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Molecular characterization of papillary renal cell carcinoma

Renal cancer is subdivided in major subtypes based on histologic features seen under the light microscope. Major subtypes include clear cell, papillary, and chromophobe renal carcinomas, as well as a number of emerging subtypes. Papillary renal carcinoma accounts for up to 20 percent of kidney cancers and is the subject of the most recent analysis of 161 papillary renal cell carcinomas by The Cancer Genome Atlas Research Network. Papillary renal cell carcinoma occurs as a sporadic tumor or in association with hereditary renal carcinoma syndromes. Hereditary papillary renal cell carcinoma is associated with germline *MET* mutations and hereditary leiomyomatosis, and renal cell cancer syndrome is associated with germline fumarate hydratase mutations, although both genes can be somatically mutated in sporadic papillary renal cell carcinoma. Trisomy of chromosomes 7 and 17 are common in this cancer. Histologic subclassification of papillary renal cell carcinoma has more recently subdivided these cancers into type I and type II carcinomas. Type I is defined by scant cytoplasm and low-grade nuclei, whereas type II carcinomas have abundant eosinophilic cytoplasm and high-grade nuclei and are associated with a more aggressive disease course. The histologic type I and type II subclassifications of papillary renal cell carcinoma are supported by data in which type I carcinomas showed frequent *MET* alterations that included changes at the gene, mRNA, and protein phosphorylation levels, and type II tumors showed activation of the NRF2-antioxidant response element pathway. In addition, type II carcinomas could be further subdivided into three variants that correlated with patient survival: those with *CDKN2A* alterations, those with translocation of the *TFE3* or *TFEB* genes, and those with a CpG island methylator phenotype (CIMP). The results of this study suggest that molecular subclassification of papillary renal cell carcinoma may be feasible in routine practice and could significantly complement the histologic analysis of these cancers

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