

## OBJECTIVES

The present thesis investigated mechanisms underlying the impaired blood flow to contracting skeletal muscle with aging and the effects of exercise training on regulation of blood flow and functional sympatholysis in young and older healthy male subjects.

### Specific aims and hypothesis:

Paper I:

Aim: to evaluate the effect of inhibiting the main enzyme involved in cGMP degradation, PDE5, on blood flow and O<sub>2</sub> delivery in contracting skeletal muscle of young and older men.

Hypothesis: potentiation of cGMP signaling would increase blood flow, O<sub>2</sub> delivery and O<sub>2</sub> uptake in contracting skeletal muscle of older but not young human subjects during submaximal exercise engaging a small muscle mass.

Paper II:

Aim: to determine whether the increase in exercise hyperemia with potentiation of cGMP signaling (paper I) was associated with an improved functional sympatholysis and/or improved efficacy of local vasodilator pathways in older men during exercise engaging a small muscle mass.

Hypothesis: potentiation of cGMP signaling would increase circulating ATP levels and improve functional sympatholysis in the exercising leg of older men.

Paper III:

Aim: to examine training-induced adaptations in the regulation of skeletal muscle blood flow and oxidative metabolism during submaximal exercise engaging a small muscle mass in older men.

Hypothesis: potentiation of cGMP signaling would increase blood flow and O<sub>2</sub> uptake in contracting skeletal muscle during exercise in older but not in young subjects before training, and that a period of exercise training would improve cGMP signaling so that the effect of potentiating cGMP signaling would be diminished.

Paper IV:

Aim: to examine effects of exercise training on  $\alpha$ -adrenergic responsiveness and functional sympatholysis in young and older habitually active men.

Hypothesis: eight weeks of exercise training would improve functional sympatholysis during knee-extensor exercise and lower  $\alpha$ -adrenergic responsiveness in the resting leg in both groups.