SerpinA1, a Protease Inhibitor Associating with Various Tumours: a Possible Diagnostic Biomarker for Progression of Cutaneous Squamous Cell Carcinoma

The incidence of non-melanoma skin cancer, including basal cell carcinoma and squamous cell carcinoma (SCC), is increasing globally. The long-term prognosis for patients with metastatic disease (6%) is poor and no specific molecular markers for progression of cutaneous SCC are currently available. The authors of this article found serpin peptidase inhibitor clade A member 1 (serpinA1) to be a novel tumour cell-associated biomarker for progression of cutaneous SCCs.

Below is a summary of a paper by Farshchian et al. The full reference for the article is: *Farshchian M, Kivisaari A, Ala-aho R, Riihilä P, Kallajoki M, Grénman R, Peltonen J, Pihlajaniemi T, Heljasvaara R, Kähäri V-M. Serpin peptidase inhibitor clade A member 1 (SerpinA1) is a novel biomarker for progression of cutaneous squamous cell carcinoma. Am J Pathol 2011; 179, 1110–1119.*

SerpinA1, also known as alpha1-proteinase inhibitor or alpha1-antitrypsin (AAT) is a highly effective inhibitor of neutrophil elastase. Patients with AAT deficiency carry an increased risk of emphysema and liver disease. Elevated expression of AAT is associated with invasive and metastatic potential and poor prognosis in lung, colorectal, and gastric carcinoma. Furthermore, serpinA1 is among 129 genes whose elevated expression has been found to be associated with progression of oesophageal squamous dysplasia.

The research group analysed the expression of the entire serpin family in skin SCC cells, using an oligonucleotide-based microarray technique. Comparison of levels of serpin gene expression revealed elevated expression of serpinA1 in SCC cell lines compared with normal keratinocytes. The results were verified with quantitative real-time polymerase chain reaction (PCR), revealing 50-fold ($p=0.03$) up-regulation of serpinA1 mRNA in cutaneous SCC cell lines compared with normal keratinocytes. SerpinA1 protein was also found in Western blot analysis in all studied SCC cell lines. In HaCaT and Ha-*ras*-transformed HaCaT cell lines, which represent an *in vitro* model for different stages of SCC tumour progression, the metastatic cell line expressed serpinA1 mRNA at the highest level, while the non-tumourigenic HaCaT cells expressed serpinA1 at low levels. Positive immunostaining for serpinA1 was especially pronounced in tumours with aggressive potential: all of the 12 recessive dystrophic epidermolysis bullosa-associated SCCs expressed serpinA1 in tumour cells. Tumour cell-associated serpinA1 staining was also detected in all chemically induced mouse skin SCCs studied ($n=17$).

Based on these results, the authors propose serpinA1 as a novel biomarker for cutaneous SCC progression. The pathogenetic mechanism is unknown, but the anti-apoptotic effect, natural killer cell activity inhibition and mitogenic action of the C-terminal part of serpinA1 have been suggested to play a role.

The first authors of the study, Mehdi Farshchian and Atte Kivisaari, work at Turku University Central Hospital. Atte Kivisaari defended his thesis on molecular markers of SCC at Turku University in January 2012. The study group, headed by Professor Veli-Matti Kähäri, has elucidated the role of various proteinases in the growth and progression of skin cancer and in wound repair since the 1980s.

Sari Suomela, Country Editor, Finland
Finnish Institute of Occupational Health, Control of Hypersensitivity Diseases, Helsinki, Finland. E-mail: sari.suomela@ttl.fi