

## 1.1 ABSTRACT

### **Extracellular matrix proteins in hereditary melanoma of the MeLiM miniature pig**

Malignant melanoma is one of the most aggressive skin tumours and also the most frequent cause of death in these diseases. Its incidence has increased in white populations worldwide about 4% per year during last decades. Melanoma is curable in 95% of patients if detected early. However, metastatic melanoma is usually lethal. The MeLiM (Melanoma-bearing Libečov minipigs) strain of miniature pigs with hereditary malignant melanoma (established at the Institute of Animal Physiology and Genetics, the Academy of Sciences of the Czech Republic in Liběčov) is an suitable animal model for study. Multiple skin tumours already appear at birth or they develop shortly thereafter. About one third of affected piglets die during the first 2 months of age due to melanoma progression and organ metastases. Spontaneous regression of melanoma is found in other animals. Numerous biochemical and histopathological similarities with human melanoma were found in this model.

The aim of this work was to complete missing information about extracellular matrix proteins, adhesive molecules as well as matrix metalloproteinases and to accomplish basic monitoring of these proteins using immunological techniques. Expression and localization of chosen proteins was observed in progressing and spontaneously regressing melanomas. Expression of alpha6 and beta4 subunits of integrin, alphaVbeta 3 integrin, fibronectin, collagen IV, laminin, tenascin C and MMP-2 was found in blood vessels of progressing melanomas where they probably participate in tumour neoangiogenesis. High expression of tenascin C, fibronectin and MMP-2 as well as localization of laminin and collagen IV in connective sheaths of blood vessels suggest that progressing porcine melanoma is very similar to human melanoma. The first signs of spontaneous regression were observed since the 6<sup>th</sup> week of age. Increased collagen IV expression, decreased tenascin C expression and disappearance of both fibronectin and MMP-2 found during this process are probably related to remodelling of melanoma into the fibrous tissue.

Ascertained results extend information about malignant melanoma in minipig of the MeLiM strain found up to now for farther interesting aspects. They

show its considerable resemblance of human melanoma thus confirming suitability of the MeLiM model for study of this cancer disease.

**Key words**

**Melanoma, MeLiM, spontaneous regression, immunohistochemistry, alfa6 subunit of integrin, beta4 subunit of integrin, alfaVbeta3 integrin, fibronectin, collagen IV, laminin, tenascin C, MMP-2**