Sarcopenia, insulin resistance and metabolic syndrome
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INTRODUCTION: Sarcopenia is the process defined by the progressive loss of muscle mass and decline in muscle quality and function due to aging. It seems to be frequently accompanied by the ectopic deposition of adipose tissue, causing a condition called sarcopenic obesity. A vicious cycle between the loss of muscle mass and the accumulation of intramuscular fat might be associated with the metabolic syndrome via a complex interplay of factors including oxidative stress, mitochondrial dysfunction, proinflammatory cytokines production and insulin resistance (Fig. 1).
Lifestyle interventions (physical exercise and nutrient supplementation) have been proved to be effective in modulating molecular pathways impaired during aging and thus curbing cellular events responsible of sarcopenic obesity.
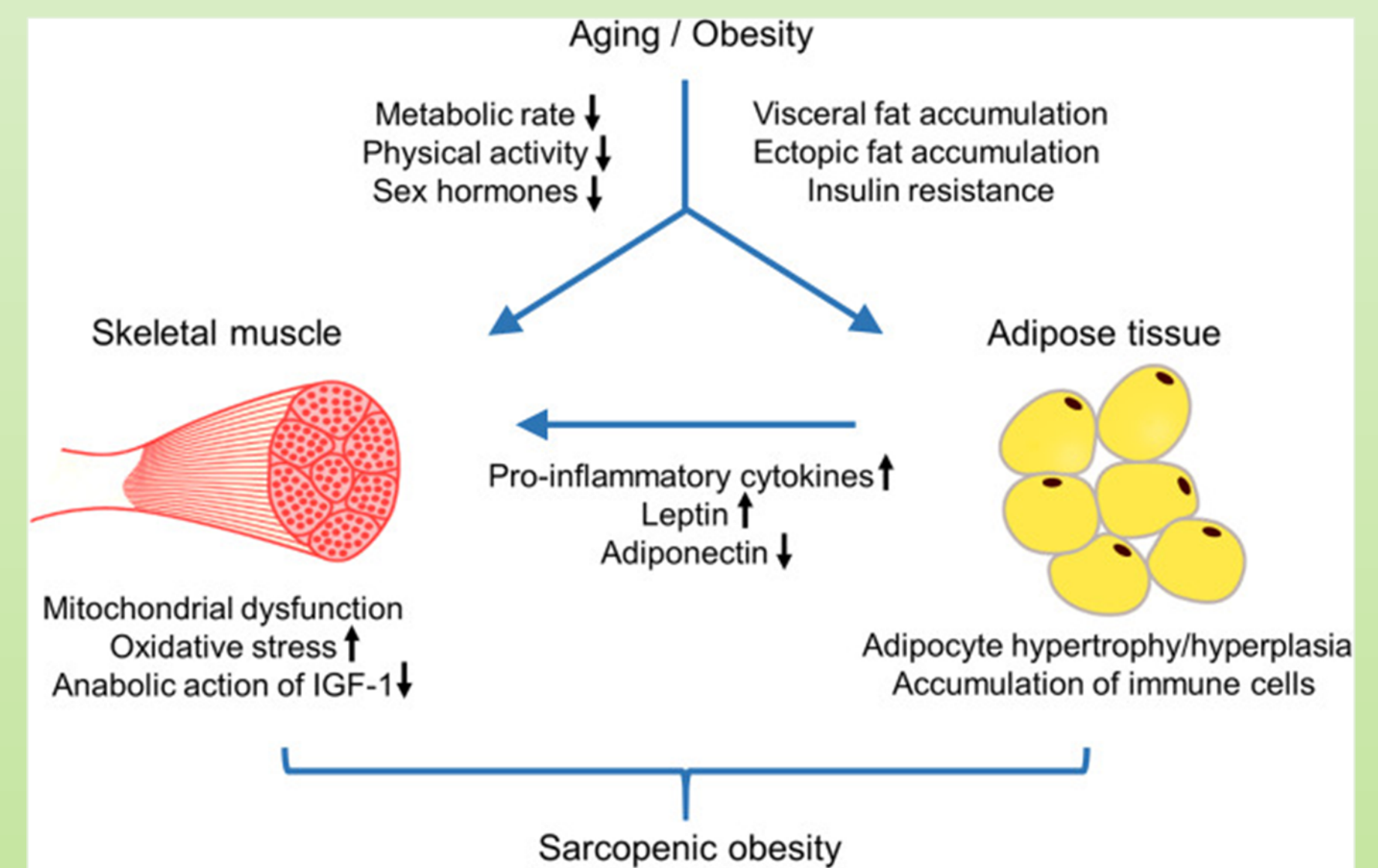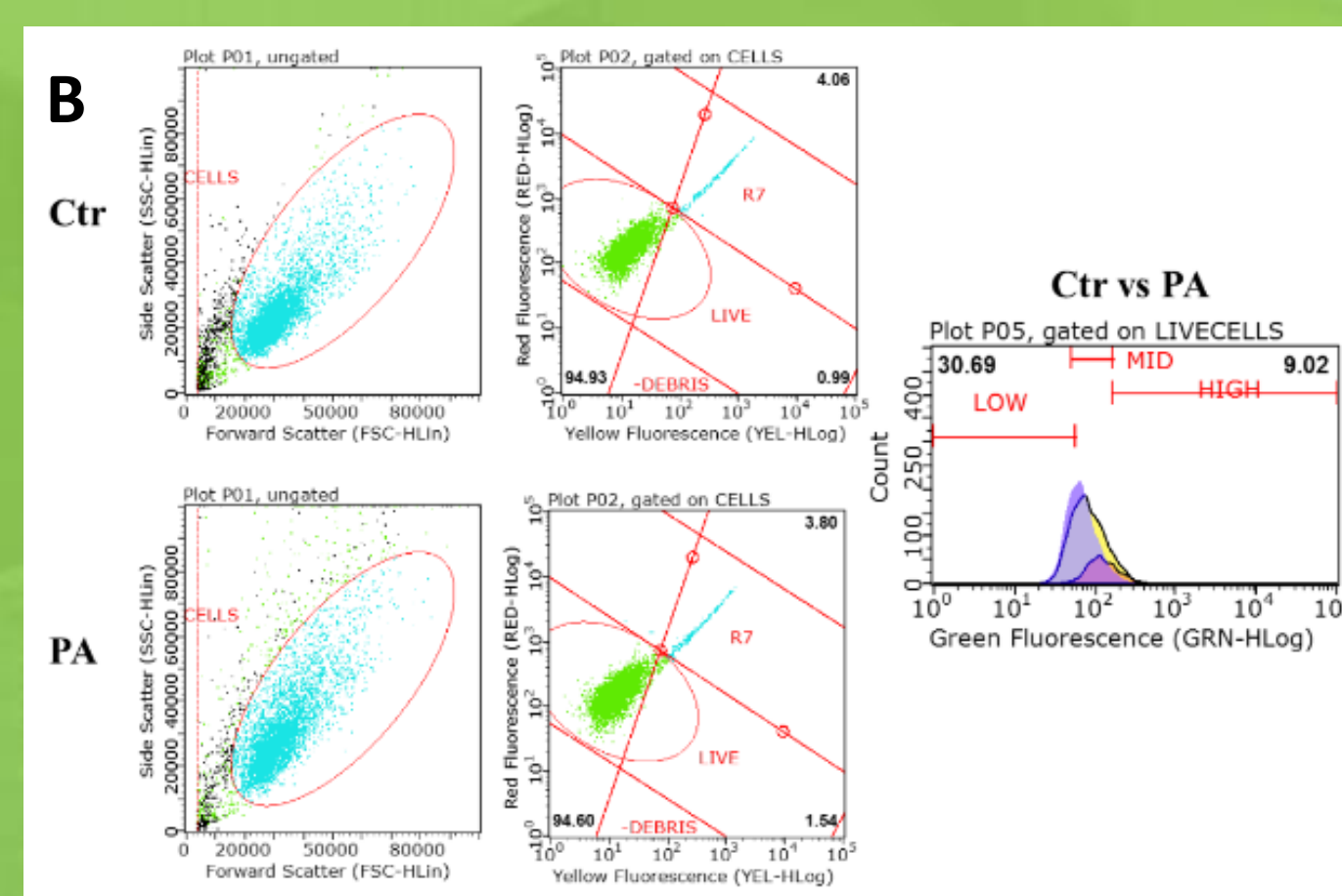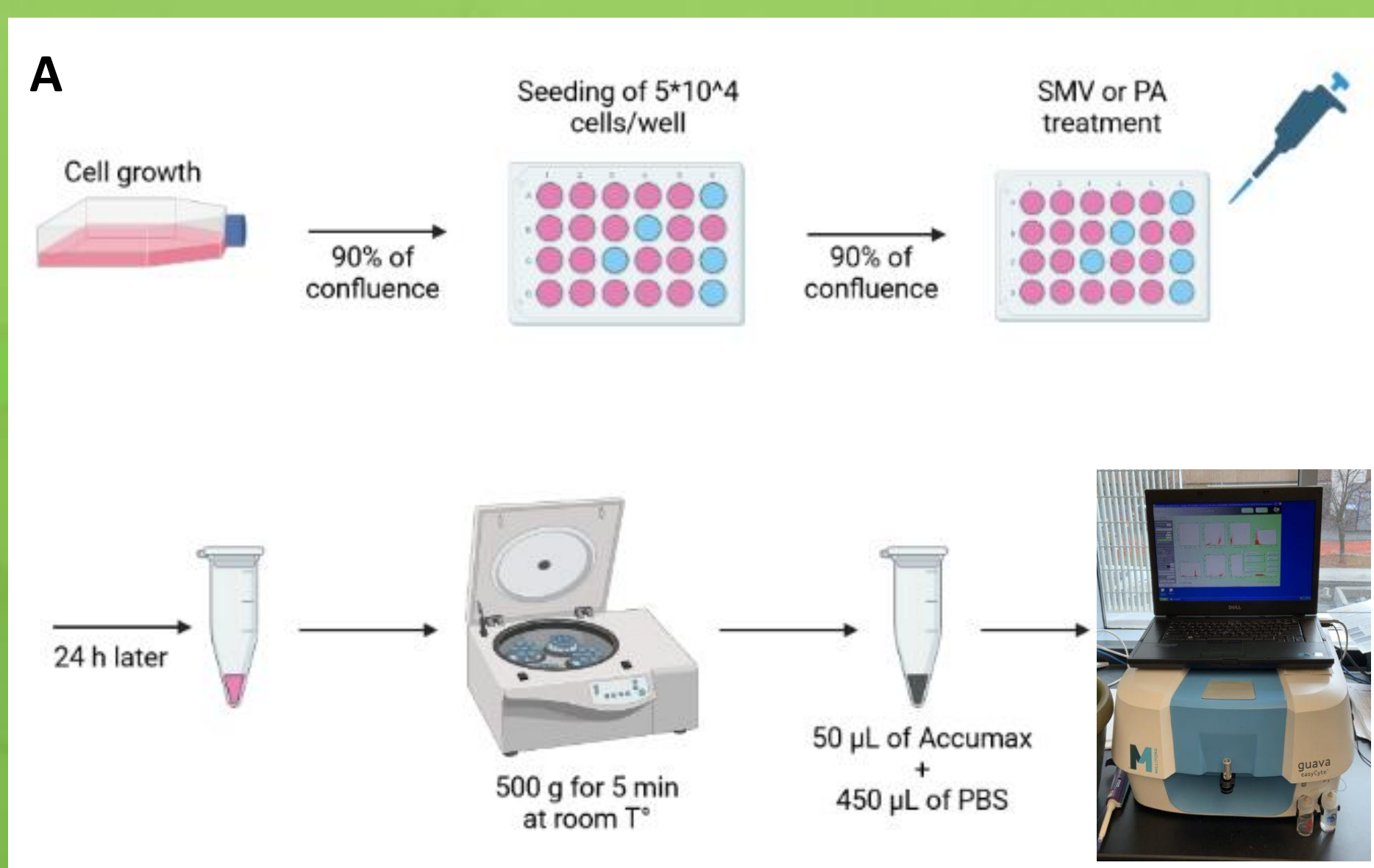

Fig. 1: Schematic biological pathways that lead to Sarcopenic Obesity during aging

AIM OF THE PROJECT: This PhD project aims to characterize the biology of specific myokines secreted by skeletal muscle during exercise. The crosstalk of myokines with adipokines will be investigated in order to analyze if oxidative stress and pro-inflammatory conditions can be modulated in order to curb the development of insulin resistance in sarcopenic obesity.
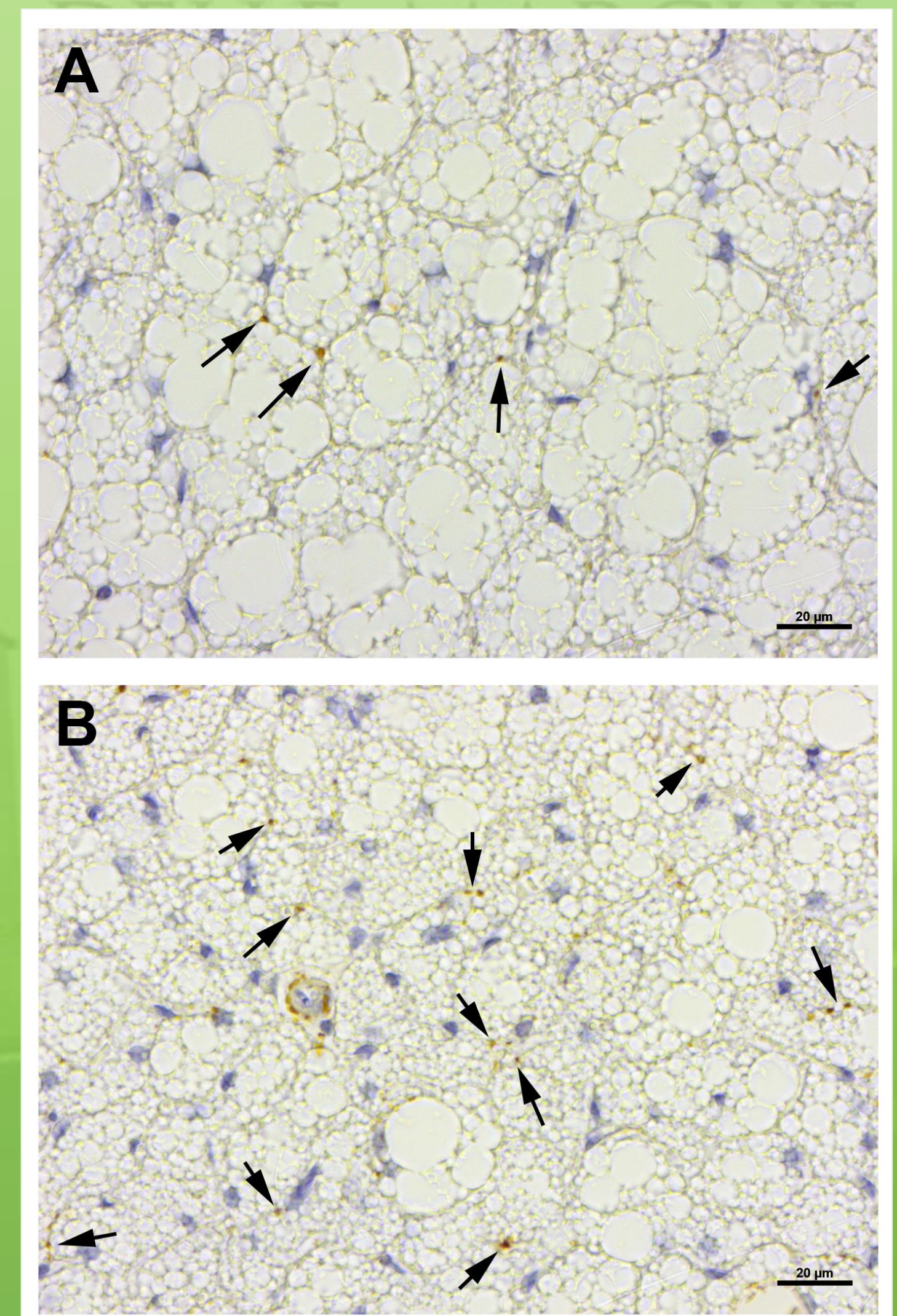
METODOLOGY AND PRELIMINARY RESULTS: It will mainly be applied a morpho-functional approach using in-vitro system mimicking physical exercise in normal, insulin resistant-induced and senescent myotubes. In-vivo setting will be used to validate if lifestyle interventions can modulate specific neuroendocrine function and prevent skeletal muscle loss in aging mice and reduce the development of insulin resistance.
The major results obtained in the first period of the PhD program regard the acquisition and the standardization of the techniques needed for the research project. Specifically, cell culture system and flow cytometry analysis were approached, as well as tissue processing and immunohistochemistry for morphological evaluation. The next step will be to perform immunofluorescence analyzes and confocal microscopy.

In-vivo analysis

Fig. 3: IHC on brown adipose tissue of mice fed with high fat diet. IR was induced by high fat diet in two different stains of mice (A and B). The modulation of nerve fibres density was evaluated by TH staining (arrows)

In-vitro experiments

Fig. 2: A. C2C12 culture treated with SMV and PA to evaluate mitochondrial toxicity and insulin resistance.
B. Intracellular ROS production analyzed with DCFH2-DA+ViaCount.

ENDPOINTS FOR THE FIRST YEAR:
- Assessing whether certain myokines have a protective effect on different myotubes models (insulin resistant, senescent and oxidative stress-induced myotubes)
- To set up myotube cell culture and to test the *in-vitro* physical activity stimulation system
- To identify some reliable biomarkers of neuromodulation to be used for morphological assay

References:
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Rubio-Ruiz ME, Guarner-Lans V, Pérez-Torres I, Soto ME. Mechanisms Underlying Metabolic Syndrome-Related Sarcopenia and Possible Therapeutic Measures. International Journal of Molecular Sciences. 2019; 20(3):647.