

P065 Reprogramming of translation in C2C12 myoblasts during differentiation

Mark Willett, Jed McDonald and Simon Morley

*School of Life Sciences, University of Sussex, Falmer,
Brighton BN1 9QG*

The differentiation of skeletal muscle cells is a highly ordered systematic process. Following the proliferation of myoblasts, regulatory factors are expressed which include those that result in rapid withdrawal from the cell cycle and the subsequent formation of myocytes. Following this, synthesis of contractile muscle proteins and proteins which facilitate membrane fusion result in the terminal differentiation of myocytes into multinucleated myotubes. This complex multi-step process suggests that the modulation of both specific and global mRNA expression is likely to be highly regulated at a post-transcriptional level.

Our experiments investigating methionine incorporation into protein suggest that high rates of protein synthesis are maintained during terminal differentiation independently of mTOR signalling, when mTOR is specifically inhibited post 24 hours. Differentiation is completely abrogated when mTOR is inhibited for the entire time-course, suggesting that mTOR dependent signalling is essential for earlier stages of differentiation. We also present data that investigates the effect on differentiation of specific inhibition of the mRNA helicase eIF4A, and investigate interactions between the canonical initiation factors (including recruitment of specific isoforms of eIF4GI and eIF4GII into eIF4F) as well as their relative mRNA and protein expression during the differentiation process.

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