node dissection was offered. *Discussion and Conclusion:* Non-urothelial bladder cancers are uncommon neoplasms and include neuroendocrine tumor, squamous cell carcinoma, adenocarcinoma, micropapillary, plasmocytoid and sarcoma. According to microscopic features, two forms of bladder neuroendocrine tumor have been described in literature: Small- and large-cell. SCCB is a very rare, poorly differentiated neuroendocrine tumor accounting for 0.5-1.0% of all bladder neoplasms (1) and characterized by a highly aggressive course. Patients affected are considered at highest-risk of metastatic spread and poor prognosis. Risk factors are not completely known. It has been suggested they may be similar to those for other bladder cancer types, including smoking, professional exposure or prolonged contact with aromatic amines. SCCB commonly arises from cells of the endocrine and nervous systems differently expressed within the human bladder; upper urinary tract, urethra and prostate may also be involved. Differently from common urothelial cancer, neuroendocrine lesions are histologically graded according to (Ki-67 index) rather than cellular polymorphism (2): when the urothelial histotype coexists, the WHO 2004 grading system (3) is used to classify the urothelial variant. On immunohistochemistry, SCCB is reactive for neuroendocrine markers such as synaptophysin, chromogranin and periodically for cytokeratin 7 and 20. The TNM system is currently used to staging these neoplasms. Clinical presentation is variable depending tumor location, staging and visceral-lymph node involvement. Treatment depends on several factors such as age, performance status, stadiation, stage, symptomatic hematuria. Radical cystectomy represents the gold standard; according to European Association of Urology guidelines, curative cystectomy is optional in patients older than 80 years but might be performed in cases of symptomatic hematuria as palliative intention whenever hemostatic resection is inconclusive. A multimodal treatment may be also offered combining surgery with chemotherapy regimens. The prognosis remains poor due to the high risk of metastasis; median overall survival is 1 to 5 years. In our case, the patient refused active treatment and best supportive care was offered.

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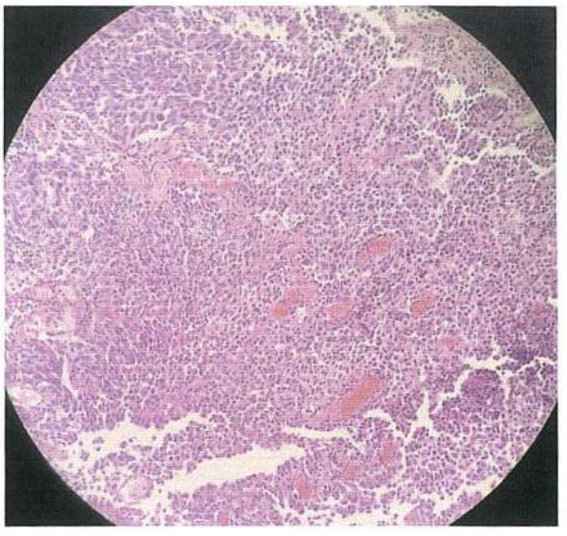

Figure 1. *Microscopic finding showing the small-cell carcinoma of the bladder (original magnification ×400).*

4
INHIBITION OF AUTOPHAGY REDUCES CELL PROLIFERATION AND MIGRATION BY P53 RESTORING IN ccRCC CELLS

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Background: Clear-cell renal cell carcinoma (ccRCC) is one of the most frequent lethal urological tumors and accounts for about the 3-4% of all diagnosed human cancer (1). One-third of patients undergoing surgical resection will develop disease recurrence or distance metastases (mRCC), with overall survival at lower than 3 years. Mutations of some tumor-suppressor genes, including the cyclin-dependent kinase Inhibitor 2A (*CDKN2A*), the tumor protein 53 (*TP53*), and the phosphatase and tensin homolog (*PTEN*), as well as the activation of different protein kinases, including the mammalian target of rapamycin (mTOR), contribute to cell growth and progression of kidney carcinoma. The activation

of mTOR leads to the synthesis of the mouse double minute 2 homolog (MDM2) protein ligase and induces the degradation of P53 by the proteasome machinery in KJ29 and Caki-2 kidney carcinoma cells (2). Down-regulation or mutation of *P53* may be associated with poor prognosis in renal cancer. Interestingly, P53-mutant proteins are able to activate autophagy that may drive cancer cells to grow, migrate and survive, contributing to disease progression. Here, we investigated the role autophagy might play in tumor progression and metastasis in kidney cancer. *Materials and Methods:* Analysis of autophagy was carried out in KJ29 and Caki-2 ccRCC cells by western blot using antibodies against the autophagic marker light chain 3 (LC3) protein. Autophagy was inhibited by specific short hairpin RNAs (shRNAs) silencing the autophagy related 7 (*ATG7*) gene. The expression of P53, E-cadherin, vimentin and P21 proteins was evaluated by immunoblot. Cell proliferation was analyzed by CellTiter assay (3), while cell migration was measured by groove re-colonizing assay in wild-type and *ATG7*-silenced ccRCC cells. For the analysis of cell migration, ccRCC cells were grown at confluence and detached by a sterile tip in order to produce a groove between the cells. The groove re-colonization was calculated by ImageJ software using a phase contrast microscope equipped with a CCD camera. The presence of P53 in autophagosomes was detected by immunofluorescence under fluorescence microscopy. Briefly, kidney carcinoma cells were co-transfected with a plasmid expressing wild type P53 linked to green fluorescent protein and a recombinant vector expressing sequences for miR501-5p (2). Next, cells were treated with an LC3 antibody conjugated with rhodamine and washed three times. Images were acquired by a CCD camera and processed by ImageJ program. Statistical analysis was carried out using ANOVA and *t*-test, as appropriate, with $p<0.05$ considered statistically significant. *Results:* ccRCC cells overexpressing *miR501-5p* showed an increased level of autophagy. This process affected the turnover of P53 in ccRCC cells by protein degradation into autophagosomes. The co-localization of P53-GFP with autophagic vesicles, especially in cells overexpressing the miR501-5p, indicated that some P53 is destroyed by the autophagic system. Silencing of *ATG7* gene significantly reduced autophagy and restored the P53 level in ccRCC cells. Moreover, the re-activation of P53 expression by autophagy inhibition strongly stimulated expression of cell-cycle inhibitor P21, which is positively regulated by tumor suppressor P53. As expected, the inhibition of autophagy by *ATG7* silencing reduced cell proliferation and migration in both KJ29 and Caki-2 cells. Reactivation of P53 by autophagy inhibition increased the expression of the epithelial marker E-cadherin and reduced the level of the mesenchymal protein vimentin in kidney carcinoma cells. These data indicate that autophagy may promote cell proliferation and migration in kidney cancer cells. *Discussion and Conclusion:* We described that the overexpression of *miR501-5p* correlates with poor prognosis in kidney cancer (2). Moreover, we found that the up-regulation of this miR may activate autophagy in ccRCC cells, suggesting that that this process may be associated with the progression of kidney carcinoma. The increase of autophagy causes inhibition of tumor suppressor P53. In fact, this protein is 'caught' and degraded by autophagosomal ingestion. On the other hand, the inhibition of autophagy leads to an increase in P53 expression and consequently to the synthesis of the cell-cycle inhibitor P21. Thereby the reduction of autophagy negatively affects cell proliferation, slowing growth of kidney carcinoma cells. Moreover, the epithelial to mesenchymal transition was inhibited through the up-regulation of E-cadherin and the reduction of mesenchymal marker vimentin in ccRCC cells with reduced autophagy. Taken together, these findings suggest that autophagy may affect cancer progression by the inactivation and degradation of P53, contributing to disease progression. In light of these observations, the inhibition of autophagy could open up new perspectives for the treatment of kidney carcinoma.

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5
EARLY COMPARISON BETWEEN ROBOT-ASSISTED RADICAL PROSTATECTOMY AND HEMI-GLAND CRYOABLATION IN ONCOLOGICAL AND FUNCTIONAL OUTCOMES

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Background/Aim: Cryo hemi-ablation (Cryo) is a minimally invasive procedure that preserves tissues around foci of