

PAX3 controls the adaptive response of skeletal muscle stem cells to environmental stress

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ABSTRACT

We have identified a molecular link between the Aryl hydrocarbon Receptor (AhR) environmental stress pathway and Pax3/Pax7 developmental genes during craniofacial development. Since Pax3/7 are key regulators of muscle stem cells (muscle satellite cells), we investigated the cellular and molecular impact of chronic 2,3,7,8-Tetrachlorodibenzo-p-Dioxin (TCDD) exposure on skeletal muscle and satellite cells in the adult. We combined in vivo and ex vivo approaches, in order to analyze the impact of chronic exposure to TCDD in several muscles such as tibialis anterior and biceps brachii. While all MuSCs express the transcription factor PAX7, we show that a muscle-specific subset also express PAX3 and exhibit resistance to environmental stress. Upon systemic TCDD treatment, PAX3-negative MuSCs display impaired survival, atypical activation and sporadic differentiation through the xenobiotic Aryl Hydrocarbon Receptor. We further show PAX3-positive MuSCs become sensitized to environmental stress when PAX3 function is impaired and that PAX3-mediated induction of mTORC1-dependent G(alert) is required for protection. Our study therefore identifies a functional heterogeneity of MuSCs in response to environmental stress controlled by PAX3.

Relaix 教授は著明な骨格筋発生学の研究者で、PAX3,PAX7 の研究は特に知られています。今回は PAX3 の環境ストレスに対する役割についてご講演いただきます。ぜひご聴講ください。

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