

**P025** Muscle-Specific mTOR Inactivation Leads to a Severe Myopathy

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Recent studies have implicated mTOR as an important regulator of skeletal muscle growth and metabolism. However, it is not known whether mTOR-dependent mechanisms are also involved in the maintenance of muscle integrity. Therefore, we inactivated mTOR specifically in differentiated mouse skeletal muscle and show that the mutant mice develop a severe myopathy displaying characteristics of dystrophies and metabolic myopathies. Our data suggest that mTOR is required for the proper expression of the dystrophin-glycoprotein complex in a novel rapamycin-insensitive mechanism, in addition to effects on the expression of genes critical for energy metabolism. In addition, mTOR mutant muscle exhibits increased Akt and S6K activities, a molecular signature of dystrophic muscles, indicating that this feature is due to satellite cell-driven regeneration. Collectively, our results demonstrate a critical role for mTOR in the maintenance of muscle fiber integrity and suggest that alterations of mTOR-mediated physiological processes could contribute to the pathogenesis of a broad range of myopathies.