



Editorial: The Influences of Early Life Experiences on Future Health and Productivity

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Editorial on the Research Topic

The Influences of Early Life Experiences on Future Health and Productivity

Livestock industries are increasingly focusing on improving lifetime performance and productivity while reducing environmental impact and cost of production. The perinatal period is a unique opportunity to shape an animal phenotype throughout life. Identifying challenges and opportunities for manipulating early life conditions to develop more resilient and less vulnerable animals is a growing area of interest. This Research Topic provides a comprehensive overview of the current knowledge about the influence that early life experiences have on the offspring, the potential underlying mechanisms leading to phenotypic outcomes later in life, and discussions on potential opportunities to yield positive outcomes thorough management interventions targeting key developmental windows focusing primarily in livestock species.

The conditions experienced during early life developmental periods can influence the offspring long-term phenotype by modulating their development, physiology, behavior, resilience, and vulnerability to disease, ultimately impacting health productivity. The Developmental Origins of Health and Disease, or *developmental programming*, refers to maternal/paternal influences at critical periods in pre and peri-conceptual, fetal or neonatal development with resulting persistent postnatal effects on the offspring (Gillman, 2005; Hanson and Gluckman, 2008). Initially demonstrated in humans, this concept extends to livestock species at large (Wu et al., 2006; Chavatte-Palmer et al., 2018). Considerable efforts have been made to understand how these influences during specific stages of gestation and early postnatal life might impact the developmental trajectory of the offspring differently, long-term, and often irreversibly. The developing fetus responds to stimuli or challenges imposed to the dam and conveyed by the placenta in mammals (Barker and Thornburg, 2013) or directly to the egg in birds, causing changes in gene expression due to epigenetic modifications (including DNA methylation, histone modifications and non-coding RNAs) that can influence organ development, structure, and/or function and ultimately exert long-term effects on the postnatal offspring. Numerous examples of influences, including but not limited to nutrition, drugs, pathogens, toxins, or stress, with the potential to program the fetus exist in livestock, some of which are featured in this Research Topic.

In beef cows, nutrient fluctuations during pregnancy (i.e., over or undernutrition) affect fetal development, with long-term impacts on muscle development hindering the quality of meat and production efficiency (Du et al., 2017). In this Research Topic, Moriel et al. summarizes the recent

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literature demonstrating how developmental programming could be explored by beef producers to enhance offspring health and performance (e.g., growth, immune function, and reproduction) by managing cow body condition score during pregnancy. These authors also discuss the positive outcomes of maternal supplementation of protein and energy, polyunsaturated fatty acids and increasing the frequency of specific nutrients including trace minerals, specific amino acids, and vitamins in maternal diets. In dairy cattle, exposure to elevated environmental temperature and humidity during pregnancy affects fetal development with long-term implications in health, survivability, and productivity (Laporta et al., 2020). Pigs gestated under heat stress conditions have an increased postnatal stress response and an increase in maintenance energy requirements (Johnson and Baumgard, 2019).

Sheep models of maternal inflammation during gestation can alter placental and fetal development leaving offspring at an increased risk of metabolic and even neurological disorders. In this Research Topic, Hicks and Yates outline the implications of excessive cytokine activity during compromised pregnancies. This prenatal inflammatory programming is likely one of many mechanisms contributing to offspring metabolic inadequacy which tends to be muscle centric and therefore, targeting anti-inflammatory therapeutics could produce innovative mitigation strategies during maternal inflammatory insults. Another contributing factor of the offspring thrifty phenotype outlined by Gibbs and Yates involves adrenergic pathway adaptations during fetal programming. These adaptations to adrenergic sensitivity in multiple tissues during compromised pregnancies yields lifelong metabolic dysfunction. Due to fetal nutrient partitioning skeletal muscle can be disproportionately affected by fetal growth restriction leading to slowed postnatal growth in ruminants and pigs. Herein, Liu et al. reviewed the life course impact of fetal exposure to elevated glucocorticoids during pregnancy on muscle development and function of the offspring. These authors highlight the role of glucocorticoids in the epigenetic regulation of the hypothalamus-pituitary axis in skeletal and cardiac muscle development and metabolism in numerous animal models, including livestock.

Furthermore, maternal insults can influence long-term changes to offspring productivity such as wool production in sheep (Magolski et al., 2011). Also, food preference has been shown to be influenced by maternal nutrition in domestic species, thus affecting food intake and subsequent production (Altbäcker et al., 1995; Simitziset al., 2008). Some of these observations extend to non-mammalian species such as poultry, where, for example, in ovo supplementation with nutrients affects the capacity of eggs to hatch, chick growth and health as well as meat quality (Roto et al., 2016). In this Research Topic, Andrieux et al. discusses programming strategies manipulating incubation temperature and dietary strategies, including the availability of methyl donors. These authors highlight the importance of timing,

duration, and intensity of these interventions to yield positive outcomes that might benefit the poultry industry.

In recent years, it has become more apparent that *postnatal early life experiences*, particularly the first weeks or months of life outside the womb, can influence the offspring developmental trajectory and productive outcomes later in life. Early life nutrition management (i.e., plane, frequency, quantity, and quality) has been shown to influence gut and rumen development, as well as the establishment of gut microbiota in dairy calves with long-lasting implications on production (Song et al., 2021). Postnatal exposure to elevated temperature and humidity significantly reduces dry matter intake with negative consequences on health and growth performance in dairy calves (Dado-Senn et al., 2020). In pigs, maternal programming *via* milk derived factors in early postnatal life have been implicated in reduced fecundity and litter size over multiple parities (Bagnell and Bartol, 2019) whereas maternal welfare improvement during gestation increases offspring neonatal survival (Merlot et al., 2022). In this Research Topic, Harvey et al. discusses how nutritional management during early postnatal life (e.g., early weaning strategies) might enhance carcass characteristics in feedlot cattle and exert advantageous reproductive outcomes in females. Other neonatal factors with the potential to influence the offspring long-term include social and housing conditions, husbandry practices, level of exposure to pathogens or infectious environments, among many others. Adcock discusses the long-term consequences and implications that early life painful and often routine procedures such as disbudding or tail docking might have for farm animal welfare and physiology. These authors compiled evidence supporting that experiencing painful events, sustained stress, or injuries leading to exacerbated inflammation, may have repercussions later in life that may be passed to the offspring.

Finally, in this Research Topic, Vautier and Cadaret, sum up the current knowledge on trans- and inter-generational programming in ruminant species. The programming effects of maternal insults such as under- or over-nutrition, heat stress, inflammation or glucocorticoid exposure vary depending on the insult, its timing and duration, with an important role of placental adaptation. Sex-related effects are observed which may affect gonadal development, hence affecting offspring subsequent fertility. In addition, several studies demonstrate intergenerational programming effects in ruminants, indicating that observations in humans and animal models are also found in ruminants.

So far, underlying epigenetic mechanisms have been poorly explored in ruminant species, although recent work on the paternal line has related the sperm epigenome to bull's fertility (Costes et al., 2022). As demonstrated in rodent models, epigenetic responses vary according to the individual's genotype, and there is a need for mechanistic studies aimed at the understanding of genetics/epigenetic interactions as well as interactions between different insults also known as the exposome.

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