

* Synthetic summary of the thematic objectives of Challenge 3:

« Individual locomotion impacts autonomy, a key factor of human health and of special concern in the context of ageing. Preserving an active locomotor system as long as possible thus has a major influence on the quality of human life... To address the issue of individual mobility we consider that an integrative approach combining exploration of both the muscular system (development, metabolism, physical activity) and various intervening factors on locomotor apparatus and function (pain, nutrition, epigenetic, dysbiosis, chronic diseases) needs to be considered... The Scientific Research Challenge 3 is based on multidisciplinary approaches, strong public-private partnerships and aims at completing complementary objectives at the medical, technical, economic and social levels, which will allow a deeper understanding of the musculoskeletal system involved in mobility in both normal and pathological situations. With such a multimodal approach, it will define new models for sustainable living in good health, will help to prevent sedentary lifestyle and will allow designing treatments tailored to each individual...

Three main research actions will aim to acquire cutting-edge knowledge of the mechanisms driving or impeding individual mobility and to propose new therapeutic orientations:

- i) We will assess the metabolic responses to exercise and to nutritional and hormonal factors associated with reduced mobility in order to identify biomarkers of altered conditions of locomotion. Results will lead to the development of preventive and curative nutritional strategies-
- ii) Muscle development will be studied in both normal and pathological situations with a particular focus on programming stem cells for applications in regenerative medicine Genetic and epigenetic regulations controlling or affecting mobility will be investigated,
- iii) Pathophysiological mechanisms of pain and dysbiosis in inflammatory and painful diseases affecting mobility (chronic and metabolic diseases) will be assessed and new therapeutic targets will be identified and drugs and probiotics developed...

Moreover, *a health and social project* will be designed to optimize mobility and locomotor capacities during care and throughout life:

- i) Because a better consideration of mobility is likely to reduce morbidity and mortality, evaluations of locomotor capacities will be carried out in the hospital setting with physiologists, and the Clermont-Ferrand University Hospital and the Jean Perrin Cancer Centre will further work to optimize long-term physical activity and capacities for in- and out-patients. In addition, surveys of patient mobility at home will be performed using adapted sensors developed in association with Strategic Scientific Challenge 2.
- ii) In collaboration with the local administrative authorities, we will develop preventive actions and monitor the social impact of Strategic Scientific Challenge 3.