catecholamine sources did not decrease Met-enkephalin responses to restraint stress but may indicate the involvement of additional regulators of opioid synthesis and

release, apart from catecholamines, such as acetylcholine, insulin, and ghrelin.

This short review on the role of Met-enkephalin in modulating stress responses showed that, despite extensive scientific research, several questions regarding opioid peptides in birds remain unresolved:

1. Met-enkephalin is produced by multiple organs. It remains unclear which, if any, are the major sources of circulating Met-enkephalin.
2. It is also unclear to what extent, if any, erythrocytes, leukocytes, and/or thrombocytes release or degrade Met-enkephalin.
3. It remains uncertain whether Met-enkephalin exerts its effects via paracrine and endocrine mechanisms.
4. Plasma concentrations of total Met-enkephalin (generated by enzymatic hydrolysis of plasma proteins) greatly exceed those of native pentapeptide Met-enkephalin. It remains unclear the extent to which total Met-enkephalin reflects larger cleavage products of proenkephalin and/or binding of Met-enkephalin to plasma proteins.
5. There is a series of extended Met-enkephalin peptides in cattle. It remains unclear whether these peptides are also found in chickens and other birds, whether they are secreted in response to stimuli, and what their physiological actions are.
6. There are no published reports on the effects of stress and other physiological interventions on circulating concentrations of Leu-enkephalin, prodynorphin-derived peptides, or nociceptin in chickens or other birds.
7. There are few published reports (<5) on the effects of stress and other physiological interventions on circulating concentrations of  $\beta$ -endorphin in chickens or other birds.

Answers to the abovementioned questions will clarify the role of endogenous opioids in stress and may facilitate opioid peptides being indicators of stress/failures in welfare. Moreover, it is speculated that research on opioid peptides will provide new bases for dissecting the multiple facets of stress and the responses to these.

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## References

- Barna, I., Koenig, J. I., and Péczely, P. (1998). Characteristics of the proopiomelanocortin system in the outdoor-bred domestic gander. II. Seasonal and circadian rhythmicity; effect of ether stress and lipopolysaccharide administration. *Gen. Comp. Endocrinol.* 109, 52–59. doi:10.1006/gcen.1997.7002
- Goldstein, A., Tachibana, S., Lowney, L. I., Hunkapiller, M., and Hood, L. (1979). Dynorphin-(1-13), an extraordinarily potent opioid peptide. *Proc. Natl. Acad. Sci. USA.* 76 (12), 6666–6670. doi:10.1073/pnas.76.12.6666
- Hylka, V. W., and Thommes, R. C. (1991). Avian beta-endorphin: alterations in immunoreactive forms in plasma and pituitary of embryonic and adult chickens. *Comp. Biochem. Physiol. C* 100, 643–648. doi:10.1016/0742-8413(91)90054-W
- Kilpatrick, D. L., Taniguchi, T., Jones, B. N., Stern, A. S., Shively, J. E., Hulihan, J., et al. (1981). A highly potent 3200-dalton adrenal opioid peptide that contains both a [Met]- and [Leu]enkephalin sequence. *Proc. Natl. Acad. Sci. U. S. A.* 78, 3265–3268. doi:10.1073/pnas.78.5.3265
- Kolta, M. G., Pierzchała, K., Houdi, A. A., and Van Loon, G. R. (1992). Effect of diabetes on the levels of two forms of Met-enkephalin in plasma and peripheral tissues of the rat. *Neuropeptides* 21 (1), 55–63. doi:10.1016/0143-4179(92)90152-m
- Pierzchała, K., and Van Loon, G. R. (1990). Plasma native and peptidase-derivable Met-enkephalin responses to restraint stress in rats. Adaptation to repeated restraint. *J. Clin. Invest.* 85 (3), 861–873. doi:10.1172/JCI114513
- Pierzchała-Koziec, K., and Van Loon, G. R. (1994). Effects of nicotine on the concentration of native and cryptic Met- and Leu-enkephalin in peripheral tissues. *J. Physiol. Pharmacol.* 45 (2), 319–330.
- Pierzchała-Koziec, K., Kępys, B., Oeltgen, P., and Scanes, C. G. (2018). Developmental changes in the pituitary-adrenocortical axis and plasma enkephalin concentration in response to isolation stress in growing lambs. *Folia Biol.* 66, 53–61.
- Pierzchała-Koziec, K., Dziedzicka-Wasylewska, M., and Scanes, C. G. (2019). Isolation stress impacts Met-enkephalin in the hypothalamo-pituitary-adrenocortical axis in growing Polish Mountain sheep: a possible role of the opioids in modulation of HPA axis. *Stress* 14, 1–9. doi:10.1080/10253890.2018.1553947
- Scanes, C. G., and Pierzchała-Koziec, K. (2024a). Disparate effects of stressors on Met-enkephalin system parameters and on plasma concentrations of corticosterone in young female chickens. *Anim. (Basel)* 14 (15), 2201. doi:10.3390/ani14152201
- Scanes, C. G., and Pierzchała-Koziec, K. (2024b). Morphine influences circulating and tissue concentrations of met-enkephalin and proenkephalin (PENK) expression and plasma concentrations of corticosterone in chickens. *Poult. Sci.* 103, 103712. doi:10.1016/j.psj.2024.103712

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- Scanes, C. G., Jaszczka, K., Gajewska, A., and Pierzchała-Koziec, K. (2025). Effects of cholinergic and opioid antagonists on *in vitro* release of Met-enkephalin, somatostatin and insulin-like growth factor-1 by and PENK expression in crop, proventriculus and duodenum of newly hatched chickens. *Anim. (Basel)* 15 (12), 1702. doi:10.3390/ani15121702

- Stern, A. S., Lewis, R. V., Kimura, S., Rossier, J., Gerber, L. D., Brink, L., et al. (1979). Isolation of the opioid heptapeptide Met-enkephalin [arg6, Phe7] from bovine adrenal medullary granules and striatum. *Proc. Natl. Acad. Sci. U. S. A.* 76, 6680–6683. doi:10.1073/pnas.76.12.6680

- Stern, A. S., Jones, B. N., Shively, J. E., Stein, S., and Udenfriend, S. (1981). Two adrenal opioid polypeptides: proposed intermediates in the processing of proenkephalin. *Proc. Natl. Acad. Sci. U. S. A.* 78, 1962–1966. doi:10.1073/pnas.78.3.1962

- Tian, J., Jiao, X., Wang, X., Geng, J., Wang, R., Liu, N., et al. (2018). Novel effect of methionine enkephalin against influenza A virus infection through inhibiting TLR7-MyD88-TRAF6-NF-κB p65 signaling pathway. *Int. Immunopharmacol.* 55, 38–48. doi:10.1016/j.intimp.2017.12.001

- Tian, J., Fu, W., Xie, Z., Zhao, Y., Yang, H., and Zhao, J. (2024). Methionine enkephalin (MENK) protected macrophages from ferroptosis by downregulating HMOX1 and ferritin. *Proteome Sci.* 22, 2. doi:10.1186/s12953-024-00228-x

- Van Loon, G. R., Pierzchała, K., and Houdi, A. A. (1991). Nicotine-induced alterations in peripheral tissue concentrations of native and cryptic Met- and Leu-enkephalin. *Neuropeptides* 19(1):35–41. doi:10.1016/0143-4179(91)90071

- Van'T Veer, A., Yano, J. M., Carroll, F. I., Cohen, B. M., and Carlezon, W. A., Jr. (2012). Corticotropin-releasing factor (CRF)-induced disruption of attention in rats is blocked by the κ-opioid receptor antagonist JD1c. *Neuropsychopharmacology* 37, 2809–2816. doi:10.1038/npp.2012.151

- Wang, X., Jiao, X., Meng, Y., Chen, H., Griffin, N., Gao, X., et al. (2018). Methionine enkephalin (MENK) inhibits human gastric cancer through regulating tumor associated macrophages (TAMs) and PI3K/AKT/mTOR signaling pathway inside cancer cells. *Int. Immunopharmacol.* 65, 312–322. doi:10.1016/j.intimp.2018.10.023

- Zhao, D., Plotnikoff, N., Griffin, N., Song, T., and Shan, F. (2016). Methionine enkephalin, its role in immunoregulation and cancer therapy. *Int. Immunopharmacol.* 37, 59–64. doi:10.1016/j.intimp.2016.02.015



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# A career reflection: lifetime achievements in avian neuroanatomy and physiology

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academic support, chickens, food intake, funding, reproduction, sabbatical leaves, stress

## Background and past education

My parents valued education and made sure all three of their children attended college. After graduation from Bucknell University with a B.S. degree in Biological Sciences, I received an offer to attend graduate school and received an M.S. degree from Bucknell University and a PhD from the University of Georgia (UGA). My mentor was Dr. Carl W. Helms who obtained his PhD from Harvard University. His major advisor was Professor Ernst Mayr, regarded as one of the greatest evolutionary biologist of the 20th century. Dr. Helms studied the complete annual cycles of migratory birds that wintered in different areas of the south and central U.S. and migrated to Canada to breed. I focused on investigating the annual cycle of the White-throated Sparrow, *Zonotrichia albicollis* and utilized a surgical procedure that removed targeted neurons from the brain of living birds. I addressed the hypothalamus and found that surgically removing a small structure at the base of the hypothalamus, the ventromedial hypothalamic nucleus, resulted in disruption of a bird's annual cycle. Specifically, the procedure caused obesity that mimicked the remarkable weight gain migratory birds display every spring to store up fat reserves prior to their rigorous flight to their breeding grounds in Canada. The same surgical procedure also significantly increased water consumption. Unexpectedly, the operation inhibited gonadal development and molting of feathers and completely terminated a specific behavior during the nighttime called *Zugunruhe*. The German term applies to migratory birds, when maintained in cages designed to record motor activity patterns, particularly hopping from one perch to another throughout a typical 24-h day. Nocturnal migratory birds will display robust motor activity at night, during the spring and fall when they would initiate their flight to their breeding grounds in spring and their return flight to their wintering grounds in the southern U.S. The increased nocturnal activity is regarded as equivalent to a bird's desire to migrate. It was the first time in a migratory bird that removal of a specific hypothalamic structure resulted in obesity and the loss of specific behavioral processes characteristic of the annual cycle of migratory birds (Kuenzel and Helms, 1967; 1970; 1974; Kuenzel, 1974). Upon completing a PhD at UGA, my major professor encouraged me to pursue an academic career. I still remember his kind words.

An important obligation remained. I was in ROTC at Bucknell University. I therefore entered the U.S. Army for 2 years and was sent to the Medical Service Corps (MSC), Ft. Sam Houston, TX. I and others served as military instructors and taught human anatomy and physiology to soldiers. Soldiers remaining at Ft. Sam Houston would be trained as combat medics. During the second year at the MSC, at Ft. Sam, I was asked to serve as Chief, Basic Science Branch and was promoted from first lieutenant to captain. Thereafter, I obtained a National Institutes of Health (NIH) Postdoctoral Fellowship and

spent 3 years at Cornell University experimenting with chickens under the direction of the neuroendocrine expert, Dr. Ari van Tienhoven. Additionally, the positive experience in the laboratory of Dr. Ari van Tienhoven, encouraged me to apply for a faculty position and was fortunate to spend half of my career (26 years) in the Poultry Science (POSC) Department (Dept.) at the University of Maryland, College Park, MD and am currently working in the POSC Dept. at the University of Arkansas, Fayetteville that began in 2000.

## Academic roles at the Univ. of Maryland (UMD) and Univ. of Arkansas, Fayetteville (UAF)

At both the UMD and UAF, I was hired primarily to (a) produce original research and (b) teach courses (three courses at UMD, two courses at UAF). Additionally, a third role was to serve on committees, from international ones down to university committees. The order of importance for the 3 roles at both UMD and UAF was to build a reputation in a particular research area, followed by teaching and service on committees. In research, I have focused on the avian brain, specifically its anatomy and physiology. What was so valuable at both institutions was the opportunity to teach courses in the disciplines that were relevant to my research interests. The major academic discipline I wished to address was an overall knowledge of avian neuroendocrine physiology. The specific research area was to develop knowledge of neural structures involved with the anterior pituitary gland. This would include contributing new, anatomical and functional knowledge of the regulation of specific neuroendocrine processes. At both UMD and UAF, I have contributed new knowledge to three avian neuroendocrine areas: 1) the location of structures regulating the reproductive system, 2) stress pathways and 3) seasonal regulation of food intake.

## Value of (1) academic support at UMD/UAF, (2) two group meetings, (3) sabbatical years, (4) funding

There were four processes/events experienced that enabled me to contribute a few advancements associated with avian brain function: 1) Academic structure and support at UMD and UAF provided support for a technical assistant person, 2) two group meetings that focused on avian neuroanatomy, 3) sabbatical leaves were encouraged by UMD and UAF, 4) both universities have an Agricultural Experiment Station that has an annual, competitive grants program providing funding for research programs involving crops, and/or agricultural animals designed to improve food production or agribusiness. Success in this program has provided opportunities for faculty to be successful in national grants programs due to the successful data collection from a previous experiment station grant. Funding I received was also used to support presentations at scientific meetings and publications in journals. Additionally, one objective throughout my career was to train graduate students to become knowledgeable and comfortable in pursuing a specific research area and develop an ability to communicate their research results not only to specific

scientific audiences, but also to their local public community when appropriate.

Note that the four processes/events emphasized previously were not sequential. In fact, all four were interactive throughout my career. In my chosen research field, avian neuroanatomy, I have always been intrigued by determining the specific location of structures within the brain, finding their appropriate name and abbreviation, their product and receptors, and critical tests to complete for demonstrating their specific function/s.

During my career, I was invited to join two groups of scientists. There was a significant overlap of specific individuals in different named groups. The first one was the Thinktank, organized by Dr. Anton (Tony) Reiner at the University of Tennessee Health Science Center, Memphis, TN. Years later, the Nomenclature Forum was initiated by Dr. Eric Jarvis, Howard Hughes Medical Institute, The Rockefeller University, NY, NY; the latter was supported by NSF and NIH. Both groups addressed critical issues in the avian literature. A persistent use of inappropriate terms for brain structures had occurred, based upon outdated assumptions of homology to mammalian structures, particularly in the forebrain that needed to be changed. I have kept in touch with Dr. Reiner and Dr. Jarvis over the years with issues that have surfaced regarding the use of appropriate terms and acronyms for avian neural structures.

In 1988 I published a book with Manju Masson titled 'A Stereotaxic Atlas of the Brain of the Chick, *Gallus domesticus*' that showed the accurate location, name and its abbreviation (acronym) for all known neural structures throughout the brain of a chick. It was published by The Johns Hopkins University Press (Kuenzel and Mason, 1988). It was the first stereotaxic atlas of an avian brain displaying complete sets of images in three planes: coronal, sagittal and horizontal sections. A total of 500 copies of the book were produced by The Johns Hopkins University Press (TJHUP). Two or 3 years ago I received a letter from TJHUP that they released all rights to me and Manju for that book. I therefore copied the book and placed it on my website with the University of Arkansas and Scholarworks at the University of Arkansas. Individuals can download the book for no charge. To date, I was informed that 739 downloads have occurred. Currently I am working on a second edition of the stereotaxic atlas as the present publication is totally out-of-date. I am planning to complete the second edition with a colleague, Parker Straight, by the end of February 2026 with all known structures, their names, acronyms and specific locations.

The Third Academic process, listed as, (3) sabbatical years, in the previous, underlined sub-heading, significantly helped me during the years at UMD and UAF. Specifically, it was the granting of sabbatical departures for 1 year from each home university. I have taken four, 12-month sabbaticals and all were spent in a foreign country. The first occurred at the Roslin Institute, Edinburgh, Scotland. The funding of the sabbatical leave was supported by a Fulbright-Hayes Senior Research Fellowship. Five publications resulted: (1) Kuenzel (1982), *Physiol. Behav.* (2) Kuenzel and van Tienhoven (1982), *J. Comp. Neurol.* (3) Kuenzel (1983), *Bird Behav.* (4) Mass and Kuenzel (1983) *Devel. Brain Res.* (5) Kuenzel and Sharp (1985), *British Poultry Sci.*

The publication, (Kuenzel and van Tienhoven, 1982), stimulated me to start the 6-year process of developing our first stereotaxic atlas of the chick brain as it identified the accurate location of several hypothalamic nuclei and all circumventricular organs in the avian brain. A second publication revealed that parasagittal knife cuts that isolated the entire length of the hypothalamus from lateral neural connections resulted in a premature activation of the reproductive system. Data demonstrated that the surgical procedure produced increases in luteinizing hormone (LH) that significantly contributed to advancement of reproductive function, (Kuenzel and Sharp, 1985). Clearly the first sabbatical leave provided the stimulus for me to initiate developing a book, the stereotaxic atlas (Kuenzel and Mason, 1988).

The second sabbatical leave occurred at Justus Liebig University Giessen, Germany and was supported by a Fulbright-Hays Senior Research Fellowship. Professor Andreas Oksche was Chair of the Department of Anatomy and Director of a research center where I worked for a year that focused on research addressing extraretinal photoreceptors. Dr. Sabine Blähser was the professor whom I worked with at the center. Publications that occurred were: Kuenzel and Blähser (1991) and Kuenzel and Blähser (1994), both published in Cell and Tissue Research. The 1991 paper was the first to describe a complete distribution of gonadotropin-releasing hormone (GnRH) neurons and fibers throughout the avian brain, while the second described the distribution of vasoactive intestinal polypeptide (VIP) neurons, with an emphasis on the lateral septal organ. Dr. Oksche developed the concept of extraocular photoreception in birds that have photo-neuroendocrine cells. I named the lateral septal organ (LSO) in a previous publication (Kuenzel and van Tienhoven, 1982) and our lab showed that the LSO contains a number of cerebrospinal-fluid contacting VIP neurons as well as VIP receptors that appear to function as photoreceptors. The LSO has been proposed to be one of four locations within the avian brain that houses the appropriate neurons for the initial activation of reproductive function each year in avian species. To date, controversy continues regarding which of the four proposed structures is/are essential for this critical function or whether all work in some neural pathway to activate gonadal development seasonally.

The benefit of this sabbatical leave was documenting the complete distribution of gonadotropin-releasing hormone (GnRH) neurons within the brain of the chicken that initiate and maintain gonadal development throughout the lifetime of poultry. A second important neuron, the VIP neuron, occurs within the LSO. The VIP neurons are proposed to initiate seasonal reproductive function in developing chicks due to their response to increased photostimulation during the springtime and summer (Kuenzel and Blähser, 1994).

The third sabbatical was also located in Germany, in the Institute of Animal Welfare and Animal Husbandry, formerly named the Inst. of Animal Science and Behavior, Celle, Germany. The host was Dr. Roland Grossmann. Two papers were published in the J. Comp. Neurol. and both utilized the technique of *in situ* hybridization histochemistry (ISHH) gene expression (Kuenzel et al., 1997; Jurkevich et al., 1999). The first showed sites of gene expression of VIP throughout the brain of the chick. The second showed development of the sexually vasotocinergic cell type in the bed nucleus of the stria terminalis in chickens. ISHH

was also utilized to document gene expression of GnRH-1 and VIP in neurons and compare the specific locations with previous data on the distribution of the peptides GnRH-1 and VIP using immunohistochemistry. The agreement was quite high with only a few additional sites of mRNA where we were unable to also see the peptide produced. The overall conclusion was to continue using results of immunohistochemistry to map specific locations of structures in the avian brain.

Our lab had shifted to neuroendocrine regulation of stress when I took a fourth sabbatical leave to the College of Veterinary Medicine, Nanjing Agricultural University, Nanjing, China. The host was Dr. RuQian (Lucy) Zhou. An experiment in our lab displayed a significant sex difference in the stress response between roosters and hens. Specifically, a significantly greater amount of stress hormone, corticosterone, was released following administration of equivalent doses of either the major neural hormone corticotropin releasing hormone (CRH) and/or arginine vasotocin (AVT) in undisturbed birds (Madison et al., 2008). We discovered for the first time an additional neural structure that plays an important role in the stress response of birds, the nucleus of the hippocampal commissure (NHpC). Of interest, the NHpC is located in the septum, a region dorsal to the hypothalamus (Nagarajan et al., 2014; Nagarajan et al., 2017a; Nagarajan et al., 2017b; Nagarajan et al., 2017b made the cover of the Journal of Neuroendocrinology (J. Neuroendo.) and a podcast was produced on its website following an interview of the Editor of J. Neuroendo. with the senior author, Gurueswar Nagarajan. Dr. Nagarajan had previously received a Ph.D. in my lab and at the time of the interview was a visiting NIH Fellow. Currently he is a scientist at the Henry M. Jackson Foundation for the advancement of Military Medicine in Bethesda, MD. A substantial population of CRH neurons were found in the NHpC and were significantly larger than the classical CRH hypothalamic neurons, specifically in the paraventricular (PVN) nucleus, the major site for the stress response in mammals.

Subsequent experiments examining two very different stressors: (1) food deprivation, a stressor that gradually increases in strength with time due to the absence of essential nutrients when food is withdrawn and (2) immobilization, a stressor that is immediately stressful as each bird was placed in a harness that reduced its movement of wings and legs. Regardless of the stressor, the same sequence of gene expression occurred. In summary, using immobilization stress, the sequence of gene expression was (1) a peak of CRH gene expression within the NHpC, located in the septum, (2) a peak of CRH gene expression within the paraventricular (PVN) hypothalamic nucleus, (3) a peak of the peptide hormone, arginine vasotocin (AVT) in the PVN that sustained the stress response at the level of the brain (Kadhim et al., 2021) and also included receptors of CRH and AVT in the two brain structures as well as measured gene expression in the anterior pituitary.

## University service

For the past 28 years, I have served as the University of Arkansas Representative and previously the University of Maryland Representative for the USDA Regional Project NC-1170 Advanced Technologies for the Genetic Improvement of Poultry. In 2018, I

organized a mini-symposium with Dr. Hans Cheng entitled 'Current Interest in Gene Editing of Avian Species' during an afternoon of the Poultry Workshop supported in part by USDA Regional Project, NC-1170. Eight prominent speakers were invited who were recognized for their knowledge of gene editing. The workshop was well attended at the Plant and Animal Genome (PAG) meeting in San Diego, CA. All seats were taken throughout the entire symposium with standing room only for all speakers.

Served for 10 years (2013–2023) on the Joint Patent and Copyright Committee and was Chairman for 5 years (January 2018 to December 2023).

To date, I have had the pleasure of serving as major professor of 27 graduate students who successfully pursued a Master of Science, MS degree and 13 doctoral students who completed their PhD program. Funding of the students occurred using several programs. Primary ones included the University of Maryland and University of Arkansas at the Dept., College and Univ. levels, including the Agricultural Experiment Station, National Science Foundation (NSF), USDA Competitive Grants Program, National Institutes of Health (NIH), Arkansas Biosciences Institute (ABI) Grants, Chancellor's Innovation and Collaborative Fund and company grants programs.

Publications include: 126 Journal Papers, 1 Book, 11 Chapters in Books, 206 Abstracts from Scientific Society Meetings, 51 Papers at Conferences, Short courses or Workshops, 3 articles in Trade or Popular Press sources, and 2 Patents in which one was licensed by a company. Currently I am working on a book, the Second Edition of 'A Stereotaxic Atlas of the Brain of the Chick, (*Gallus gallus domesticus*). The authors are Parker Straight and Wayne Kuenzel and is planned for completion in 2026.

## Awards

1. Sept. 1971-September 1973 National Institutes of Health (NIH) Postdoctoral Fellow, Cornell University, Ithaca, N.Y.
2. Jan. 1981 - Jan. 1982 Fulbright-Hays Senior Research Fellowship to Great Britain, Roslin Institute, Edinburgh, Scotland (Sabbatical Year #1). Hosts: Dr. Ian Duncan and Dr. Peter Sharp.
3. 1983 Maryland Alumni Assn (MDAA) Award, College of Agriculture for Excellence in Research.
4. 1988 Excellence in Teaching Award, Poultry Science Assn, Embrex (Purina Award), presented to an individual each year.
5. Aug. 1988 - Aug. 1989 Fulbright-Hays Senior Research, Fellowship to West Germany, Justus Liebig University Giessen (Sabbatical Year #2). Host: Dr. Sabine Blahser.
6. Aug. 1996 - Aug. 1997 Institute of Animal Science and Behavior, Celle, Germany (Sabbatical Year #3). Host: Dr. Roland Grossmann; Residence for family provided.
7. 1998 Merck and Co. Award for Achievement in Poultry Science, Poultry Science Association.

8. 2000 25 Years of Service Award Univ. of Maryland, Poultry Science Dept.
9. 2000 Sigma Xi Research Award-Contribution to Science Award, Univ. of Maryland Chapter.
10. 2010 Embrex Fundamental Science Award: Outstanding achievement in basic disciplines, Poultry Science Association.
11. 2012 Elected Fellow, Poultry Science Association.
12. September 2014-June 2015 Key Lab ANSC/BioChem, College VetMed, Nanjing Agricultural University, Nanjing, China (Sabbatical Year #4). Host: Dr. RuQian (Lucy) Zhou.
13. 2023/24 Elected Fellow, American Association for the Advancement of Science (AAAS).
14. 2025 25 Years of Service Award Univ. of Arkansas, Poultry Science Dept.

## Author contributions

WK: Writing – original draft, Writing – review and editing.

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## References

- Jurkevich, A., Barth, S. W., Kuenzel, W. J., Köhler, A., and Grossmann, R. (1999). Development of a sexually dimorphic vasotocinergic system in the bed nucleus of the stria terminalis in chicken. *J. Comp. Neurol.* 408, 46–60. doi:10.1002/(sici)1096-9861(19990524)408:1<46::aid-cne4>3.0.co;2-5
- Kuenzel, W. J. (1974). Multiple effects of ventromedial hypothalamic lesions in the White-throated sparrow. *Zonotrichia albicollis*. *J. Comp. Physiol.* 90, 169–182. doi:10.1007/bf00694483
- Kuenzel, W. J. (1982). Transient aphagia produced following bilateral destruction of the lateral hypothalamic area and quinto-frontal tract of chicks. *Physiol. Behav.* 28, 237–244. doi:10.1016/0031-9384(82)90068-3
- Kuenzel, W. J. (1983). The behavioral sequence of food and water intake: its significance for elucidating central neural mechanisms controlling feeding in birds. *Bird. Behav.* 5, 2–15.
- Kuenzel, W. J., and Blähser, S. (1991). The distribution of gonadotropic releasing hormone (GnRH) neurons and fibers throughout the chick brain (*Gallus domesticus*). *Cell tissue res. Cell. Tissue Res.* 264, 481–495. doi:10.1007/BF00319038
- Kuenzel, W. J., and Blähser, S. (1994). Vasoactive intestinal polypeptide (VIP)-Containing neurons: throughout the brain of the chick (*Gallus Domesticus*), with focus upon the lateral septal organ. *Cell. Tissue Res.* 275, 91–107. doi:10.1007/BF00305378
- Kuenzel, W. J., and Helms, C. W. (1967). Obesity produced in a migratory bird by hypothalamic lesions. *BioSci* 17, 306–395.
- Kuenzel, W. J., and Helms, C. W. (1970). Hyperphagia, polydipsia and other facets of hypothalamic lesions in the White-throated sparrow. *Zonotrichia Albicollis*. *Condor* 72, 66–75. doi:10.2307/1366476
- Kuenzel, W. J., and Helms, C. W. (1974). An annual cycle study of tan-striped and white-striped White-throated Sparrows. *Auk* 91, 44–53. doi:10.2307/4084660
- Kuenzel, W. J., and Mason, M. (1988). A Stereotaxic Atlas of the Brain of the Chick (*Gallus domesticus*). The Johns Hopkins University Press, 166pp.
- Kuenzel, W. J., and Sharp, P. J. (1985). Parasagittal hypothalamic knife cuts in Male chicks: advancement of reproductive function and changes in plasma levels of luteinizing hormone and androgen. *Brit. Poult. Sci.* 26, 199–205. doi:10.1080/00071668508416804
- Kuenzel, W. J., and van Tienhoven, A. (1982). Nomenclature and location of hypothalamic nuclei and circumventricular organs in the Avian brain. *J. Comp. Neurol.* 206, 292–313.
- Kuenzel, W. J., McCune, S. K., Talbot, R. T., Sharp, P. J., and Hill, J. M. (1997). Sites of gene expression for vasoactive intestinal polypeptide throughout the brain of the chick (*Gallus domesticus*). *J. Comp. Neurol.* 381, 101–118. doi:10.1002/(sici)1096-9861(19970428)381:1<101::aid-cne8>3.0.co;2-5
- Madison, F. N., Jurkevich, A., and Kuenzel, W. J. (2008). Sexual differences in plasma corticosterone released in undisturbed chickens (*Gallus Gallus domesticus*) in response to arginine vasotocin and corticotropin releasing hormone. *Gen. Comp. Endocrinol.* 155, 566–573. doi:10.1016/j.ygcen.2007.08.014
- Mass, J. H., and Kuenzel, W. J. (1983). Precocious development of the testes effected in chicks following parasagittal knife cuts of the lateral hypothalamic area. *Devel. Brain Res.* 10, 165–169.
- Nagarajan, G., Tessaro, B. A., Kang, S. W., and Kuenzel, W. J. (2014). Identification of arginine vasotocin (AVT) neurons activated by acute and chronic restraint stress in the Avian septum and anterior diencephalon. *Gen. Comp. Endocrinol.* 202, 59–68. doi:10.1016/j.ygcen.2013.02/029
- Nagarajan, G., Kang, S. W., and Kuenzel, W. J. (2017a). Functional evidence that the nucleus of the hippocampal commissure shows an earlier activation from a stress than the paraventricular nucleus: implication of an additional structural component of the avian hypothalamo-pituitary-adrenal axis. *Neurosci. Lett.* 642, 14–19. doi:10.1016/j.neulet.2017.01.064
- Nagarajan, G., Jurkevich, A., Kang, S. W., and Kuenzel, W. J. (2017b). Anatomical and functional implications of CRH neurons in a septal nucleus of the Avian brain: an emphasis on glial-neuronal interactions via V1a receptors. *In Vitro. J. Neuroendocrinol.* 29, 1–11.

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