

4447 Human kallikreins 6 and 10 are secreted as zymogen forms in ascites fluid from ovarian cancer patients.

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Human kallikreins 6 (hK6) and 10 (hK10) are members of the human tissue kallikrein family. hK6 and hK10 are secreted serine proteases which contain 244 and 276 amino acids, respectively. Both hK6 and hK10 have been found to be overexpressed in epithelial ovarian carcinoma and the overexpression leads to increased hK6 and hK10 levels in serum of ovarian cancer patients. High levels of hK6 and hK10 are associated with late stage ovarian cancer. Experimental evidence has shown that hK6 has trypsin-like enzymatic activity. Similarly, hK10 is predicted to have trypsin-like enzymatic activity. However, this prediction has not been experimentally confirmed. To understand the potential roles of hK6 and hK10 in ovarian cancer progression, we characterized hK6 and hK10 in the ascites fluids from ovarian cancer patients. hK6 and hK10 were purified from the ascites fluids with immunoaffinity chromatography followed by reversed-phase HPLC. N-terminal sequence of the purified proteins revealed that both hK6 and hK10 were secreted into the ascites fluid in their zymogen forms. The majority of hK6 present in the ascites fluid was in its free zymogen form, with a small proportion bound to protease inhibitors. However, all hK10 detected was present in the ascites fluid in its free form. Our results support the hypothesis that human tissue kallikreins may participate in an enzyme cascade reaction within the ascites fluid.

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