

Molecular Markers for Progression of Squamous Cell Carcinoma of the Skin

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Atte Kivisaari defended his PhD thesis in Turku, Finland, on 27 January 2012. The thesis was supervised by Professor Veli-Matti Kähäri, Department of Dermatology and Venereology, University of Turku and Turku University Hospital, Finland. The opponent was Associate Professor Kaisa Tasanen-Määttä, Department of Dermatology, University of Oulu and Oulu University Hospital, Oulu, Finland. The thesis is available at: <http://www.doria.fi/handle/10024/73890>.

The incidence of non-melanoma skin cancer (NMSC) is increasing. Ultraviolet (UV) light is a major risk factor for the development of cutaneous squamous cell carcinoma (SCC). Cutaneous SCCs that develop to chronic ulcers are known to progress and metastasize more easily than UV-induced SCCs. Matrix metalloproteinases (MMPs) are a group of proteolytic enzymes that are thought to have a role in cancer growth and invasion.

The molecular background for progression of cutaneous SCC was examined by immunohistochemistry (IHC) using tissue samples of recessive dystrophic epidermolysis bullosa (RDEB)-associated SCC, sporadic UV-induced SCC, and SCC precursors. IHC studies using tissue microarray (TMA) technique revealed overexpression of MMP-7 and MMP-13 in SCC tumour cells. MMP-7 expression was enhanced especially in the SCC tumour cells of the RDEB-associated SCCs. Studies with SCC cell lines showed that tumour cell derived MMP-7 activated heparin-binding epidermal growth factor-like growth factor (HB-EGF), which enhanced the growth of SCC tumour cells.

Furthermore, it was shown that type VII collagen (COL7) is expressed in sporadic SCC tumour cells. Interestingly, it was shown that SCC-associated MMP-13 is capable of cleaving COL7 *in vitro*. COL7 cleavage may have a role in the progression of cutaneous SCC.

Studies on the serine proteinase inhibitor gene family using SCC tumour cell gene array, quantitative real-time polymerase chain reaction (PCR), SCC cell lines, normal human epidermal



Fig. 1. Atte Kivisaari defended her PhD thesis in Turku, Finland on 27 January 2012. The opponent was Associate Professor Kaisa Tasanen-Määttä. Professor Veli-Matti Kähäri acted as custos.

keratinocytes and IHC of TMA samples showed that serine proteinase inhibitor clade A, member 1 (serpinA1, alpha-1-antitrypsin) is expressed and produced by human SCC tumour cells, but not by normal keratinocytes. Moreover, serpinA1 expression was shown to correlate with the progression of cutaneous SCC using transformed HaCaT-cell lines and mouse chemically induced skin SCC model. SerpinA1 may serve as a novel biomarker for the progression of cutaneous SCC.

This study elucidated putative mechanisms of the progression of cutaneous SCC and revealed novel biomarker candidates for the progression of SCC of the skin.