Dr PAUL GREGOREVIC

MUSCLE BIOLOGY AND THERAPEUTICS

Our research is focused on elucidating the mechanisms that regulate the development and adaptation of skeletal muscles, and developing novel interventions to combat the loss of skeletal muscle mass and function commonly associated heritable and acquired diseases, and the aging process.

Research Brief
Frailty associated with loss of skeletal muscle mass and strength is a leading cause of death among a significant proportion of the elderly population, and patients with a host of medical conditions. Impaired muscle function is also a predictor of incidence and severity of heart disease, diabetes and metabolic syndrome. The goal of the Laboratory for Muscle Research and Therapeutics is to understand the cellular mechanisms that regulate muscle growth, wasting and metabolism, so that we can develop new methods of preventing or treating the symptoms of muscle-related diseases. Our studies also examine these mechanisms in the context of cardiac adaptation, and disease.

The research places a particular emphasis on employing recombinant viral vectors designed and manufactured in-house as a means to selectively alter gene expression in mouse models, combined with established and cutting-edge techniques spanning the disciplines of biological/biomedical science. Employing the advantages of gene delivery technologies enables interrogation of the cellular mechanisms controlling muscle adaptation in vivo with a combination of speed, precision, and efficacy not attained using other approaches. Our expertise with gene delivery technologies is also transferable to the genetic manipulation of other tissues, as evident from Dr Gregorevic’s team providing custom-made viral vectors for >20 research teams world-wide to manipulate gene expression in skeletal, cardiac and smooth muscle; vasculature; hepatic, pancreatic, renal, reproductive and adipose tissues in the last 3 years.

Methodologies
• Design and in-house manufacture of recombinant viral vectors
• Mouse models of heritable and acquired neuromuscular disorders & muscle trauma
• In vivo administration of gene delivery technologies
• Functional assessment of skeletal muscle contractility in vitro, in situ, in vivo
• In vivo metabolic phenotyping
• Analysis of gene expression via Next Generation Sequencing
• Western blotting, histology/histochemistry, qRT-PCR, cell culture

Selected Publications
Recombinant viral vectors: Gene delivery tools for studying and treating muscle related diseases

Investigating the role of the Transforming Growth Factor-β (TGFβ) signalling network in health & disease