

## MicroRNA expression patterns in post-natal mouse skeletal muscle development

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**Introduction:** MicroRNA (miRNAs) are small non-coding RNA molecules that act as transcriptional regulators, primarily by repressing the expression of their specific gene targets. In mature organisms, miRNAs play a major role in the maintenance of skeletal muscle homeostasis and facilitate the adaptation of muscle structure, function and metabolism in response to internal and external stress signals. In this study, we investigated the expression patterns and putative roles of miRNAs during the early post-natal development stages of the mouse *quadriceps* muscle.

**Methods:** Twenty C57BL/6 mice were sacrificed at the age of 2 days (n=4), 2 weeks (n=5), 4 weeks (n=5) and 12 weeks (n=6) and RNA was extracted from the muscle. MiRNA expression was assessed using the TaqMan Array Rodent MicroRNA A+B Cards Set v3.0. The Expression Suite software was used to extract and normalize the data using the global normalization function. Linear trend in cycle threshold values (Ct) were assessed using a robust regression model; Kruskal-Wallis' test was used to compare time Ct values for miRNAs with no significant trend. Predicted Ct values from a robust quadratic model were used to classify miRNAs into clusters of Ct profiles using the Wald's distance. For each cluster, top cellular functions and miRNA-mRNA target interactions were determined using the online software package Ingenuity System Interactive Pathway Systems.

**Results:** Out of the 768 miRNA measured, 354 (46%) were significantly expressed in muscle in at least one of the time points (Ct<32). Thirty of these miRNAs (8%) were expressed at one time point only. Collective miRNA expression levels significantly decreased (43%) or increased (16%) with time ( $P<0.05$ ). Out of 10 miRNAs clusters, 8 were selected for further analysis based on the significance levels of the linear and the Kruskal-Wallis' tests. The most highly ranked cellular functions likely to be regulated by each miRNA cluster included cellular development, cellular growth and proliferation, cell death and survival, DNA replication and protein synthesis.

**Conclusion:** This study provides an overview of the role and regulation of miRNAs in neo-natal and post-natal mouse skeletal muscle samples. Our results collectively suggest that miRNAs play an essential regulatory role during the very-early muscle development stages, and that their expression levels tend to decrease as the muscle grows and matures.