

MASTER 2 BMC PARCOURS GENOPATH ANNÉE 2021-2022

Titre du sujet de stage : Cellular interactions involved in physiological muscle repair

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Sujet de stage :

Skeletal muscle is a highly dynamic tissue that regenerates *ad integrum* after an injury. We previously demonstrated that the different stages of skeletal muscle repair greatly rely on the dynamic interplay between muscle stem cells (MuSCs) and their environment including immune cells (Arnold et al., 2007) (*i.e.*, macrophages), fibro-adipogenic progenitor (FAPs)/fibroblasts (Mackey et al., 2017) and endothelial cells (Latroche et al., 2017). However, these mechanisms have been essentially described using non-physiological models of injury (*e.g.*, injection of toxin) that damage all the myofibers but remain totally unknown when the muscle is “mechanically” damaged by different strenuous exercises (*i.e.*, from a mild to a severe injury as this occurs in Human (Fouré and Gondin, 2021)).

This project will investigate how inflammatory, vascular and connective cells control skeletal muscle repair in a physiological model of exercise-induced muscle injury. The cellular interactions involved in muscle repair will be investigated using 3D histology, flow cytometry and *in vivo* live imaging (Lau et al., 2016) with mouse strains allowing MuSCs and macrophage tracking. We will focus on tissue resident macrophages versus monocyte-derived macrophages to define their roles according to the magnitude of muscle injury. We will also evaluate the effects of non-pharmacological approaches on the recovery of muscle homeostasis.

This project will provide the first cellular (and molecular) analysis of muscle regeneration after a physiological injury and illustrate the potential benefits of therapeutic interventions.

Technologies utilisées : Histology, immunostaining, cell biology, flow cytometry, *in vivo* live imaging (biphoton microscopy).

Mots clés : Skeletal muscle injury, stem cells, cellular interactions, macrophages

Publications d'intérêt :

Arnold, L., Henry, A., Poron, F., Baba-Amer, Y., van Rooijen, N., Plonquet, A., et al. (2007). *J. Exp. Med.* 204, 1057–1069. doi:10.1084/jem.20070075.

Fouré, A., and Gondin, J. (2021). *Exerc Sport Sci Rev* 49, 59–65. doi:10.1249/JES.000000000000239.

Latroche, C., Weiss-Gayet, M., Muller, L., Gitiaux, C., Leblanc, P., Liot, S., et al. (2017). *Stem Cell Reports* 9, 2018–2033. doi:10.1016/j.stemcr.2017.10.027.

Lau, J., Goh, C. C., Devi, S., Keeble, J., See, P., Ginhoux, F., et al. (2016). *Intravital* 5, e1156272. doi:10.1080/21659087.2016.1156272.

Mackey, A. L., Magnan, M., Chazaud, B., and Kjaer, M. (2017). *J. Physiol. (Lond.)* 595, 5115–5127. doi:10.1113/JP273997.