Psoriasin (S100A7), a member of the S100 family of calcium-binding proteins, is highly expressed in high-grade ductal carcinoma in situ (DCIS) and in the benign hyperproliferative skin disorder psoriasis. Both breast cancer and psoriasis are diseases which are characterized by hyperproliferation and a disturbed differentiation of the epithelial cells as well as a pronounced angiogenesis. The potential role of psoriasin in angiogenesis and the epithelial cell differentiation remain unclear. The aim of this thesis was to investigate the cellular effects of psoriasin in angiogenesis and the differentiation processes, with special emphasis on breast cancer and psoriasis.

We found that psoriasin expression was induced in mammary epithelial cells and keratinocytes by oxidative stress. Psoriasin expression was shown to induce vascular endothelial growth factor (VEGF) expression and several other pro-angiogenic factors in epithelial cells. Upon down-regulation of psoriasin, H2O2-induced expression of VEGF was decreased as well as the pro-angiogenic factors heparin-binding EGF-like growth factor (HB-EGF) and matrix metalloproteinase (MMP)-1. Extracellular psoriasin contributed to the subsequent induction of proliferation, migration and tube formation of endothelial cells. The proliferative effect of psoriasin was shown to be mediated by the receptor for advanced glycation end products (RAGE). Furthermore, psoriasin induced reactive oxygen species (ROS) in both endothelial and epithelial cells through the action of RAGE, and contributed to the expression of the pro-angiogenic factors in endothelial cells.

The expression of psoriasin was up-regulated in mammary epithelial cells and keratinocytes in response to differentiation-inducing stimuli and was shown to be regulated by pathways involved in epithelial cell differentiation. Upon psoriasin down-regulation the shift towards a more differentiated CD24+-phenotype of mammary epithelial cells was abolished. Furthermore, the expression of the differentiation markers involucrin, desmoglein 1, transglutaminase 1 and CD24 was decreased in keratinocytes upon down-regulation of psoriasin expression. In vivo we demonstrated a gradient of psoriasin expression in the psoriatic epidermis, with intense expression in the suprabasal differentiated layers, and a similar staining pattern between psoriasin and the differentiation marker CD24 in DCIS tumors.

In conclusion, our findings describe psoriasin as a mediator in the angiogenic process and a contributor of epithelial cell differentiation. Consequently, psoriasin is possibly a contributor to the development and progression of breast cancer and psoriasis and a potential target in the treatment of these diseases.
Psoriasin (S100A7), a member of the S100 family of calcium-binding proteins, is highly expressed in high-grade ductal carcinoma in situ (DCIS) and in the benign hyperproliferative skin disorder psoriasis. Both breast cancer and psoriasis are diseases which are characterized by hyperproliferation and a disturbed differentiation of the epithelial cells as well as a pronounced angiogenesis. The potential role of psoriasin in angiogenesis and the epithelial cell differentiation remain unclear. The aim of this thesis was to investigate the cellular effects of psoriasin in angiogenesis and the differentiation processes, with special emphasis on breast cancer and psoriasis.

We found that psoriasin expression was induced in mammary epithelial cells and keratinocytes by oxidative stress. Psoriasin expression was shown to induce vascular endothelial growth factor (VEGF) expression and several other pro-angiogenic factors in epithelial cells. Upon down-regulation of psoriasin, H2O2-induced expression of VEGF was decreased as well as the pro-angiogenic factors heparin-binding EGF-like growth factor (HB-EGF) and matrix metalloproteinase (MMP)-1. Extracellular psoriasin contributed to the subsequent induction of proliferation, migration and tube formation of endothelial cells. The proliferative effect of psoriasin was shown to be mediated by the receptor for advanced glycation end products (RAGE). Furthermore, psoriasin induced reactive oxygen species (ROS) in both endothelial and epithelial cells through the action of RAGE, and contributed to the expression of the pro-angiogenic factors in endothelial cells.

The expression of psoriasin was up-regulated in mammary epithelial cells and keratinocytes in response to differentiation-inducing stimuli and was shown to be regulated by pathways involved in epithelial cell differentiation. Upon psoriasin down-regulation the shift towards a more differentiated CD24-phenotype of mammary epithelial cells was abolished. Furthermore, the expression of the differentiation markers involucrin, desmoglein 1, transglutaminase 1 and CD24 was decreased in keratinocytes upon down-regulation of psoriasin expression. In vivo we demonstrated a gradient of psoriasin expression in the psoriatic epidermis, with intense expression in the suprabasal differentiated layers, and a similar staining pattern between psoriasin and the differentiation marker CD24 in DCIS tumors.

In conclusion, our findings describe psoriasin as a mediator in the angiogenic process and a contributor of epithelial cell differentiation. Consequently, psoriasin is possibly a contributor to the development and progression of breast cancer and psoriasis and a potential target in the treatment of these diseases.