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4444 Human kallikrein 8 protein (hK8) in ovarian cancer cytosols: A new marker of favorable prognosis.

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Human kallikrein 8 (hK8/neuropsin/ovasin/PRSS19; encoded by the *KLK8* gene) is a member of the kallikrein family of secreted serine proteases. Previous reports indicate that *KLK8* is regulated by steroid hormones, differentially expressed in ovarian cancer tissues and that tissue *KLK8* mRNA is a marker of favourable prognosis in ovarian carcinoma. Recent evidence shows that the hK8 protein is elevated in 55% of ovarian tumor tissues and 62% of ovarian cancer patient sera, compared to normal, suggesting that hK8 is a prospective diagnostic ovarian cancer biomarker. Given the above, the aim of the present study was to determine if tissue hK8 bears any prognostic significance in ovarian cancer. Using a newly developed ELISA, hK8 levels were quantified in 136 ovarian tumor extracts and correlated with various clinicopathological variables and outcome [progression-free survival (PFS), overall survival (OS)], over a median follow-up period of 42 months. hK8 concentration in ovarian tumor cytosols ranged from 0 to 478 ng/mg of total protein, with a median of 30 ng/mg. An optimal cutoff value of 25.8 ng/mg total protein (75^{th} percentile) was selected, based on the ability of hK8 values to predict the PFS of the study population, to categorize tumors as hK8-positive or negative. Women with hK8-positive tumors most often had lower grade tumors (G1), no residual tumor after surgery and optimal debulking success ($p < 0.05$). Univariate and multivariate Cox regression analyses revealed that patients with hK8-positive tumors had a significantly longer PFS and OS than hK8-negative patients ($p < 0.05$). Kaplan-Meier survival curves further confirmed a reduced risk of relapse and death in women with hK8-positive tumors ($p = 0.001$ and $p = 0.014$, respectively). These results indicate that hK8 is an independent marker of favourable prognosis in ovarian cancer.

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