Function and clinical relevance of kallikrein-related peptidases and other serine proteases in gynecological cancers.

Abstract:
Gynecological cancers, including malignant tumors of the ovaries, the endometrium and the cervix, account for approximately 10% of tumor-associated deaths in women of the Western world. For screening, diagnosis, prognosis, and therapy response prediction, the group of enzymes known as serine (Ser-)proteases show great promise as biomarkers. In the present review, following a summary of the clinical facts regarding malignant tumors of the ovaries, the endometrium and the cervix, and characterization of the most important Ser-proteases, we thoroughly review the current state of knowledge relating to the use of proteases as biomarkers of the most frequent gynecological cancers. Within the Ser-protease group, the kallikrein-related peptidase (KLK) family, which encompasses a subgroup of 15 members, holds particular promise, with some acting via a tumor-promoting mechanism and others behaving as protective factors. Further, the urokinase-type plasminogen activator (uPA) and its inhibitor PAI-1 (plasminogen activator inhibitor-1) seem to play an unfavorable role in gynecological tumors, while down-regulation of high-temperature requirement proteins A 1, 2 and 3 (HtrA1,2,3) is associated with malignant disease and cancer progression. Expression/activity levels of other Ser-proteases, including the
type II transmembrane Ser-proteases (TTSPs) matriptase, hepsin (TMPRSS1), and the hepsin-related protease (TMPRSS3), as well as the glycosyl-phosphatidylinositol (GPI)-anchored Ser-proteases prostasin and testisin, may be of clinical relevance in gynecological cancers. In conclusion, proteases are a rich source of biomarkers of gynecological cancer, though the enzymes’ exact roles and functions merit further investigation.