UNIVERSITY OF LIMERICK, IRELAND

FACULTY OF EDUCATION AND HEALTH SCIENCES

IRCSET PhD Research Scholarship Project

An *In Vivo* Microdialysis Study of Skeletal Muscle Response to Exercise and Nutrient Intake in Humans.

Candidates interested in being put forward for an IRCSET PhD Scholarship to progress this 3y PhD programme of research should contact either Professor Dick FitzGerald (dick.fitzgerald@ul.ie) or Professor Phil Jakeman (phil.jakeman@ul.ie)

Deadline for application is Feb 8th 2010

Brief Outline of Project Proposal follows

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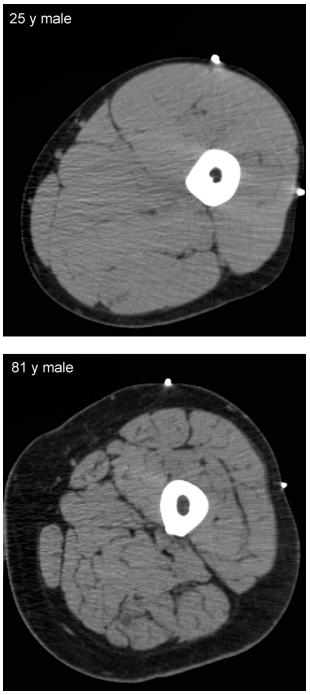
An *In Vivo* Microdialysis Study of Skeletal Muscle Response to Exercise and Nutrient Intake in Humans.

The plasticity of human skeletal muscle is well documented. Skeletal muscle can increase in size (hypertrophy) in response to physical activity (e.g. resistance training), a process that can be enhanced by appropriately timed nutrient (protein) intake. Equally, skeletal muscle can reduce in size (atrophy) by disuse or through the venerable process of aging (age-related sarcopenia). Sarcopenia is a progressive, insidious process characterized by 3–8% reduction in lean muscle mass per decade after the age of 30 years (see MRI image on left). It is thought to affect 30% of individuals over 60 years of age and more than 50% of those over 80 years. Research on the mechanisms contributing to sarcopenia includes studies focusing on protein metabolism and cell signalling, voluntary or imposed reductions in physical activity, protein energy malnutrition and reduced anabolic efficiency to protein ingestion. Relevant to sporting performance and sarcopenia, nutrient regulation of skeletal muscle metabolism is an exciting field of study. Researchers in the Department of Physical Education and Sport Sciences @ UL have a well-cited track record in the study of the acute and chronic effect of exercise on skeletal muscle function, adaptation and metabolism. Grant funding from The Wellcome Trust, Enterprise Ireland, Embark (IRCSET) and a recent Research Enhancement Grant to Food and Health @UL fuels the research initiative in this area.



The Proteins and Peptides Group located in the Department of Life Sciences is funded from various sources including: the Higher Education Authority Programme for Research in Third Level Institutions, Enterprise Ireland & industry through the Food for Health Ireland initiative, IRCSET, Department of Agriculture Fisheries and Food and the Marine Institute.

Project Description

This project focuses on the role of dietary protein, the type, amount and timing of protein intake to preserve skeletal muscle mass and hence the prevention and/or management of sarcopenia. We are looking to profile the regulatory amino acid and peptide content (Cohen and Hall, 2009) of dialysate of the interstitium of skeletal muscle sampled by *in vivo* microdialysis.

BACKGROUND: Resistance exercise exerts a contractile force sufficient to induce a change in protein and amino acid turnover in skeletal muscle. In brief, protein catabolism is increased and anabolism suppressed *during* the exercise bout with post-exercise feeding determining the magnitude and direction of post-exercise protein turnover. If non-fed then skeletal muscle protein catabolism remains elevated and anabolism suppressed, the net effect being catabolic to muscle. If fed then anabolic processes predominate and net anabolism or increased muscle protein synthesis (MPS) ensues for approximately 2-3h. Essential amino acids are potent regulators of MPS in the post-exercise phase, non essential amino acids having little or no effect. Insulin-like growth factors (IGFs) and related peptides act to promote muscle protein synthesis. The circulating concentration of IGFs is modified by nutrient feeding, but the effect

of a change in circulating IGFs on muscle interstitial concentration of IGF is unknown. Within skeletal muscle IGFs act in synergy with essential amino acids to promote muscle protein synthesis.

AIMS: The aim of this study is to utilize *in vivo* microdialysis to investigate the changes in interstitial concentration of essential amino acids and regulatory peptides of muscle protein synthesis following resistance exercise with and without feeding a soluble whey protein optimised to provide a nutrient supply to skeletal muscle. In this work we build upon our previous studies of the bioavailability of key regulatory amino acids following whey protein feeding (Power, Jakeman & Hallihan., 2009) and microdialysis of amino acids (McCormac, Jakeman *et al*, *in press*) regulatory growth factors (Berg, *et al*, 2006) following resistance exercise. The approach is to utilise the discriminatory properties of a 20kDa and 100 kDa microdialysis catheter to measure changes in the skeletal muscle metabolites such as amino acids and regulatory peptides in response to exercise and nutrient feeding. A preliminary analysis of the microdialysate peptide/protein content has provided information on the range and approximate molecular mass of the high abundance peptides/proteins present (see below,

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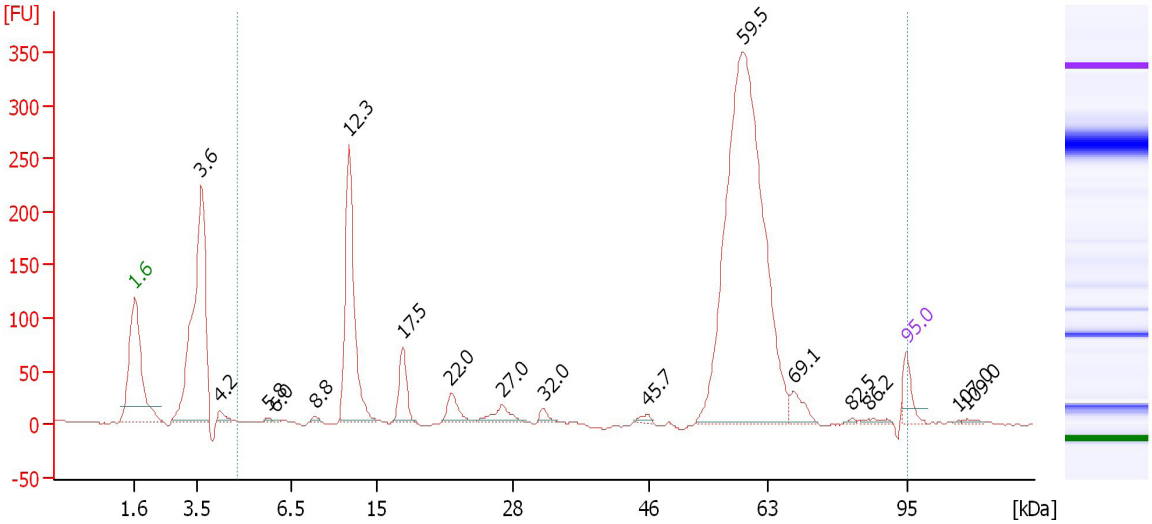

RESEARCH MILESTONES: Three research milestones have been identified:

1. separation of amino acid and peptide fractions contained within microdialysates of human skeletal muscle by UPLC;
2. analysis/identification of selected components of the microdialysate peptide fraction by LC-MS/MS;
3. application of 1&2 above to the study of skeletal muscle response to nutrient feeding with and without resistance exercise.

The latter two milestones are expected to occur following the PhD confirmation process.

METHODS OF RESEARCH: The main techniques to be used in this research are *in vivo* microdialysis along with UPLC and LC-MS located within the research laboratories of the principal investigators..

COLLABORATION: Post-graduate researcher to receiving IRCSET scholarship funding (http://www.ircset.ie/Default.aspx?tabid=68). The student appointed will work in close collaboration with researchers within the two departments. The principal researchers also maintain collaborative links with other Universities within and outside of Ireland and

opportunities may arise for the student to visit/work in these laboratories should the need arise.

References:

Berg U, Gustafsson T, Sundberg CJ, Carlsson-Skwirut C, Hall K, Jakeman P and Bang P. Local changes in the insulin-like growth factor system in human skeletal muscle assessed by microdialysis and arterio-venous difference technique. *Growth Hormone and IGF Research,* 2006;16(4): 217-224.

Cohen A and Hall MN. An amino acid shuffle activates mTORC1. *Cell,* 2009;136: 399-400.

Power O, Jakeman P & Hallihan A. Human insulinotropic response to oral ingestion of native and hydrolysed whey protein. *Amino Acids*. 2009:37(2):333-9.

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