Overexpression of the human tissue kallikrein genes KLK4, 5, 6, and 7 increases the malignant phenotype of ovarian cancer cells.

The human tissue kallikrein family of serine proteases (hK1-hK15 encoded by the genes KLK1-KLK15) is involved in several cancer-related processes. Accumulating evidence suggests that certain tissue kallikreins are part of an enzymatic cascade pathway that is activated in ovarian cancer and other malignant diseases. In the present study, OV-MZ-6 ovarian cancer cells were stably co-transfected with plasmids expressing hK4, hK5, hK6, and hK7. These cells displayed similar proliferative capacity as the vector-transfected control cells (which do not express any of the four tissue kallikreins), but showed significantly increased invasive behavior in an in vitro Matrigel invasion assay (p<0.01; Mann-Whitney U-test). For in vivo analysis, the cancer cells were inoculated into the peritoneum of nude mice. Simultaneous expression of hK4, hK5, hK6, and hK7 resulted in a remarkable 92% mean increase in tumor burden compared to the vector-control cell line. Five out of 14 mice in the 'tissue kallikrein overexpressing' group displayed a tumor/situs ratio greater than 0.198, while this weight limit was not exceeded at all in the vector control group consisting of 13 mice (p=0.017; chi2 test). Our results strongly support the view that tumor-associated overexpression of tissue kallikreins contributes to ovarian cancer progression.