

## Micro RNA profile associated with the dystrophin level in Becker muscular dystrophy

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Becker (BMD) and Duchenne muscular dystrophy (DMD) are allelic disorders arising from mutations in the dystrophin gene. In-frame mutations lead to the milder BMD while out-of-frame mutations disrupt the reading frame and lead to the severe DMD with lack of dystrophin. A therapeutic strategy for skipping specific exons in dystrophin and restoring the open reading frame has been successfully applied in DMD; this “converts” the out-of-frame deletion in DMD to BMD-like in-frame deletion. Micro RNAs (miRs) are small RNA sequences that regulate gene expression post-transcriptionally. Specific miRs are important regulators of skeletal muscle maintenance. In order to better understand the role of miRNAs associated with different levels of dystrophin, we performed small RNA sequencing in the muscle samples of BMD patients harbouring deletions relevant to ongoing exon skipping studies in DMD. A total of 12 miRs with significant difference between BMD and controls were identified including miRs regulating inflammation (miR-146b, miR-155, miR21) and vascular angiogenesis (miR-378). BMD patients with dystrophin 70–80% of control levels had high expression of miR-425, involved in the regulation of the myostatin signalling pathway. There was a significant up-regulation of miR-144 and miR-451 in BMD with lower amounts of dystrophin (60–70% of control). These miRNAs are also up-regulated in aged skeletal muscles. The age-associated changes include loss of muscle mass and altered cycles of degeneration and regeneration leading to inflammation that also occurs in DMD and BMD. This suggests a role of miR-144 and miR-451 in the dystrophic processes. The validation of the identified miRs is ongoing and will help to establish the role of the dysregulated miRs in the pathological process in dystrophic muscles. In addition to being used as biomarkers, miR425, miR-144 and miR-451 could potentially be utilised as therapeutic targets.