



Institut NeuroMyoGène

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## **INMG seminar**

**Friday February 1<sup>st</sup> 2019 11:00**

Amphi 2bis

Faculté de Médecine Lyon Est

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

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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 analyse 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.

## SELECTED PUBLICATIONS

Cellular localization of the cell cycle inhibitor Cdkn1c controls growth arrest of adult skeletal muscle stem cells. Mademtzoglou D, Asakura Y, Borok MJ, Alonso-Martin S, Mourikis P, Kodaka Y, Mohan A, Asakura A, **Relaix F**.

Elife. 2018 Oct 4;7. pii: e33337.

SOXF factors regulate murine satellite cell self-renewal and function through inhibition of  $\beta$ -catenin activity. Alonso-Martin S, Auradé F, Mademtzoglou D, Rochat A, Zammit PS, **Relaix F**.

Elife. 2018 Jun 8;7. pii: e26039.

Reciprocal signalling by Notch-Collagen V-CALCR retains muscle stem cells in their niche. Baghdadi MB, Castel D, Machado L, Fukada SI, Birk DE, **Relaix F**, Tajbakhsh S, Mourikis P.

Nature. 2018 May;557(7707):714-718.

n Situ Fixation Redefines Quiescence and Early Activation of Skeletal Muscle Stem Cells. Machado L, Esteves de Lima J, Fabre O, Proux C, Legendre R, Szegedi A, Varet H, Ingerslev LR, Barrès R, **Relaix F**, Mourikis P.

Cell Rep. 2017 Nov 14;21(7):1982-1993

Pax3 and Pax7 play essential safeguard functions against environmental stress-induced birth defects. Zalc A, Rattenbach R, Auradé F, Cadot B, **Relaix F**.

Dev Cell. 2015 Apr 6;33(1):56-66.

Antagonistic regulation of p57kip2 by Hes/Hey downstream of Notch signaling and muscle regulatory factors regulates skeletal muscle growth arrest. Zalc A, Hayashi S, Auradé F, Bröhl D, Chang T, Mademtzoglou D, Mourikis P, Yao Z, Cao Y, Birchmeier C, **Relaix F**.

Development. 2014 Jul;141(14):2780-90.

Six homeoproteins directly activate Myod expression in the gene regulatory networks that control early myogenesis. **Relaix F**, Demignon J, Laclef C, Pujol J, Santolini M, Niro C, Lagha M, Rocancourt D, Buckingham M, Maire P.

PLoS Genet. 2013 Apr;9(4):e1003425.

Lack of in vivo functional compensation between Pax family groups II and III in rodents. Hayashi S, Rocancourt D, Buckingham M, **Relaix F**.

Mol Biol Evol. 2011 Oct;28(10):2787-98.

Neural crest cell lineage restricts skeletal muscle progenitor cell differentiation through Neuregulin1-ErbB3 signaling. Van Ho AT, Hayashi S, Bröhl D, Auradé F, Rattenbach R, **Relaix F**.

Dev Cell. 2011 Aug 16;21(2):273-87.