Kallikreins are potential biomarkers for pancreatic and colon cancer

Human kallikreins are a cluster of 15 serine protease genes located in the chromosomal band 19q13.4, a non-randomly rearranged region in many solid tumors, including pancreatic cancer. We utilized the SAGE and EST databases of the Cancer Genome Anatomy Project to perform in-silico analysis of kallikrein gene expression in normal and cancerous pancreatic and colon tissues and cell lines using virtual Northern blotting (VNB), digital differential display (DDD) and X-profiler. Two kallikreins, KLK6 and KLK10, are significantly up-regulated in pancreatic cancer. We probed two normal and six pancreatic cancer SAGE libraries with gene-specific tags for each of these kallikreins. KLK6 was found to be expressed in 5/6 cancer libraries and showed the most marked (5-fold) increase in average expression levels in cancer vs. normal. These data were verified by screening the EST databases, where all mRNA clones isolated were from cancerous libraries, with no clones detected in normal pancreatic tissues or cell lines. X-profiler comparison of two pools of normal and cancerous pancreatic libraries further verified the significant increase of KLK6 expression levels in pancreatic cancer. DDD data showed a 13-fold increase in KLK10 expression in pancreatic cancer.

Three kallikrein genes, KLK6, 8 and 10 are overexpressed in colon cancer compared to normal colon, while one kallikrein, KLK1, is down-regulated. While no expression of KLK6 was detected in normal colon, KLK6-specific tags were detectable in two cancer libraries. Similar results were obtained by EST screening; no KLK6 clones were detected in any of the 28 normal libraries examined, while ten KLK6 EST clones were found in colon adenocarcinoma. KLK10 was not detectable in normal colon. Gene-specific tags were however, detectable with high density in colon cancer and seven EST clones were found to be expressed in colon adenocarcinoma.

We conclude that hK6 and hK10 (the proteins encoded by the KLK6 and KLK10 genes) and hK6, hK8 and hK8 should be examined as tissue or serological markers of pancreatic and colon cancers, respectively.