**Subacute endotoxemia: a molecular study to understand the pathogenesis of -cell dysfunction and impaired insulin sensitivity in cats**

**Summary / Zusammenfassung**

This project is part of the studies performed by the Diabetes Research Group which is a joint appointment between the Clinic for Small Animal Internal Medicine (Prof. Dr. Claudia Reusch), the Institute for Veterinary Physiology (Prof. Dr. Thomas Lutz) and the Institute of Virology (Prof. Dr. Mathias Ackermann).

Diabetes mellitus is the most frequently diagnosed endocrinopathy in cats. It is generally accepted that impaired insulin secretion by pancreatic -cells and reduced insulin sensitivity of muscle, liver and adipose tissue are important factors in the development and progression of diabetes mellitus. Obesity and diabetes are characterized by a state of chronic low-grade inflammation. The activation of inflammatory signaling pathways in these states is causally linked to insulin resistance and to the impairment of β-cell function. However, insulin resistance is also a common disorder in acute inflammatory settings. Proinflammatory cytokines are also believed to be implicated in the pathophysiology of insulin resistance in any disease associated with inflammatory conditions. Cytokines also modify insulin secretion by pancreatic -cells in experimental models.

The aim of this project is to clarify whether low-grade induced inflammation and activation of the innate immune system in cats are involved in impaired β-cell function and insulin sensitivity, and whether inflammatory cytokines play a primary role in glucose metabolism in this species. We wish to clarify some of the functional effects and molecular aspects of subacute endotoxemia as a potential primary cause of the insurgence of insulin resistance and diabetes mellitus in cats. Using our established model of chronic IV infusions in cats (e.g., to model chronic hyperglycemia), cats are chronically infused with lipopolysaccharide. β-cell function (fasting insulin level, arginine stimulation test) and peripheral insulin sensitivity (intravenous glucose tolerance test) are assessed. Tissue biopsies (i.e. pancreas, omental and subcutaneous adipose tissue and skeletal muscle) are used to determine specific mRNA expression profiles and the respective protein abundances (e.g. adiponectin, PPARγ, IL-6, IL-8, MCP-1, TLRs). In addition, macrophages and neutrophils are quantified in tissue sections of pancreatic islets and adipose tissue. Circulating factors (adiponectin, insulin, IL-6, IL8, TNFα and FA) will be determined in serum.

We believe that our model will be of general benefit to understand the relationship between chronic inflammation and metabolic changes in animals and humans.

**Publications / Publikationen**


**Keywords / Suchbegriffe**
cat; infection; LPS; insulin resistance; diabetes mellitus

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