

**#4194 The Prognostic Value of Human KLK8 (Neuropsin/Ovasin) in Ovarian Cancer and Evidence for Alternative Splicing.** Angeliki Magklara, Andreas Scorilas, Dionyssios Katsaros, Stefano Fracchioli, Irene Rigault de la Longrais, R. Piccinno, George M. Yousef, and Eleftherios P. Diamandis. *Department of Obstetrics and Gynecology, Gynecologic Oncology Unit, University of Turin, Turin, Italy, Mount Sinai Hospital and Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Canada.*

KLK8 (neuropsin/ovasin) is a new member of the human kallikrein gene family which consists of enzymes with serine protease enzymatic activity. Recent reports have implicated KLK8 in ovarian cancer with a potential clinical value for disease diagnosis or prognosis as well as a possible therapeutic target. We undertook this study to evaluate the role of KLK8 in ovarian carcinoma by examining its expression, at the mRNA level, in ovarian tumors. We found that KLK8 expression is an independent and favorable prognostic marker for ovarian cancer. Patients with higher KLK8 expression in the tumor have lower grade disease ( $P=0.007$ ), small residual tumor left after surgery ( $P=0.044$ ), live longer (progression-free survival,  $P<0.001$ ; overall survival,  $P=0.034$ ) and relapse less frequently. In multivariate analysis, higher KLK8 expression was significantly associated with longer disease-free survival (HR=0.57,  $P=0.027$ ). We also identified two novel mRNA splice variants of the KLK8 gene (type 3 and 4), which are abundantly expressed in many tissues. Sequence analysis revealed that these variants were missing whole exons, and the predicted proteins would be devoid of the essential amino acids of the catalytic triad; therefore they are expected to be enzymatically inactive. The new variants were also expressed in ovarian tumors, but statistical analysis failed to establish any potential prognostic value. These results suggest that KLK8 is a novel, favorable prognostic marker in ovarian cancer. Since KLK8 encodes for a predicted secreted protein, its detection in serum may aid in ovarian cancer diagnosis and prognosis.