

Overall research theme:

Hypoxic dilation of coronary arteries - possible mechanisms

Latest update:

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Characteristics of the research group:

Interdisciplinary: cardiology (OF), basic vascular research (US) and endocrinology (CHG).

Running projects: Titles and abstracts:

Hypoxic dilation of coronary arteries - possible mechanisms

Coronary artery dilatation to hypoxia is an important protective response that increases flow to endangered myocardium. The mechanisms triggering hypoxic dilatation are unknown. With novel methodologies, in part developed by our group, our aim is to investigate four possible mechanisms of hypoxic vasodilatation that may act in concert:

1. An energy limitation mechanism.
2. Phosphorylation of heat shock protein 20 as an alternative to myosin light chain phosphorylation.
3. Endogenous production of the potent vasodilator adenosine.
4. Altered liberation of endothelial vasoactive substances (NO, prostacyclin, endothelin-1).

All studies are performed on left anterior descending coronary arteries from hogs obtained at a local slaughterhouse. The arteries are investigated as intact cylindrical segments in a pressure myograph. The experimental set-up allows control of transmural pressure and longitudinal length while artery diameter is automatically determined by video imaging. A microdialysis catheter is placed in the smooth muscle interstitium of the coronary artery mounted in the pressure myograph. The minute amounts of dialysate challenge the analytical accuracy and have resulted in extensive international collaboration. The study perspective is to increase the understanding of the processes involved in regulation of coronary artery tone during myocardial ischemia.

Recent publications related to the projects described above:

Frøbert O., Gregersen H., Bjerre J., Bagger J.P., Kassab G.S.: Relation between zero-stress state and branching order of porcine left coronary arterial tree. *American Journal of Physiology*, 1998, 275: H2283-H2290.

Frøbert O., Mikkelsen E.O., Bagger J.P.: The influence of transmural pressure and longitudinal stretch on K^+ - and Ca^{2+} - induced coronary artery constriction. *Acta Physiologica Scandinavica*, 1999, 165: 379-385.

Tanko L.B., Simonsen U., Frøbert O., Bagger J.P., Gregersen H., Mikkelsen E.O.: Vascular reactivity to nifedipine and Ca^{2+} in vitro: the role of preactivation, wall tension and geometry. *European Journal of Pharmacology*, 2000, 387: 303-312.

Tanko L.B., Simonsen U., Matrougui K., Gregersen H., Frøbert O., Bagger J.P., Mikkelsen E.O.: Axial stretch modifies contractility of porcine coronary arteries by a protein kinase C-dependent mechanism. *Pharmacology & Toxicology*, 2001, 88: 89-97.

Frøbert O., Mikkelsen E.O., Bagger J.P., Gravholt C.H.: Measurement of interstitial lactate during hypoxia-induced dilatation in isolated pressurised porcine coronary arteries. *Journal of Physiology*, London, 2002, 539: 277-284.