Age-associated changes in lymphocyte metabolism of dairy calves

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Introduction

Dairy calves have the necessary immune cell machinery to mount an effective immune response. However, their lymphocytes often fail to fully respond to parenteral vaccination until 6 months of age, limiting vaccine effectiveness during the first months of life. Lymphocytes' mitochondrial functionality drives effector functions critical for vaccine responsiveness. However, the extent to which lymphocyte mitochondrial function changes with age and could explain this poor vaccination response remains unknown. Thus, we aimed to determine how the mitochondrial function of dairy calf lymphocytes changes with age from birth to immunologic maturity. Given lymphocyte dependency on mitochondrial efficiency, we hypothesized that the mitochondrial efficiency of dairy calf lymphocytes increases with age.

Materials and methods

In this cross-sectional study, groups of 4 Holstein calves were sampled at birth before colostrum consumption (0), 1, 2, 3, 4, 6, 8, 16 and 24 weeks of age. Mid-lactation cows (n = 4) were also sampled to provide a reference of a mature immune response. Whole blood was collected, and B, CD4, CD8 and gamma delta T lymphocytes were isolated using magnetic-activated cell sorting. Mitochondrial function was assessed in each T lymphocyte subset using extracellular flux analysis, reporting non-mitochondrial oxygen consumption, basal respiration, maximal respiration, spare respiratory capacity, proton leak and the oxygen consumption rate (OCR) to extracellular acidification rate (ECAR) ratio. The OCR to ECAR ratio indicates the relative proportions of oxidative phosphorylation and glycolysis cells use, providing a more holistic image of cell metabolism. Significant differences ($P < 0.05$) were determined using Kruskal-Wallis tests and the Dunn method for all pairwise comparisons.

Results

CD4+ cells had higher non-mitochondrial oxygen consumption at 3 weeks relative to 0 and 16 weeks. Also, the OCR to ECAR ratio for 0 weeks was lower than in adults. CD8+ cells had a higher OCR to ECAR ratio at 3 weeks than at 2 weeks. Gamma delta T-cells had higher basal respiration at 2 weeks compared to 24 weeks, and maximal respiration of 3 weeks was higher than 16 weeks. B-cells had higher maximal respiration at 1 week than at 16 weeks, and the proton leak at 1 week was higher than at 0 weeks. Overall, there was no pattern of changes in any of the studied mitochondrial outcomes across age groups.

Significance

In conclusion, our results do not support the existence of differences in the mitochondrial function of dairy calf lymphocytes associated with age. The mitochondria of calf lymphocytes do not function differently than adult lymphocytes. Therefore, mitochondrial efficiency is not likely an underlying factor for reduced vaccine responsiveness in dairy calves.

