



**Karolinska  
Institutet**

**Institutionen för Onkologi och Patologi**

# Assessment of prognostic markers in benign and malignant melanocytic tumours.

## AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska Institutet  
offentligen försvaras i den lilla föreläsningssalen 1tr, Astrid Lindgrens  
Sjukhus, Solna

**Fredagen den 9 december 2011, kl. 9:15**

**av Vitalijs Svjatoha**

MD, MSc.

*Huvudhandledare:*

Docent Edneia Tani  
Institutionen för Onkologi och Patologi  
Karolinska Institutet

*Fakultetsopponent:*

Prof. Christian Ingvar  
Kliniska vetenskaper  
Lunds Universitet

*Bihandledare:*

Prof. Lamber Skoog  
Institutionen för Onkologi och Patologi  
Karolinska Institutet

*Betygsnämnd:*

Prof. Erik Larsson  
Institution för Immunologi, Genetik och  
Patologi  
Uppsala Universitet

Prof. Anders Hjerpe  
Institution för Laboratoriemedicin  
Karolinska Institutet

Docent Giuseppe Masucci  
Institutionen för Onkologi och Patologi  
Karolinska Institutet

**Stockholm 2011**

## **Abstracts.**

Cutaneous melanoma is a malignant tumour that arises from pigmented skin cells – melanocytes, represents the most rapidly increasing cancer worldwide which is causing significant public health problem. During the past decade a significant progress has been made in the understanding of genesis and progression of melanocytic lesions. However treatment of malignant melanomas is in a majority of cases limited to surgical excision of the primary tumours or metastases. In advanced metastatic disease there are few treatment options. The present thesis reviews current knowledge on epidemiology, ethiology, pathology and treatment options of the benign and malignant melanocytic tumours and concentrates on the analysis of several molecules that are thought to play a role in the processes of cell growth, apoptosis, division, motility and adhesion as well as regulation of cytoskeletal components, protein phosphorylation, cell-cycle and cell survival. Archival material from fine needle aspirates as well as formalin-fixed tumour tissue was used in the study. Primary benign and malignant melanocytic tumours as well as metastatic melanomas were included in the study. The expression of the following proteins in malignant and benign melanocytic tumours was analyzed: S100, CD40, CD44, Bcl-2, Ki-67, COX-2 and HSP90. The expression patterns of the proteins were correlated to pathomorphological properties of the tumours as well as clinical parameters. Moreover, a presence of the BRAF gene mutation V600 has been analyzed in metastases from malignant melanomas. We found that melanocytic tumours are heterogeneous in respect to expression of the analyzed proteins as well as mutational status. Analysis of biomarkers and genetic aberrations might therefore be of importance for predicting the biological behaviour of the tumours. The results of the study are discussed in the light of eventual prognostic, diagnostic and therapeutic application of the analyzed proteins and mutational status.