AMERICAN SOCIETY OF CLINICAL ONCOLOGY
www.asco.org

Human kallikrein 11 (hK11) and 15 (hK15) expression in ovarian cancer: New independent predictive and prognostic factors.

Sub-category: Prognostic Factors
Category: Tumor Biology/Immunobiology/Human Genetics
Meeting: 2003 ASCO Annual Meeting

Abstract No: 3462
Citation: Proc Am Soc Clin Oncol 22: 2003 (abstr 3462)
Author(s): S. Fracchioli, C. A. Borgono, G. M. Yousef, I. A. Rigault de La Longrais, M. Puopolo, M. Massobrio, E. P. Diamandis, D. Katsaros; University of Turin, Turin, Italy; University of Toronto, Toronto, Canada
Abstract: Human kallikreins (hKs) are serine proteases present in diverse biological tissues and fluids where they are implicated in both physiological and pathological processes. The kallikrein genes, denoted KLK1-KLK15, are located on chromosome 19q13.4 and encode for the corresponding kallikrein enzymes, hK1-hK15. Many kallikreins were found to be differentially expressed in epithelial ovarian cancer (EOC), including hK11 and hK15, recently cloned. Both hK11 and hK15 expression is under the regulation of steroid hormones at the transcriptional level. We hypothesized that hK11 and hK15 may be implicated in ovarian carcinogenesis, and may serve as novel ovarian cancer biomarkers. We evaluated hK11 levels using a highly sensitive and specific immunoassay, and hK15 expression by quantitative RT-PCR, in 104 and 168 consecutive patients with EOC, respectively. Results were correlated with clinicopathological variables, progression-free (PFS) and overall survival (OS). The median follow-up was of 67 months. hK11 positive tumors (>0.54ng/mg of total protein) were significantly associated with early stage (I/II), menopausal status, response to chemotherapy (all $p<0.05$), decreased risk of relapse ($p=0.007$) and death ($p=0.005$). Multivariate analyses confirmed the independent positive prognostic value of hK11 for OS ($p=0.025$). Similarly, in the subgroup of patients with grade 1-2 tumors, hK11-positivity was associated with higher OS in both uni- and multivariate analysis ($p<0.05$). Lastly, in women with optimal debulking after surgery, hK11 positivity was associated with slower disease progression. On the other side, hK15 overexpression resulted to be a significant predictor of reduced PFS ($p<0.001$) and OS ($p<0.009$), and this association kept its significance in the multivariate analysis. Our results indicate that hK11 and hK15 are two novel independent prognostic markers in patients with EOC with opposite behaviour. Given the above, it is plausible to hypothesize that human kallikreins function together in the normal physiology of the ovary and in promoting or inhibiting ovarian carcinogenesis at different stages.