

# Pig models of early-stage cardiovascular disease

Malene Muusfeldt Birck, PhD thesis 2011

According to the World Health Organization, cardiovascular disease (CVD) is the leading cause of death worldwide. This PhD thesis focuses on atherosclerosis, which is an important contributor to the growing burden of CVD. In order to reduce the number of people suffering from atherosclerosis, risk factors that may initiate and progress atherosclerosis have been identified. Conventional risk factors such as smoking, hypertension, diabetes, obesity and hypercholesterolemia are not the only factors that can contribute to the development of atherosclerosis which can then cause CVD. Inflammation has been shown to play an important role in the development of atherosclerosis and this has increased the focus on infection as a possible risk factor. In early life, infection often causes inflammation and, hence, infection may have an impact on the initiation of atherosclerosis.

The aim of this PhD project was to develop a pig model with endothelial dysfunction and early atherosclerosis lesions based upon infection-induced inflammation.

The results are presented in three articles:

– **Infection-induced coronary dysfunction and systemic inflammation in piglets are dampened in hypercholesterolemic milieu**

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– **Intimal changes in the coronary artery of infected hypercholesterolemic minipigs**

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– **A novel method for trans-uterine identification of piglets**

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The thesis substantiates that the pig is a good animal model for atherosclerosis research.

The results show that repeated infection is associated with endothelial dysfunction and that the degree of impairment is related to the pathogen burden. Hypercholesterolemia seems to modulate the infection-induced inflammatory response, reducing inflammation and lessening severe dysfunction. In the morphological study, the combination of hypercholesterolemia and infection seemed to speed up atherogenesis as increased numbers of foam cells were present in the subendothelial space of infected animals, compared to non-infected animals fed a cholesterol diet. Infection was also associated with increased endothelial cell death and degenerative changes. Further studies are needed to take a closer look at the interaction between infection, inflammation and altered lipid metabolism and its role in atherogenesis. In addition, the somewhat contradictory findings between the functional and the morphological studies deserve further investigation.

This thesis has shed light on some new aspects of atherosclerosis and also stresses the importance of applying preventive measures early in life. The results reveal new and interesting knowledge about the dynamics of infection-induced inflammation, hypercholesterolemia and endothelial dysfunction and should hopefully encourage additional studies about this topic.

Two additional articles based on this PhD project have been published:

– **Expression studies of the obesity candidate gene FTO in pig.**

M. B. Madsen, M. M. Birck, M. Fredholm, S. Cirera (2010) *Biotechnol.* Vol. 21 (1), 51-63

– **Expression profile of miR-122 and its target CAT-1 in high-cholesterol fed minipigs (*Sus scrofa*)**

S. Cirera, M. M. Birck, P. K. Busk, M. Fredholm (2010) *Comparative Medicine* Vol. 60 (2), 136-141.