Our research is focussed on understanding cellular and molecular mechanisms associated with obesity and type 2 diabetes. Our team performs studies in cell based systems and animals in order to have an integrative view of metabolic dysfunction linked to obesity and diabetes.

**Research Brief**

Our research is focused on identifying genes/proteins that are important in pathways that may impair insulin action and then to develop pharmaceutical therapies that either activate or block the pathway of interest. We currently have two such candidates. Together with N-Gene Pharmaceuticals we have developed a drug (BGP-15) currently in a multi-centre clinical trial for type 2 diabetes (see Chung et al. PNAS 2008). In addition, in a paper published in 2012 (Gehrig et al. Nature 2012) we showed that this drug has pre-clinical efficacy for the treatment of Duchenne Muscular Dystrophy and we are about to commence human clinical trials in this disease. In addition, based on our previous work targeting the IL-6 family of cytokines (see Carey et al. Diabetes 2006; Watt et al. Nat Med. 2006) we have developed another peptide in pre-clinical development.

**Methodologies**

- Mouse Metabolic phenotyping
- Euglycemic Hyperinsulinemic clamps in conscious mice
- In vivo electroporation
- qRT-PCR, Northerns, Westerns, immunoprecipitation, kinase assays, cell culture

**Selected Publications**

**Concept of Myokines** *(from Pedersen & Febbraio Nat Rev Endo, 2012)*

- Myokines are cytokines or other peptides that are produced, expressed and released by muscle fibres
- Myokines may exert autocrine, paracrine or endocrine effects
- Myokines may balance and counteract the effects of adipokines
- The muscle–cell secretome consists of several hundred secreted products
- Identified myokines include myostatin, LIF, IL-6, IL-7, BDNF, IGF-1, FGF-2, FSTL-1 and irisin

**The drug BGP-15 can activate HSP72 and improve the pathology associated with Duchenne Muscular Dystrophy** *(from Gehrig et al. Nature 2012)*

![Images showing the effects of BGP-15 on muscle tissue]

- UCP-1
- Lipolysis
- IL-6
- IRF
- Follistatin
- Hepatic glucose production during exercise
- Hepatic CXCL-1 production
- Promotes endothelial function and revascularization
- GLP-1 to increase Insulin secretion