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Titel des Beitrags:
Human kallikrein 5: a potential novel serum biomarker for breast and ovarian cancer.

Abstract:
The kallikrein family is a group of 15 serine protease genes clustered on chromosome 19q13.4. Human kallikrein (hK) gene 5 (KLK5) is a member of this family and encodes for a secreted serine protease (hK5). KLK5 was shown to be differentially expressed at the mRNA level in breast and ovarian cancer. Until now, detection of hK5 protein in either biological fluids or tissues has not been described due to lack of suitable reagents and methods. The aim of this study was to develop immunological reagents and a sensitive and specific fluorometric immunoassay (ELISA) for hK5, to examine the presence of hK5 in human tissues and biological fluids, and to study the possible clinical utility of hK5 as a biomarker for endocrine-related malignancies. Recombinant hK5 protein was produced and purified using a Pichia pastoris yeast expression system. The protein was used as an immunogen to generate mouse and rabbit polyclonal anti-hK5 antibodies. A sandwich-type microplate immunoassay (ELISA) was developed using these antibodies, coupled with a time-resolved fluorometric detection technique. The ELISA assay was then used to measure hK5 in various biological fluids, tissue extracts, and serum samples from normal individuals and patients with various malignancies. The hK5 ELISA immunoassay has a lower detection limit of 0.1 micro g/liter, is specific for hK5, and has no
cross-reactivity with other homologous kallikreins. The dynamic range is 0.1-25 micro g/liter, and within-run and between-run coefficients of variation within this range are <10%. hK5 is found in many tissues, with the highest expression levels seen in the skin, breast, salivary gland, and esophagus. hK5 is present at relatively high levels in milk of lactating women. Whereas the levels of hK5 are almost undetectable in serum of normal individuals (male and female) and patients with diverse malignancies, higher concentrations were found in a proportion of patients with ovarian (69%) and breast (49%) cancer. High levels were also detected in ascites fluid from metastatic ovarian cancer patients and in ovarian cancer tissue extracts. In conclusion, we report development of the first immunofluorometric assay for hK5 and describe the distribution of hK5 in biological fluids and tissue extracts. Our preliminary data indicate that hK5 is a potential biomarker in patients with ovarian and breast cancer.