

## 7 Summary

### **The bovine corpus luteum as an model for Angiogenesis, Anti-Angiogenesis and vascular regression**

The bovine corpus luteum is an excellent model for controlled vascular development and regression. The aim of this study was to examine the pattern of blood vessel growth and regression during the development and luteolysis of the corpus luteum. A potential coherence between the morphometric results and factors involved in angiogenesis, namely VEGF, VEGF-R2 and Ang-2 should be pointed out.

Each step of angiogenesis and particularly anti-angiogenesis should be documented with regard to vascular density and apoptosis. 47 bovine corpora lutea from different stages of the oestrous cycle were examined by light- and electron-microscopy, lectin histochemistry, immunohistochemistry and TUNEL-Test. An important result of this study was that the corpus hemorrhagicum could be divided into three zones: the central zone of the developing corpus luteum consisting of erythrocytes and fibrin; the outer zone characterized by erythrocytes, connective tissue and VEGF-positive macrophages which might stimulate migration and proliferation of endothelial cells during early luteal angiogenesis. In the early and late regressing corpus luteum many macrophages could be observed which might be responsible for the programmed cell death of endothelial cells.

The most important result of the present study was that during late luteal regression a new angiogenic phase sets in. A moderate increase of capillaries becomes obvious and the VEGF-immunolabelling is high during late regression. It is possible that the new angiogenic phase in the regressing corpus luteum is not only important for regression of the corpus luteum but also for the development of the corpus luteum of the following cycle.

The results of this study show further more an increase of capillaries and blood vessel lumina in stadium 10 of the corpus albicans. Therefore it may be that the corpus albicans is organized from the outer to the inner zone.

For the first time VEGF-R2 and Ang-2 could be shown in vascular smooth muscle cells of the bovine corpus luteum indicating that these two factors are important mitogens for vascular smooth muscle cells in the bovine ovary.

Ultrastructural analysis shows that the obliteration of blood vessels by cells causes a reduction of blood flow which might trigger programmed cell death of luteal endothelial cells.

Another important result of this study was that high-performance cows show a more intensive luteal angiogenesis than other cows. This may indicate that ovarian dysfunctions in these animals are the result of an increased angiogenesis or a defect of anti-angiogenesis.