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Author Block: *Constantina Petraki, Panagiotis A. Papanastasiou, Vassiliki N. Karavana, Eleftherios P. Diamandis.* Evangelismos Hospital, Athens, Greece, Hygeia Hospital, Athens, Greece, University of Toronto and Mount Sinai Hospital, Toronto, ON, Canada

Human tissue kallikreins are members of a large multigene family of fifteen serine proteases (the genes designated as KLK1-KLK15 and their encoded proteins as hK1-hK15). In addition to the established role of hK3 (PSA) in prostate cancer, many members of the KLK gene family have been proposed as new biomarkers for other cancers, including breast, ovarian and testicular cancer. Most studies are based on quantitative methods and especially, RT-PCR and ELISA measurements. Recently, we have immunohistochemically evaluated most of the above hKs in normal and malignant tissues. In general, most hKs were immunohistochemically revealed in a variety of tissues, indicating that these proteins are not tissue-specific (except for hK2 and hK3 which have prostate-restricted expression). It is worth mentioning that tumors arising from tissues expressing hKs, also showed an immunohistochemical expression (IE). As glandular epithelia constitute the main IE sites, all hKs were expressed in adenocarcinomas of the stomach, colon, pancreas, breast, ovary and prostate. This finding implicates kallikreins in the progression of cancer. Furthermore, urothelial carcinomas, papillary and follicular thyroid carcinomas, gliomas, prolactinomas and hormone-producing pancreatic tumors showed variable kallikrein immunoexpression. In series of prostate, renal cell, colon and urothelial carcinomas, we have studied the correlation of hK IE with the histological type and clinical behavior of these tumors. Our main findings were that the IE of several hKs had a positive correlation with the histological grade and pathological stage of colon, renal cell and prostate cancer. Furthermore, some hKs were independent unfavorable predictors of overall survival for these carcinomas. The hK IE in urothelial carcinomas was variable, without any statistically significant correlation with histological grade or pathological stage. We conclude that it is now possible to immunohistochemically localize many kallikreins in diverse malignancies for the purpose of evaluating these molecules as prognostic and predictive biomarkers.

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