Tumor protective role(s) for KLK6 in breast cancer

The cDNA encoding KLK6 was originally identified by mRNA differential display as being highly overexpressed in a primary breast tumor but completely inactivated in its lung metastasis, and the vast majority of metastatic breast cancers suppressor (Anisowicz, Sotiropoulou et al. Mol Med 2: 624-636, 1996). Based on this expression pattern, it was suggested that the encoded protein -a novel serine protease- may function to protect against tumor progression and that it is likely deregulated at the level of transcription, therefore, it represents a putative Class II tumor. Re-expression of KLK6 in non-expressing MDA-MB-231 breast tumor cells by vector-mediated stable cDNA transfection, resulted in marked reversal of their malignant phenotype, manifested by lower cell proliferation rates and saturation density, marked inhibition of anchorage-independent growth, and reduced cell motility (not shown) and their dramatically reduced ability to form tumors when implanted in SCID mice, as shown here. Interestingly, inhibition of tumor growth was observed at physiological concentrations of KLK6 (C12wt, C11wt) but not when KLK6 was highly overexpressed (C5wt) as observed in a subset of breast tumors. In addition, differential proteomic profiling revealed that KLK6 re-expression results in significant downregulation of vimentin that represents an established marker of epithelial-to-mesenchymal transition (EMT) of tumor cells and in concomitant upregulation of calreticulin and epithelial markers cytokeratin 8 and 19, indicating that KLK6 may play a protective role against tumor progression that is likely mediated by inhibition of EMT. Taken together, these findings suggested that normally KLK6 exerts protective roles against breast cancer.