東北大学大学院農学研究科
食と農免疫国際教育研究センター
CFAI 特別セミナー

2023年10月30日 月 13:00-14:00

会場：第４講義室

Assessing genetic and epigenetic contributions to the ovine stress response phenotype using bacterial endotoxin

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When livestock are reared using intensive farming practices, they experience increased stress that can adversely affect animal health and production, and climate change is predicted to be an amplifying factor. Producers have become reliant on antimicrobials to prevent and treat diseases caused by microbial stressors however, this global practise is facing increasing restrictions because it has contributed to the development of antimicrobial resistant pathogens, some of which are zoonotic. Selective breeding based on a health trait such as stress responsiveness may be a strategy to improve population level stress resilience, and this would help to mitigate adverse outcomes attributed to stress. Stress responsiveness is a moderately heritable trait, but estimates vary with phenotyping methods. Bacterial lipopolysaccharide (LPS) endotoxin has been widely used across species as a microbial stressor. When an LPS immune challenge is carried out on sheep, it elicits a classical acute-phase response (APR) that manifests as fever, anorexia and temporal increases in serum cytokine and stress hormone (cortisol) levels that model an acute bacterial infection. Bacterial LPS is a biologically relevant stressor implicated in numerous disorders including mastitis, sepsis, acidosis, and leaky gut syndrome, all of which are exacerbated by heat stress. Our group has been using LPS to stress phenotype sheep for several years. We have demonstrated that the peak cortisol response to LPS is correlated with immune responsiveness, and telomere length, which is a predictive marker of ageing. This phenotype is moderately heritable ($h^2 \cong 0.3$), and we have identified several genetic markers associated with stress responsiveness using this phenotyping platform. Interestingly, LPS immune challenge during pregnancy alters ovine fetal neuroendocrine-immune programming, and this is retained into adulthood. The mechanisms by which this occurs are currently unknown, however, epigenetic mechanisms that include microRNA (miRNA) have been implicated in fetal reprogramming. Recently, we identified 45 ovine miRNAs (35 upregulated and 10 downregulated) that were differentially expressed (DE) during the peak stress response to LPS immune challenge, most of which are found on ovine chromosome 18. Further analysis of high (HSR), middle (MSR) and low (LSR) stress responding sheep from a population of 112 animals revealed 3 upregulated and 7 downregulated DE miRNA (HSR versus MSR and LSR). Functional analysis of these DE miRNAs revealed roles in Ras and MAPK signaling, cytokine signaling, adaptive immune system and transcriptional pathways in the HSR sheep. In contrast, metabolic pathways were enriched in the LSR sheep. Collectively, these studies reveal roles for miRNAs in the ovine stress response that should be investigated further to elucidate their contribution to regulating mRNA expression during LPS-induced stress, and genetic and epigenetic variation in stress responsiveness.

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