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**Invited talk: Exercise:
Understanding physiology and
molecular mechanisms – A pathway
to therapies**

Mark Hargreaves

*University of Melbourne, Melbourne,
VIC, Australia*

There is convincing epidemiological evidence that regular physical activity, including structured exercise, is associated with improved health outcomes. This appears to be partly related to the total exercise energy expenditure. Over the years, many physiologists have examined the integrative biology of exercise to better understand physiological responses to homeostatic challenges. These insights have often been used to identify the physiological limits of, and the optimal strategies to enhance, athletic performance. Increasingly, studies in exercise biology provide new ideas on the mechanisms by which exercise exerts its beneficial effects on health. With increased application of emerging techniques in molecular and cell biology, there is now even greater understanding of the molecular mechanisms underpinning the adaptive responses to acute and chronic exercise. This information has the potential to optimise exercise interventions and to identify novel therapeutic strategies, including potential “exercise mimetics”, although whether full recapitulation of exercise effects can be achieved by one, or several, pharmacological agents is debated. Another prospect emerging from the ‘omics’ era is greater understanding of the physiological and molecular bases of individual variation in responses to exercise. Although the technology remains ahead of the biology, analysis of the large data sets being generated from exercise studies may one day result in precision “exercise medicine” and a really personalised trainer.

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**Invited talk: Mapping complex
molecular networks underlying
exercise using global
phosphoproteomics**Nolan Hoffman^{1,2,*}, Benjamin L. Parker², Rima Chaudhuri², David E. James^{2,3}¹ *Mary MacKillop Institute for Health Research, Melbourne, VIC, Australia*² *Charles Perkins Centre, School of Life and Environmental Sciences, The University of Sydney, Sydney, NSW, Australia*³ *School of Medicine, The University of Sydney, Sydney, NSW, Australia*

Exercise is essential in regulating energy metabolism and remains the most promising therapy for obesity and type 2 diabetes. However, the intricate cellular signalling networks underlying tissue responses to exercise-stimulated metabolic and mechanical stress are not fully understood. Global, unbiased discovery approaches are warranted to map these complex, interconnected molecular networks that promote the systemic health benefits of exercise.

Protein phosphorylation is central to a range of exercise-induced tissue adaptations including regulation of skeletal muscle metabolism and contraction. Therefore, we previously undertook a global mass spectrometry-based phosphoproteomic analysis comparing human skeletal muscle biopsies before and after a high-intensity exercise bout [1]. This revealed over 1000 exercise-regulated phosphorylation sites on over 500 proteins, including a majority of kinases and phosphites never previously implicated in exercise signalling. Furthermore, novel exercise-regulated substrates of the energy-sensing AMP-activated protein kinase (AMPK) were uncovered using this global approach. Ongoing studies will be discussed that are aimed at determining how components of the acute exercise signalling network are impacted by skeletal muscle contraction and nutrient availability.

Collectively, multidisciplinary global phosphoproteomics and targeted physiological approaches have led to the discovery of exercise biological targets and new roles for kinases such as AMPK. This rapidly expanding frontier in understanding the molecular underpinnings of exercise will aid development of therapeutic strategies to improve human health and target obesity-related pathophysiology.