

MUSCLE DYSFUNCTIONS IN CHRONIC KIDNEY DISEASE PATIENTS

CONTEXT

Loss of mass and dysfunction of skeletal muscles are common comorbidities in Chronic Kidney Disease (CKD) patients. They are associated with an increased risk of mortality, lead to reduced physical activity, and impact quality of life.

Previous studies have highlighted in skeletal muscle of CKD patients an activation of atrophy pathways, a fiber type transition from type I (slow) to type II (fast), an alteration in mitochondrial structure, as well as activation of autophagy and mitophagy. However, the mechanisms involved are still poorly understood. In particular, data are still lacking concerning the impact of hemodialysis on skeletal muscle cells.

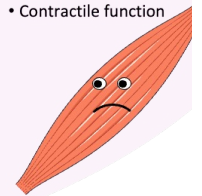
CHRONIC KIDNEY DISEASE



- Hemodialysis
- Uremic toxins
- Inflammation
- Protein energy wasting
- Denutrition
- Deregulation of myokine secretion

MUSCLE DYSFUNCTIONS

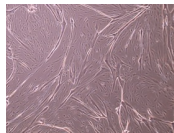
- Regeneration
- Metabolic functions
- Contractile function



Experimental model:

Healthy controls
CKD patients

Human primary muscle cells



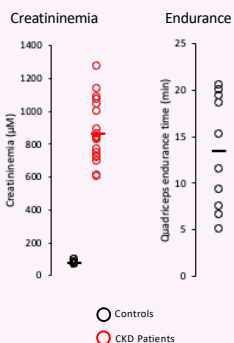
Primary muscle cells (3 days differentiation). Phase contrast microscopy (x80)

OBJECTIVES

The primary objective of this project is to study whether primary muscle cells from CKD patients display altered function or capacities.

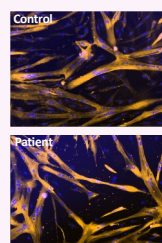
The second objective is the development of a standardized study protocol for primary muscle cells, combining recording of calcium response and contractile response to electric and chemical stimuli.

A. Clinical characteristics



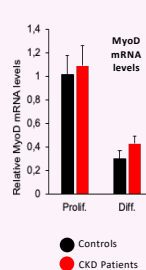
B. Morphological and biochemical assays

Immunofluorescence

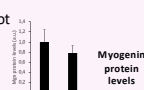


Primary muscle cells (3 days differentiation) MyosinHC (orange) and Hoechst (blue) staining - Epifluorescence microscopy (x100)

qRT-PCR



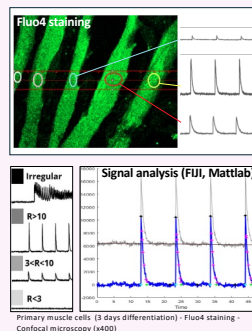
Western blot



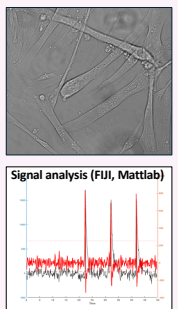
C. Functional assays (live microscopy)

Electric / Chemical stimulation

→ Calcium response



→ Contractile response



TASKS

- Characterize primary muscle **cell differentiation** in presence and in absence of various treatments
- Study **myokines** gene expression and secretion
- Characterize primary muscle cell **calcium response** and **contractile response**
- Set up a reproducible protocol enabling characterization of **primary muscle cell contractile capacities**

PREREQUISITES

- ✓ Interest in working with cellular models
- ✓ Skills in biochemistry and microscopy will be appreciated
- ✓ Candidate should be curious, precise, organised, autonomous
- ✓ Candidate should have an interest in the development of new techniques and protocols