

1.5 Scope of this thesis

This study is supposed to elucidate the role of phospholipase D in differentiation and apoptosis of epidermal cells. The comprehension of the expression, regulation and function of phospholipase D in these cellular processes may provide new aspects of therapy in diseases established by aberrance of these processes. One hyperproliferative disease of the skin is *psoriasis vulgaris*. Previously, HaCaT cells as a model for basal keratinocytes were reported to express phospholipase D1b and phospholipase D2. Growth hormones often act via receptor tyrosine kinases and phospholipase D may be activated by mechanisms involving tyrosine phosphorylation. Therefore, phosphorylation of phospholipase D1 in HaCaT cells shall be investigated using the antibody α NChPLD1 and a specific assay of phospholipase D1 activity. Deficient differentiation can be another cause of hyperproliferation. Differentiation and apoptosis of keratinocytes share several features. For instance, in both processes ceramide levels greatly increase and a cornified envelope is formed. In the leukaemia cell line HL60 differentiation was accompanied by an increase of phospholipase D1 expression. Thus, the expression of phospholipase D and of several differentiation-associated genes in ceramide-treated HaCaT keratinocytes shall be examined using polymerase chain reaction based methods.

Malignant melanoma is a serious cancerous neoplasm of pigment forming cells, melanocytes and nevus cells. The great metastatic potential of malignant melanoma is the reason for its bad prognosis. Phospholipase D is involved in proliferation and apoptosis which are key features of tumour progression. Moreover, its role in cytoskeletal reorganisation which is a major aspect of metastatic deformation makes it a most interesting target. The expression and regulatory properties of phospholipase D in diverse cell lines derived from malignant melanoma shall be investigated on transcriptional, translational and activity level. Possible distinctions between melanocytes and melanoma cells as well as within melanoma cells of different origin shall be described. The influence of therapeutic intervention for the treatment of malignant melanoma shall be characterised in respect of their influence on phospholipase D. In this regard, monomeric G-proteins as regulatory proteins of phospholipase D activity are of interest.