2016

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Abstract

Skeletal muscle regeneration relies on myoblast stem cell differentiation and is a crucial response to muscle injury caused by trauma and numerous diseases. In skeletal myoblasts, cell death and differentiation are mutually exclusive biological endpoints that are both induced by culture in differentiation media. MyoD, the master muscle-specific transcription factor, is well-known to regulate the expression of muscle specific genes such as myogenin and the ensuing differentiation. However, we have previously reported that MyoD also plays a critical role in the expression of PUMA and apoptosis, rather than myogenin and differentiation, in a subset of myoblasts, thus diminishing the regeneration. It is, therefore, critical to understand the molecular events that distinguish between this coordinate regulation of differentiation and apoptosis by MyoD. p38 kinase is known to be required for the expression of myogenin. Herein, we report that pharmacological inhibition of p38, while diminishing the expression of myogenin, actually enhances the expression of PUMA. Since myoblast cell cultures are asynchronous, we hypothesized that cell cycle position may contribute to this molecular distinction. To investigate this possibility, we have successfully synchronized cultures and experiments are underway to determine the effect of cell cycle position on PUMA expression versus differentiation specific gene expression.