Up-Regulation of Plakophilin-2 and Down-Regulation of Plakophilin-3 Are Correlated with Invasiveness in Bladder Cancer

Introduction and Objectives: Plakophilin (Pkp) proteins are associated with the binding of cadherin to intermediate filaments of the cytoskeleton. The aim of the present study was to examine Pkp2 and 3 expression levels in bladder cancer, in particular their levels during cellular growth and invasion.
Materials and Methods: The relative mRNA and protein expression levels of Pkp2 and 3 in bladder cancer cell lines were determined using quantitative real-time PCR and western blot analyses. The cellular localization of Pkp2 and 3 proteins in bladder cancer cells was also assayed using immunohistochemistry. The proliferation and invasive activities of bladder cancer cells were evaluated using cell growth and *in vitro* cell invasion assays, and were compared to those of bladder cancer cells treated with Pkp2 and 3 small interfering RNAs.
Results: Pkp2 mRNA and protein levels were elevated, and those of Pkp3 were reduced, in bladder cancer cells that are known to exhibit increased proliferation and invasive activity. Pkp2/3 protein expression was predominantly observed in the cytoplasm of invasive bladder cancer cells and tissues. Pkp2 knockdown inhibited, and Pkp3 knockdown enhanced, invasion of bladder cancer cells but these knockdowns did not alter cell proliferation.
Conclusions: We conclude that high Pkp2, and low Pkp3, expression is associated with bladder cancer cell invasion and that neither Pkp2 nor Pkp3 is associated with cell proliferation. We further hypothesize that accumulation of Pkp2 and 3 in the cell cytoplasm, rather than their recruitment to the cell membrane, is related to an increased ability of the tumor to invade and metastasize.