Instituto de Medicina Molecular João Lobo Antunes

Master Project Proposal

Title: Mechanisms of nuclear positioning in skeletal muscle cells

Synopsis:

Position of the nucleus is important for cellular activities such as cell division, cell migration and multicellular organism development. The cytoskeleton plays an important role in nuclear positioning either by anchoring or moving the nucleus within the cell.

In our lab we are interested in understanding how does the cytoskeleton regulates nuclear positioning during muscle formation (1,2,3). We are also curious to know how mutations in proteins associated with muscular dystrophies interfere with nuclear position during myofiber formation (figure 1 and 2) (4).

We propose to study how these proteins are involved in the physical connection between the nucleus and the actin cytoskeleton during muscle formation. We use state-of-the-art microscopy techniques (multicolor time-lapse fluorescent microscopy, photo-activation and photoswitchable techniques, fluorescence recovery after photobleaching - FRAP) combined with molecular biology, biochemistry and micromanipulation (microinjection) approaches to address this process both *in vitro* and *in vivo* (figure 1 and 2). The mechanisms of nuclear positioning during muscle formation that we will identify are potential targets for therapies to inhibit abnormal nuclear positioning in muscle disorders.

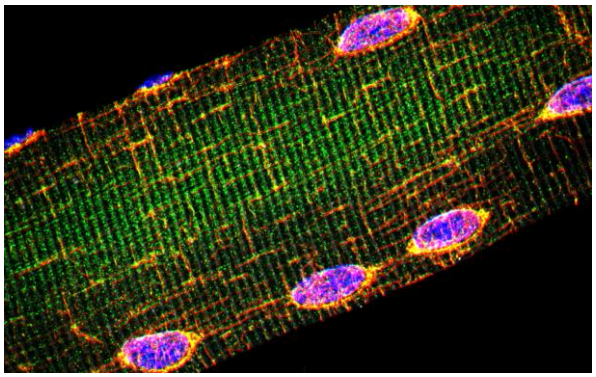

Figure 1.
Isolated myofiber with pheripheral nuclei.

Green - Gamma actin
Red – Microtubules
Blue - Nucleus

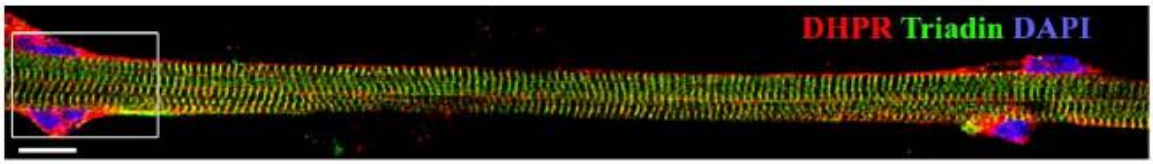

Figure 2- Skeletal muscle fiber, differentiated in vitro, with peripheral nuclei (blue) and fully formed triads (Red and Green).

Supervisor: *Edgar Gomes, EGomes Lab, edgargomes@medicina.ulisboa.pt*
Webpage of the group: https://imm.medicina.ulisboa.pt/en/investigacao/labs/gomes-lab/

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Remunerated or volunteer training: Volunteer