

PhD Student **Ole Emil Andersen, MD**

**Place of enrolment:** Aarhus University, Faculty of Health

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**Title of project:** The Metabolic Effects of  $\beta$ -hydroxybutyrate on Working Skeletal Muscle

## **ABSTRACT**

### *Background:*

Skeletal muscle mitochondria deteriorates during ageing which possibly leads to impaired muscle insulin sensitivity and fitness. Recently, ingestion of the ketone body  $\beta$ -hydroxybutyrate (BHB), has been shown to enhance metabolic efficiency in the working heart muscle through improved mitochondria substrate metabolism. It is not clear whether similar beneficial effects of BHB occur in skeletal muscle.

### *Aim:*

To establish the effects of BHB on muscular fatigue, mitochondrial function, and functional capacity of working skeletal muscles.

### *Methods:*

We composed the project of three studies: 1) An *in vitro* rodent study where we determine how acute incubation and dietary supplementation with BHB affect fatigue, muscle excitability, and gene expression of proteins related to glucose, ketone and fat metabolism in isolated rat muscles. 2) A  $^{31}\text{P}$ -MRS human study where we employ non-invasive scans to evaluate the effects of BHB infusion on metabolic efficiency, mitochondrial function (maximal oxidative capacity), and intramyocellular pH in the working *tibialis anterior* muscle of young and elderly subjects matched by physical activity. 3) A human exercise study where we assess functional capacity following acute ketone ester ingestion in prediabetics and physically active subjects on a cycle ergometer.

### *Perspectives:*

The proposed project will provide valuable insight into ketone metabolism in skeletal muscle with the potential to establish novel dietary strategies for prevention and treatment of age- or diabetes-related metabolic deficiencies. Further, this projects diverse methodologies and requirements for interdisciplinary collaborations provides a strong foundation for a PhD-project.