Relevance of periostin splice variants in renal cell carcinoma

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The extracellular matrix N-glycoprotein periostin is thought to enhance tumor invasion. In this study, the expression patterns of periostin and its splice isoforms were investigated in renal cell carcinoma (RCC). Periostin mRNA expression patterns were characterized in 30 fresh-frozen RCCs in normal fetal and adult renal tissues by both isoform-specific and nonspecific RT-PCR and by gene expression array analysis. Its protein expression was analyzed by immunohistochemistry, using tissue microarrays with tissue from 1007 RCC patients. Periostin mRNA in RCC was increased, as observed in both RT-PCR and gene microarray analyses, with significantly higher expression in the clear cell than in the papillary subtype. Four of eight periostin isoforms, identified in fetal kidney by direct sequencing, have not been described to date. Three isoforms could be detected in both RCC and matched non-neoplastic tissue, and one of them was expressed more frequently in RCC. Periostin protein was detected in both mesenchymal cells of the tumor stroma and epithelial tumor cells. Greater amounts of periostin in tumor epithelia correlated with the presence of sarcomatoid differentiation, higher tumor stage, lymph node metastases, and poor overall survival in the clear cell subtype. In conclusion, periostin expression in tumor epithelia may contribute to sarcomatoid differentiation and more aggressive behavior of RCC. The presence of a tumor-associated periostin isoform suggests splice-specific regulation in RCC tissue.