Scientific programme

The objective of our group is to understand the **muscular pathophysiological mechanisms** involved in the development of chronic diseases (Chronic Obstructive Pulmonary Disease, COPD; type 2 diabetes), muscular dystrophies (FacioScapuloHumeral Dystrophy, FSHD; Duchenne Muscular Dystrophy, DMD) and iatrogenicity.

By an optimisation of the synergy between basic and applied research, the identification of new pathophysiological mechanisms will allow us to develop new therapeutical strategies.

Thus, the characterisation of the dysfunction (investigations at the whole body level, analyses at the cell level using muscle biopsy) and the identification of new molecular and cellular mechanisms (biochemical analyses on tissues, cellular and animal models) build a common experimental approach used by the group going from the patient to the cell.

Our research project is focussed on three axes:

- **Muscle differentiation and remodelling**: Chicken embryo and Ciona Intestinalis are both models used for investigating basic aspects of the differentiation and myofibrillogenesis respectively in smooth muscle and striated skeletal muscle. In smooth muscle, we will investigate mainly the role of Bone Morphogenetic Protein pathway as well as the involvement of the transcriptional factor Bapx1 in the gut smooth muscle differentiation and in the pathophysiology of gut diseases such as pyloric hypertrophic stenosis and Hirschsprung disease. In striated muscle, the identification of factors which control sarcomer and myofibril assembling (especially the role of GTPases Rho) will allow to study their role in the pathophysiology of type 2 diabetes and FSHD.

- **Chronic diseases**: We will study how the striated skeletal muscle may be involved in the pathophysiology of COPD and type 2 diabetes. COPD is characterised at the muscle level by an atrophy which is a good predictor of mortality. This myopathy is certainly multifactorial, in part subsequent to muscle deconditioning, but also related to a systemic inflammation. In addition, we have recently demonstrated the involvement of oxidative stress in this dysfunction and we are now investigating whether an alteration of the protein expression profile exists in COPD patients (especially some signs of proteasome modulation activity). Thus, regarding therapeutical strategy, we will associate to exercise training (which is admitted as an efficient but incomplete therapy) an antioxidant therapy.
Then, subsequent tests in vitro will be performed to focus on the ubiquitine/proteasome activity. In type 2 diabetes, we have demonstrated that fat oxidation is reduced and that skeletal muscle accumulates fat. We will specify the molecular mechanisms as well as their relationship with insulin resistance. From a therapeutic point of view, we plan to optimize training for improving fat oxidation in skeletal muscle and in cell cultures we will investigate the efficiency of pharmacological interventions such as inhibitors of fat transporters or modulators of adipogenesis.

Muscular dystrophies: Our group will focus on two muscular dystrophies: FSHD and DMD. The group has previously established, using a proteomic technique, the map of protein misregulation in FSHD. This analysis allowed us to suspect that a mitochondrial dysfunction or an oxidative stress could participate to the development and/or the course of this disease. We are now working on the validation of this hypothesis and this would allow to conduct therapeutic assays with antioxidants. Regarding the DMD, we will study the mechanisms involved in the improvement of muscle function and dystrophic process induced by training and NO donors such as L-Arginine with the objective to specify whether a potentialisation of training by L-Arginine may have a potential therapeutic interest.

Technology transfer, patents, licences
1-Detection, localisation and dosage of biological molecules separated on an area using the measure of a property or electric effect: N°15603, Collaborations AFM, CNRS and University of Montpellier 2
2-Cartography of electrophoresis gel by physical technique. N°2833082, Collaboration AFM, CNRS and University of Montpellier 2
3-Nur-re a response element which binds dimers of Nur nuclear receptors and method of use therefore. US patent N°6,852,538

Key words
Skeletal muscle, Gut smooth muscle, Diaphragm, Chronic diseases, Myopathies, Chronic Obstructive Pulmonary Disease, Type 2 diabetes, Duchenne Muscular Dystrophy, FacioScapuloHumeral Dystrophy, Oxidant stress, Myofibrillogenesis, Muscle differentiation, Muscle plasticity, Development, Stem cells, Iatrogenicity, Mechanical ventilation, Muscle biopsy, Proteomic, Therapies, Rehabilitation, Exercise, Nutrition.

Key publications