Institut NeuroMyoGène CNRS UMR 5310 / INSERM U1217

Domaine Scientifique de la Doua - 16 rue Dubois, Bâtiment G. Mendel - 69622 Villeurbanne Cedex
Tel : (33) 0472431325 – Fax : (33) 0472432685 – www.inmg.fr

LES SÉMINAIRES DE L'INMG

Translational Control of Muscle Stem Cells

Par

Colin Crist

(Invité par Rémi Mounier)

Lady Davis Institute for Medical Research
Jewish General Hospital- Montreal – Québec – H3T 1E2 - Canada
Department of Human Genetics
McGill University
Montreal – Québec – H3A 1B1 Canada

https://cristlab.wordpress.com/

Lundi 14 novembre 2016

11 h 00

Salle Guillermond
Bâtiment L'Herbier
9, rue Raphaël DUBOIS
69100 Villeurbanne
Domaine Universitaire de La Doua

http://oscar.univ-lyon1.fr/appli~externe/plan/plans/plan_campus_ouest.html

ABSTRACT
Regeneration of adult tissues depends on somatic stem cells that remain quiescent, yet are primed to enter a differentiation program. The molecular pathways that prevent activation of these cells are not well understood. Using mouse skeletal muscle stem cells as a model, we show that accumulating transcripts specifying the myogenic program are not translated in quiescent satellite cells, but are repressed by the action of microRNAs and RNA binding proteins. Furthermore, the reversible nature of microRNA dependent silencing mechanisms may underlie the rapid activation of satellite cells that are poised to enter the myogenic program. We also show that a general repression of translation, mediated by the phosphorylation of translation initiation factor eIF2✔ at serine 51 (P-eIF2α), is required to maintain the quiescent state. Skeletal muscle stem cells unable to phosphorylate eIF2✔ exit quiescence, activate the myogenic program and differentiate, but do not self-renew. P-eIF2α ensures in part the robust translational silencing of accumulating mRNAs that is needed to prevent the activation of muscle stem cells. Additionally, P-eIF2α dependent translation of mRNAs regulated by upstream open reading frames (uORFs) contributes to the molecular signature of stemness. Finally, we show that addition of small molecule inhibitors of eIF2α dephosphorylation to muscle stem cell cultures permits their *ex vivo* expansion and engraftment into a preclinical mouse model of Duchenne muscular dystrophy.

If you wish to meet Colin Crist, please contact Rémi Mounier (remi.mounier@univ-lyon1.fr).

Selected publications:

Zismanov, V. Chichkov, V., Colangelo, V., Jamet, S. Wang, S., Syme, A., Koromilas A.E., and **Crist, C.** (2016) Phosphorylation of eIF2✔ is a translational control mechanism regulating muscle stem cell quiescence and self-renewal. Cell Stem Cell *18*, 79-90.

Crist, C.G., Montarras, D. and Buckingham, M. (2012) The muscle satellite cell is primed for myogenesis, but maintains quiescence with sequestration of *Myf5* mRNA targeted by microRNA-31 in mRNP granules. Cell Stem Cell *11,* 118-126.