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Original Article

The association of GLUT-1, Galectin 3 and Claudin 1 staining with the type of renal tumors

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Abstract

Aim: The mechanism of carcinogenesis and prognostic parameters of renal cell carcinomas(RCC) exhibiting an increasing incidence trend are still obscure. Even though new tumors types are identified, diagnostic difficulty is even experienced occasionally for the most common tumor types. Various immunohistochemical and molecular-genetic studies are conducted for tumor type identification and prognostic evaluation. The present study examined glucose transporter protein (GLUT-1), galectin-3 that is associated with cell growth, differentiation, proliferation, adhesion, angiogenesis and apoptosis, and Claudin 1, a transmembrane protein of intercellular tight junctions, immunohistochemically for the most commonly encountered renal tumors. The staining patterns were compared in terms of Fuhrman nuclear grade, stage, metastasis, and demographic data.

Material and Methods: Methods: The study consisted of a total of 99 renal tumor cases including 40 Clear Cell Renal Cell Carcinoma (CCRCC), 22 Chromophobe Renal Cell Carcinoma (CrRCC), 16 Oncocytoma and 19 Papillary Renal Cell Carcinoma (PRCC) cases.
Results: Overexpression of GLUT-1 was observed in 92.5% of CCRCC cases and 36.8% of PRCC cases whereas the loss of expression was observed in CrRCC and Oncocytoma. Claudin-1 was seen in 77.5% of the CCRCCs, 45.4% of the CrRCCs, 81.25% of the oncocytomas and 84.2% of the PRCCs. Galectin-3 was present in 90% of the CCRCCs, 81% of the CrRCCs, 50% of the oncocytomas and 21% of the PRCC

Conclusion: Diffuse membranous staining pattern was observed for GLUT-1 in case of CCRCC, however, no correlation with prognostic parameters was noticed. Claudin-1 expression was observed in high nuclear grade tumors. Thus, it may be regarded as a poor prognostic factor. Galectin 3 expression was observed in the tumors with sarcomatoid differentiation.

Keywords: Claudin; Eosinophilic; Galectin-3; GLUT-1; Immunohistochemistry; Renal Cell Carcinoma.

INTRODUCTION

Renal cell carcinoma represents approximately 2-3% of adult malignant tumors. The most common type CCRCC, makes up 70% of renal cell carcinomas and has a slightly higher prevalence in males (1.5/1) (1). Although new tumor types were introduced to the 2016 WHO classification, diagnostic difficulty is still encountered even for the most common histomorphological subtypes. Due to these problems, different immunohistochemical and molecular-genetic studies are required for differential diagnosis.

We suggest that Claudin, a member of the protein family associated with intercellular tight junctions, is one of the markers to aid in differential diagnosis. The intercellular tight junction family is composed of two major components, namely, Occludin and Claudin and it functions in the growth, proliferation, differentiation of cells as well as forms tight junctions (2).

Another marker, Galectin-3, is a 31-kDa glycoprotein associated with the growth, differentiation, proliferation, adhesion, angiogenesis, and apoptosis of the cell and expressed in numerous tumors (3,4). It is present not only in the intracellular compartment - nucleus and cytoplasm- but also on the cell surface and in the extracellular matrix (5). The third marker is GLUT-1 that localized in the cell membrane. It plays an important role in the growth, proliferation, and functioning of the cells, and serves as transporter of intracellular glucose transport. It is

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considered that GLUT-1 may be a regulatory protein in tumor growth, cancer invasion and metastasis (6).

Despite numerous newly described tumor types, we still experience diagnostic difficulties even in the most common RCC types in everyday practice. Our aim is to be able to obviate these difficulties with GLUT-1, Galectin-3 and Claudin-1, and to shed light on these prognostic parameters of RCC with these markers.

MATERIAL and METHODS

Ninety-nine cases diagnosed with CCRCC, CrRCC, P1RCC, P2RCC, oncocytomas based on the partial and radical nephrectomy specimens collected in the medical faculty of Bezmialem Foundation University between 2012-2017. The study was approved by the ethics committee board of Bezmialem University. The nuclear grade of malignant tumors was assessed according to the Fuhrman nuclear grading system whereas the stage of tumor was determined based on the TNM classification of AJCC version 2017.

Hematoxylin-eosin-stained preparations were re-evaluated for immunohistochemical staining and then blocks were selected. The images were captured using Nikon microscope.

HE sections and immunohistochemical stainings performed during diagnosis were taken into consideration while differentiating tumor types. Clear cytoplasm and immunohistochemical Vimentin positivity, Cytokeratin 7 (CK7) negativity were evaluated in favor of CCRCC whereas cells with abundant eosinophilic cytoplasm showing the solid, tubular or alveolar pattern, the presence of perinuclear and diffuse CK7 positivity, Vimentin negativity and diffuse membranous CD63 positivity were evaluated in favor of CrRCC. Tubules within degenerated or myxoid stroma, cells with solid structure, relatively uniform nuclei, regular nuclear contours, abundant granular eosinophilic cytoplasm, focal CK7 positivity, Vimentin negativity and apical CD63 positivity were accepted for oncocytoma. For papillary RCC, it was first classified as Type 1 and Type 2. But, type differentiation could not be performed due to the low number of cases. The PRCC consisted of eosinophilic cytoplasmic cells which formed papillary and tubular structures and which could show increased alignment occasionally. Among the papillary structures, there were histocytes with foamy cytoplasm. The tumor was positive for CK7 and AMACR.

Two-micron-thick slices were cut from the paraffin blocks prepared from formalin-fixed specimens of the primary tumors. The slides were stained for Galectin-3 (monoclonal mouse antibody, Thermo Fremont, USA Clone 9C4), GLUT-1 (Biogenex, Atlanta, Georgia) and Claudin-1 (Thermo-scientific). Immunohistochemical staining was performed using the automated Ventana device. The staining patterns for Galectin-3, GLUT-1, and Claudin-1 antibodies in the selected areas of tumor were assessed as membranous, cytoplasmic, basolateral, and nuclear staining. The staining patterns were compared with the demographic data, Fuhrman nuclear grades, stages, and other clinical parameters. Staining extent was graded semiquantitatively as focal (1-10%) and diffuse (>10%) and staining intensities were interpreted as weak and strong.

IBM SPSS 22.0 statistical package program was used for the statistical analysis. The Kruskal-Wallis test was used to compare continuous variables. Subsequently, the Dunn test (binary comparison) was used for the variables found to be significant, and the Chi-square test was used for categorical variables. The standard deviation, frequency, and percentage were given for descriptive statistics in case of other different situations. $p < 0.05$ was considered to indicate a statistically significant difference.

RESULTS

The present study examined a total of 99 renal tumors including 40 CCRCC, 22 CrRCC, 16 oncocytomas, and 19 PRCCs. Sixty-five patients 26 of whom had CCRCC underwent partial nephrectomy while 34 patients underwent radical nephrectomy. The Fuhrman nuclear grades of 40 CCRCC cases were as follows: Grade 1 in one case, Grade 2 in 18 cases, Grade 3 in 18 cases and Grade 4 in three cases. The mean diameters of tumors were 5.1 cm for CCRCC, 6 cm for CrRCC, 4 cm for oncocytoma and 5.5 cm for PRCC. Other demographic data were summarized in the table (Table 1). The mean follow-up periods of tumors varied between 15 and 55 months for CCRCC, 14 and 55 months for CrRCC, and 4 and 56 months for PRCC.

Table 1. Clinicopathological characteristics of the patients

		CCRCC	CrRCC	Oncocytoma	PRCC
Age		31-81	41-82	21-78	29-84
		mean 58.90	mean 58.05	mean 57.63	mean 58.89
Sex					
	Female	18	15	9	2
	Male	22	7	7	17
Clinical stage					
	I	24	19		14
	II	3	2		2
	III	12	1		
	IV	1			1
Nuclear Grade					
	1	1			
	2	18			9
	3	18			10
	4	3			
Metastasis					
	M0	31	22		19
	M1	9			
Follow-up period					
		15-55 month	14-55 month	4-56 month	

The overexpression of GLUT-1 was observed in 92.5% of CCRCC cases and 36.8% of PRCC cases whereas the loss of expression was observed in cases with CrRCC and Oncocytoma. The expression of GLUT-1 in CCRCC cases was observed in both clear and eosinophilic areas

(Figure 1). It was statistically significant in terms of differentiating from other tumors (p <0.001). The strong and membranous pattern of staining in all cases was a salient finding however no significant result was noted between membranous staining and nuclear grade or other prognostic parameters (p>0. 05).

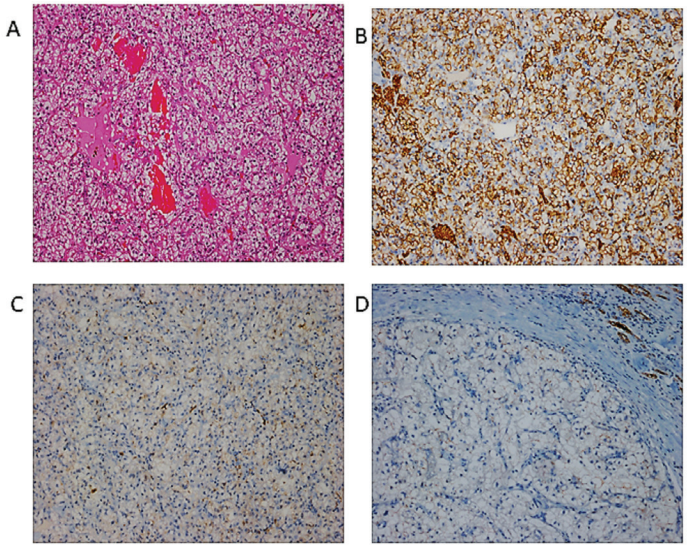

Figure 1. Clear cell renal cell carcinoma, hematoxylin and eosin stained (A). Diffuse membranous staining with GLUT-1 (B). (magnification, ×100). Negative staining with Galectin and Claudin 1(C,D), (magnification, ×100)

Staining for Claudin-1 was observed in 77.5% of the CCRCCs, 45.4% of the CrRCCs, 81.25% of the oncocytomas and 84.2% of the PRCCs (p> 0.005) (Figure 2).

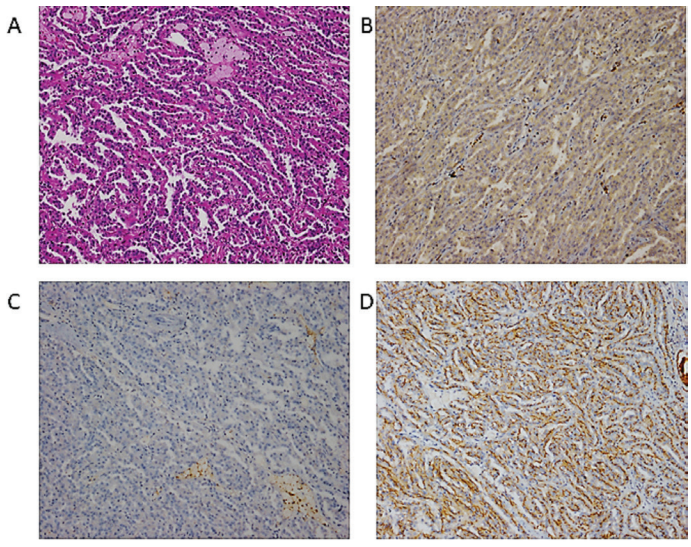

Figure 2. Papillary Renal Cell Carcinoma, hematoxylin and eosin stained (A). Negative staining with GLUT-1(B). Negative staining with Galectin 3(C). Diffuse canaliculer staining with Claudin 1(D). (magnification, ×100)

Claudin, a protein associated with tight junctions, showed high levels of staining in the oncocytomas (81.25%). Focal strong staining was observed in 69.2% of oncocytomas whereas diffuse strong staining was noted in 30.8% of them. Diffuse staining was observed in 80% of CrRCCs . Although not statistically significant, the ratio of diffuse staining was higher in the CrRCCs compared to oncocytomas. Diffuse staining for Claudin 1 was observed in 8 of 18 cases with nuclear grade 2, in 13 of 18 cases with grade 3 and in all of three cases with grade 4. No staining was detected in a grade 1 case (Figure 3).

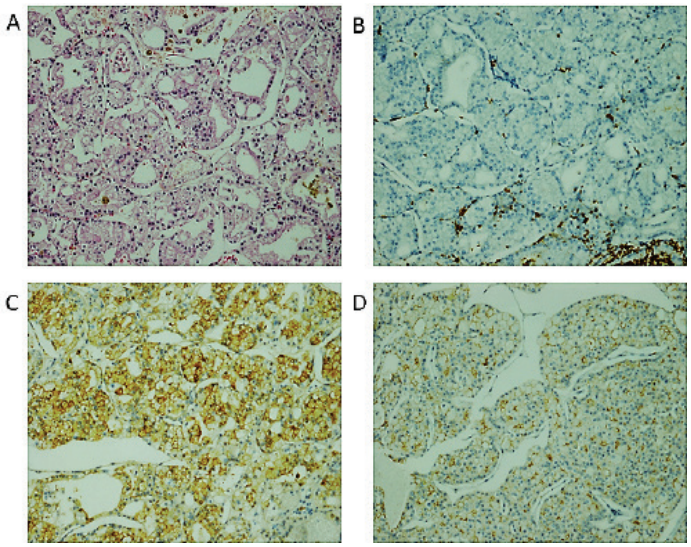

Figure 3. Chromophobe Renal Cell Carcinoma, hematoxylin and eosin stained (A). Negative staining with GLUT-1(B). Diffuse membranous staining with Galectin 3(C). Negative staining with Claudin 1(D). (magnification, ×100)

Although it did not result in a statistically significant result owing to the low number of low-grade tumors, the high rate of staining in the CCRCCs with high grades was notable. Diffuse strong staining was observed in almost all of PRCCs with nuclear grade 2 and 3 (15/16). No difference was found between Claudin 1 expression and nuclear grade. Staining for Galectin-3 was present in 90% of the CCRCCs, 81% of the CrRCCs, 50% of the oncocytomas and 21% of the PRCCs (Figure 4).

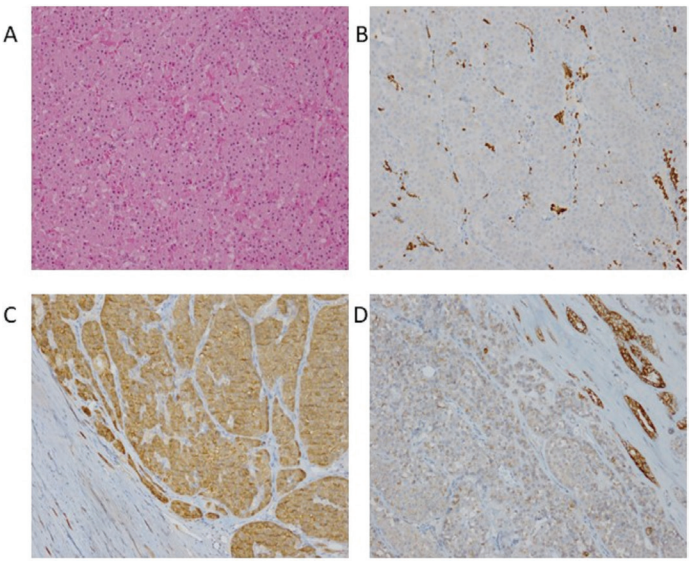

Figure 4. Oncocytoma, hematoxylin and eosin stained (A). Negative staining with GLUT-1(B). Diffuse membranous and cytoplasmic staining with Galectin 3(C). Negative staining with Claudin 1(D). (magnification, ×100)

The staining pattern was membranous and cytoplasmic in all tumor types. Staining for all three antibodies was observed in 11 cases of CCRCCs. Metastasis was observed in two of these cases while nine of them did not have any metastasis. GLUT1 and Claudin-1 positivity coexisted in 16 cases of whom 10 had metastasis. However, the Fuhrman nuclear grade was high in the cases with simultaneous diffuse and strong positivity of these two antibodies. Three cases had sarcomatoid differentiation two of which were CCRCC and one was CrRCC. Diffuse and strong staining for Galectin-3 was present only in the CrRCC with sarcomatoid differentiation, but no staining was observed for the other antibodies. Whereas diffuse strong staining was detected for all three antibodies in the CCRCC specimen (Table 2).

Table 2. Comparasion of GLUT1, CLAUDİN1 and GALECTİN3 expression levels in renal tumors

	GLUT-1		CLAUDIN 1			GALECTIN-3		
	M	C	M	C	BL	M	C	M+C
CCRCC	37 (100%)	0	11 (35.4%)	0	20 (64.5%)	3 (18.75%)	2 (12.5%)	11 (68.75)
CrRCC	0	0	3 (30%)	0	7 (70)	5 (27.7%)	1 (5.5%)	12 (66.6)
Oncocytoma	0	0	6 (46.15%)	0	7 (53.84%)	1 (12.5%)	0	7 (87.5%)
PRCC	7 (100%)	0	4 (25%)	0	12 (75%)	1 (25%)	0	3 (75%)

DISCUSSION

Renal cell carcinomas makes up 2-3% of all cancers. Its worldwide prevalence increases about 2% per year (7). More than 50% of RCC are detected incidentally during abdominal ultrasonography or computed tomography performed due to the increased use of imaging methods and other diseases (9). The increasing prevalence and mortality rate of RCC rises the number of the studies conducted to determine the factors designing treatment and affecting prognosis.

Prognostic factors can be assessed based on the TNM classification 2017 and histological factors including RCC subtype, nuclear grade, sarcomatoid differentiation, vascular invasion, and collecting duct invasion (9). Tight junction filaments considered to be helpful in differentiating the type of tumor and associated with prognosis are localized in the apical and basolateral regions of cells. They also function in the growth, proliferation, and differentiation of cell as well as forming the tight junctions (10,11,12). It is composed of two major components including occludin and claudin. Claudins are 21-28 kDa integral membrane proteins associated with intercellular tight junctions. They have approximately 24 types and composed of four transmembrane domains namely, two extracellular loops, amino and carboxyl-terminal cytoplasmic domains, and a short cytoplasmic turn. They have a large number of members in different localizations of the nephron. Claudin 1 is present in the glomerular podocytes, Claudin 1, 2 in the parietal epithelial cells, Claudin 2, 17 in the proximal tubule, Claudin 4, 7, 8 in the thick loop, Claudin 14, 16, 19 in the thick ascending loop, Claudin 3, 4, 7, 8 in the distal and collecting ductus and Claudin 18 in the collecting ducts (13,14). The studies conducted on different tumors associated with these proteins are available and they also compared these proteins with the prognostic parameters and tumor types as in the present study. Suren et. al. stated that Claudin-1 was important in differentiating benign and malignant thyroid neoplasms and a valuable marker for discriminating papillary carcinoma (97%) and follicular carcinoma (10%) as well (15). The loss of expression or over-expression of Claudin varies depending on the type of tumor (16). The loss of Claudin-1 expression was also associated with reduced lifespan and recurrence in stage II colon cancer (17). Warrier reported that Claudin-1 was expressed in both cytoplasm and cell membrane in breast carcinoma, associating the increased expression in cytoplasm with favorable prognosis (18). Membranous and basolateral staining patterns were observed in the relevant tumor types whereas cytoplasmic staining was not observed in the present study. Membranous staining was observed in lung adenocarcinomas with Claudin-1 expression and this was found to be correlated with RAS and EGFR expressions. However, no association with the prognostic parameters such as T and N stage was noted (19).

A study compared different Claudin types with the stage and grade of tumor which are the prognostic parameters of RCCs, revealing that the expression of Claudin-1 was associated with low-grade tumors while that of Claudin 2 was associated with high-grade tumors. Low expression of Claudin 1 was present in high-grade tumors. But, it did not have any correlation with the stage of tumor (20). The present study showed that its expression increased in cases with a high nuclear grade in CCRCC.

Another study comparing renal cell carcinoma subtypes showed that Claudin 1 expression in more than 2/3 of PRCCs highlights its diagnostic value for PRCCs. The PRCCs with loss of Claudin 1 expression were reported to have a more aggressive behavior. Positive staining was observed in approximately 1/4 of CCRCCs whereas it was found that its increased expression could be a poor prognostic parameter (21). The present study resulted in a very high staining rate (84.2%) in PRCCs. The rate of staining was 77.5% in CCRCC. Another study could detect no adequate finding regarding the histological origin of tumor with Claudin 1 and suggested that Claudin 7 and 8 could be used for differentiating chromophobe renal cell carcinoma and oncocytoma (22). Claudin-1 and -16 were

found to show significant expression in another study and it was determined to be important for the clinical course and biology of tumor (23). The present study revealed that staining for Claudin-1, predominantly found in the Bowman's capsule, was observed in the tumors arising from different areas of the kidney. This might be explained by the fact that Claudin 1 associated with zonula occludens 1 also affects other signaling pathways resulting in neoplastic transformation (14,17).

The expression of Claudin 1 in CCRCC was found to be high in the cases with old age, large diameter of tumor, high T stage, presence of preoperative tumor metastasis, high Fuhrman grade and presence of postoperative distant metastasis (10). However, in the present study, Claudin 1 expression was not determined to have a statistically significant association with metastasis, nuclear grade, and demographic data. There are studies indicating that the damage to tight junctions and loss of cohesion are responsible for the aggressive behavior and dedifferentiation of cancer cells (22). Although it was not found to be statistically significant in the present study, we suggest that staining with Claudin-1 is associated with high nuclear grade based on the ratios.

Another protein, Galectin-3, is a glycoprotein associated with cell growth, differentiation, proliferation, adhesion, angiogenesis, apoptosis and expressed in many tumors (3,4). The studies conducted on nontumoral lesions and tumors of the kidney are present in the literature (24). A study showed diffuse expression of Galectin-3 in the cell membrane cytoplasm and nucleus at the rate of 53.9% in CCRCC. At the same time, the loss of Galectin-3 expression was found to inhibit cell growth, decrease apoptosis and suppress invasion ability (4). CCRCCs are known to originate from proximal tubules. Despite this fact, high expression of Galectin 3 in these tumors suggests that other Galectins are displaced by Galectin-3 in the tumoral tissue (25). Another hypothesis on this subject is that tumor cells can facilitate this binding owing to the high affinity of Galectin-3 for polysaccharides (26). The study conducted using mRNA expression analysis found that Galectin-1 and 3 expression increased in male gender in CCRCCs. However, this difference was not detected between the surrounding and normal tissue (27). This may be related to the greater incidence of RCC in men (1).

Various studies were carried out to determine the role of Galectin-3 in differentiation and prognosis. Dancer et al. stated that galectin-3 expression was high in granular cytoplasmic tumors such as oncocytomas and CrRCCs whereas it was very low in PRCCs. Overexpression was noted in CCRCCs with high nuclear grade (28). Sakaki et al. reported that Galectin-3 expression was high especially in CCRCCs with distant metastasis, however, no statistically significant correlation could be detected between Galectin-3 and prognosis in these studies (3). We could neither detect a statistical correlation between Galectin-3 and prognostic parameters. However, it was found to be positive in three cases with sarcomatoid differentiation. A clear interpretation could not be made due to the low number of cases. Merseburger et al. pointed out a down-regulation of Galectin in advanced stage RCCs and stated that this condition was associated with unfavorable prognosis and reduced lifespan (29).

GLUT 1 is the most important member of the GLUT family which is also found in normal tissues. Although cytoplasmic and membranous staining occurs for GLUT-1, its staining pattern is associated with the histology and stage of tumor. The overexpression of GLUT-1 is correlated with malignant tumor characteristics such as invasive pattern, proliferation and reduced lifespan (30). Diffuse membranous staining pattern is observed in CCRCC regardless of the nuclear grade. Cytoplasmic staining which can appear as clear or eosinophilic may be observed at varying percentages across the histological subtypes of RCC (31). There are studies demonstrating that GLUT-1 expression is and is not associated with the stage or grade of tumor (31-33). The present study did not reveal any relationship between GLUT 1 and nuclear grade or stage.

CONCLUSIONS

Despite the studies on Claudin-1, GLUT-1, and Galectin-3, the markers evaluated immunohistochemically in renal tumors in the present study, there are still inconsistencies. According to our results, diffuse staining for GLUT-1 is present in CCRCC regardless of nuclear grade, and it is important in differentiating other tumors. Claudin-1 expression is higher in CCRCCs with high nuclear grade. It can be considered as a poor prognostic factor. Staining percentage is high for Claudin in PRCCs, however, no association with nuclear grade was detected. Although many expected results could not be reached, we suggest that current results will contribute to the differentiation of RCC types and to the studies on its association with prognosis. Current data needs to be supported by studies with large case series.

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REFERENCES

1. Ljungberg B, Bensalah K, Canfield S, et al. EAU guidelines on renal cell carcinoma: 2014 update. Eur Urol 2015;67:913-24.
2. Sawada N, Murata M, Kikuchi K, et al. Tight junctions and human diseases. Med Electron Microsc 2003;36:147-56.
3. Sakaki M, Fukumori T, Fukawa T, et al. Clinical significance of Galectin-3 in clear cell renal cell carcinoma. J Med Invest 2010;57:152-7.
4. Xu Y, Li C, Sun J, et al. Antitumor effects of galectin-3

inhibition in human renal carcinoma cells. Exp Biol Med (Maywood) 2016;241:1365-73.
5. Wang JL, Werner EA, Laing JG, et al. Nuclear and cytoplasmic localization of a lectin-ribonucleoprotein complex. Biochem Soc Trans 1992;20:269-74.
6. Macheda ML, Rogers S, Best JD. Molecular and cellular regulation of glucose transporter (GLUT) proteins in cancer. J Cell Physiol 2005;202:654-62.
7. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer 2013;49:1374-403.
8. Gill IS, Aron M, Gervais DA, et al. Clinical practice. Small renal mass. N Engl J Med 2010;362:624-34.
9. Sun M, Lughezzani G, Jeldres C, et al. A proposal for reclassification of the Fuhrman grading system in patients with clear cell renal cell carcinoma. Eur Urol 2009;56:775-81.
10. Shin HI, Kim BH, Chang HS, et al. Expression of claudin-1 and -7 in clear cell renal cell carcinoma and its clinical significance. Korean J Urol 2011;52:317-22.
11. Langbein L, Grund C, Kuhn C, et al. Tight junctions and compositionally related junctional structures in mammalian stratified epithelia and cell cultures derived therefrom. Eur J Cell Biol 2002;81:419-35.
12. Lee DB, Huang E, Ward HJ. Tight junction biology and kidney dysfunction. Am J Physiol Renal Physiol 2006;290:20-34.
13. Tsukita S, Furuse M, Itoh M. Multifunctional strands in tight junctions. Nat Rev Mol Cell Biol 2001;2:285-93.
14. Gong Y, Hou J. Claudins in barrier and transport function-the kidney. Pflugers Arch-Eur J Physiol 2017;469: 105-13.
15. Süren D, yıldırım M, Sayiner A, at al. Expression of claudin 1, 4 and 7 in thyoid neoplams. Oncology Letters 2017;13:3722-26.
16. Soini Y. Expression o claudins 1, 2, 3, 4, 5 and 7 in various types of tumours. Histopathology 2005;46:551-60.
17. Resnick MB, Konkin T, Routhier J, et al. Claudin-1 is a strong prognostic indicator in stage II colonic cancer: a tissue microarray study. Mod Pathol 2005;18:511-18.
18. Warrier S, Sellinger C, Beith JM, et al. Claudin-1 as a novel transcriptional target of hedgehog signaling and a predictor for outcome in breast cancer. 2013 ASCO Annual Meeting Proceedings J Clin Oncol. 31: Abstract 2013;1053.
19. Sun B, Yao Y, Pei B, et al. Claudin-1 correlates with poor prognosis in lung adenocarcinoma. Thoracic Cancer 2016;7:556-63.
20. Vırman J, Soını Y, Kujala P, at al. Claudins as Prognostic Factors for Renal Cell Cancer. Antıcancer Research 2014;34:4181-88.
21. Fritzsche F, Oelrich B, Johannsen M, et al. Claudin-1 protein expression is a prognostic marker of patient survival in renal cell carcinomas. Clin Cancer Res 2008;14:7035-42.
22. Lechpammer M, Resnick MB, Sabo E, et al. The diagnostic and prognostic utility of claudin expression in renal cell neoplasms. Mod Pathol 2008;21:1320-29.
23. men w, martın t, ruge f, et al. expression of Claudins in Human Clear Cell Renal Cell Carcinoma. Cancer Genomics Preteomics 2015;12:1-8.
24. Desmedt V, Desmedt S, Delange JR, et al. Galectin-3 in renal pathology: more than just an innocent bystander? Am J Nephrol 2016;43:305-17.
25. Delacour D, Cramm-Behrens CI, Drobecq H, et al. Requirement for galectin-3 in apical protein sorting. Curr Biol 2006;16:408-14.
26. Zhao Q, Duckworth CA, Wang W, et al. Peanut agglutinin appearance in the blood circulation after peanut ingestion mimics the action of endogenous galectin-3 to promote metastasis by interaction with cancer-associated MUC1. Carcinogenesis 2014;35:2815-21.
27. Von Klot CA, Kramer MW, Peters I, et al: Galectin-1 and galectin-3 mRNA expression in renal cell carcinoma. BMC Clin Pathol 2014;14:15.
28. Dancer J, truong L, Zhai Q, et al. Expression of Galectin-3 in renal neoplasms. Arch Pathol Lab Med 2010;134:90-4.
29. Merseburger AS, Kramer MW, HennenlotterJ, et al: Loss of galectin-3 expression correlates with clear cell renal carcinoma progression and reduced survival. World J Urol 2008;26:637-42.
30. Szablewski L. Expression of glucose transporters in cancers. Biochimica et Biophysica Acta 2013;1835:164-69.
31. Ozcan A, Shen SS, Zhai QJ, Expression of GLUT1 in primary renal tumors morphologic and biologic implications. Am J Clin Pathol 2007;128:245-54.
32. Nagase Y, Takata K, Moriyama N, et al. Immunohistochemical localization of glucose transporters in human renal cell carcinoma. J Urol 1995;153:798-801.
33. Miyakita H, Tokunaga M, Onda H, et al. Significance of 18 F-fluorodeoxyglucose positron emission tomography (FDG-PET) for detection of renal cell carcinoma and immunohistochemical glucose transporter 1 (GLUT-1) expression in the cancer. Int J Urol 2002;9:15-8.