Assessment of kallikrein-related peptidase 5 (KLK5) protein expression in tumor tissue of advanced ovarian cancer patients by immunohistochemistry and ELISA: correlation with clinical outcome.

Members of the human kallikrein-related peptidase (KLK) family, including KLK5, have been reported to play an important role in ovarian cancer progression. In the present study, we assessed KLK5 protein expression in ovarian cancer tissues by immunohistochemistry (IHC) and ELISA, and analyzed its association with clinicopathologic parameters and disease outcome in 95 patients with advanced ovarian cancer FIGO stage III/IV. KLK5 immunoeexpression was evaluated in ovarian cancer tissue microarrays by IHC using a manual semiquantitative scoring system. KLK5 antigen levels were determined in ovarian cancer tumour tissue extracts by ELISA. KLK5 protein is expressed in ovarian cancer tissue by stromal and tumor cells. Mean KLK5 immunoscore values in tumor cells (KLK5-Tc; 5.7, range 0 to 12) were higher compared to stromal cells (KLK5-Sc; 1.2, range 0 to 9) but the correlation between KLK5-Tc and KLK5-Sc was rather low (rs = 0.34, P< 0.05). No significant associations of clinicopathological parameters with KLK5-Tc, KLK5-Sc, the combined overall score KLK5-Tc+Sc, or ELISA (KLK5-E) expression values were determined,
except for KLK5-E protein expression with advanced age and high nuclear grade (G3). In univariate Cox regression analysis, elevated expression levels of KLK5-Sc are significantly linked with both prolonged overall survival (OS) (hazard ratio [HR] = 0.6, P = 0.046) and progression-free survival (PFS) (HR = 0.54, P = 0.032) of advanced ovarian cancer patients. KLK5-Tc and KLK5-Tc+Sc scores as well as the KLK5-E values were not associated with patients' outcome. In multivariable analysis, KLK5-Sc expression was found to be statistically significant for PFS. Patients with elevated KLK5-Sc had a two-fold lower risk of disease recurrence (HR = 0.53, P = 0.037) as compared to patients with low KLK5-Sc. For KLK5-Sc and OS, a trend towards statistical significance was observed (HR = 0.62, P = 0.077). These results indicate that KLK5 overexpression by stromal cells (KLK5-Sc) may be a positive modulator lowering aggressiveness of ovarian cancer.