WHITEPAPER

Uroplakin II – Increased Sensitivity in Urothelial Carcinoma

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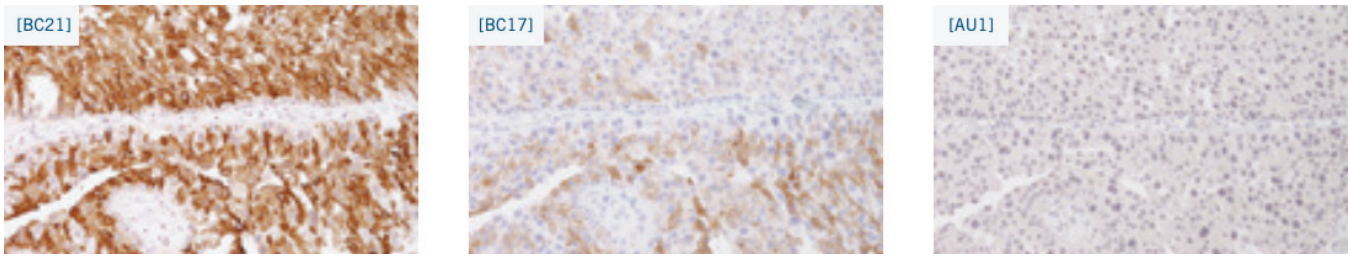
Bladder cancer is the seventh most commonly occurring cancer in the United States with 73,469 new cases reported in 2016 and is associated with high recurrence & progression rates[1].

Bladder cancer is the seventh most commonly occurring cancer in the United States with 73,469 new cases reported in 2016 and is associated with high recurrence & progression rates[1]. About 70% of superficial bladder cancer patients will experience tumor recurrence and 10-15% of this sub-population will eventually progress to muscle invasion[2]. Early diagnosis, when the disease is still at a localized stage, increases the chance of successful treatment. The survival rate for in situ urinary bladder cancer is 97%[3]. Tissue-based biomarkers for early diagnosis of bladder cancer are of major clinical need. Urothelial carcinoma (UC) of the bladder typically originates in the urothelium and accounts for more than 90% of all bladder tumors. Biomarkers expressed in the urothelium, such as uroplakins (UP), could be predictive markers of UC of the bladder. Pathologists have used UP III [AU1] to establish urothelial origin of the bladder; however, use of AU1 is limited due to its poor sensitivity.[4]

UPII [BC21] exhibited superior specificity, making it useful in the identification of tumors of urothelial origin.

Recent studies have shown a monoclonal mouse anti-UPII antibody [BC21] to demonstrate increased sensitivity in UC of the bladder when compared to mouse monoclonal UPIII antibodies [BC17 and AU1]. UPII [BC21] exhibited superior specificity, thus making it useful in the identification of tumors of urothelial origin. The highly sensitive and specific UP II [BC21] may serve as a promising tissue-based biomarker in the differential diagnosis of UC and in the detection of tumor of unknown origin, specifically in cases of metastatic bladder cancer that has spread to the prostate.[4]

The combination of GATA-3 (nuclear) and UPII (cytoplasmic/membrane) in a single color format increased both specificity and sensitivity in a single section[7,8]. GATA-3 increases the overall specificity when compared to UPII alone and it does not stain prostate adenocarcinoma or renal cell carcinoma[4,5]. Thus, two antigens, GATA-3 (nuclear) and UPII (cytoplasmic/membrane), can be recognized and discerned on the same section by a single color. This cocktail has been formulated for manual and automated IHC on a variety of platforms.



UP II (BC21) and UP III (BC17 and AU1) staining on serial sections of the same bladder cancer tissue (Grade II)[8]

Comparsion of UP II (BC21) and UP III (BC17 and AU1) on the UC of the Bladder[8]

Cancer Type	Grade	Specimens	+ Specimens	% Positive	- Specimens	% Negative
UP II [BC21]	Grade I, II & III	56	44	79%	12	21%
UP III [BC17]	Grade I, II & III	56	31	55%	25	45%
UP III [UA1]	Grade I, II & III	56	19	34%	37	66%
UP II [BC21]	Grade II	34	27	79%	7	21%
UP III [BC17]	Grade II	34	18	53%	16	47%
UP III [UA1]	Grade II	34	9	26%	25	74%
UP II [BC21]	Grade IIII	10	6	*60%	4	40%
UP III [BC17]	Grade IIII	10	6	60%	4	40%
UP III [UA1]	Grade IIII	10	4	40%	6	60%

*Total number of positive tumors cells stained was much higher in BC21 vs. BC17 and AU1

To learn more about Uroplakin II [BC21] or the Uroplakin II + GATA-3 cocktail please contact Biocare Medical at 800-799-9499 or visit the following links: https://biocare.net/product/uroplakin-ii-antibody/; https://biocare.net/product/gata-3-uroplakin-ii/.

1. Centers for Disease Control and Prevention. US Cancer Statistics: Data Visualizations 2016. 2. Frantzi M, Makridakis M, Vlahou A. Biomarkers for bladder cancer aggressiveness. Curr Opin Urol. 2012 Sep;22(5):390-6. 3. Jemal A, *et al*. Cancer statistics, 2010. CA Cancer J Clin. 2010 Sep-Oct;60(5):277-300. 4. L Hoang, *et al*. A newly developed uroplakin II antibody with increased sensitivity in urothelial carcinoma of the bladder. Arch Pathol Lab Med. 2014 Jul;138(7):943-9 5. Mohammed KH, Siddiqui MT, Cohen C. GATA3 immunohistochemical expression in invasive urothelial carcinoma. Urol Oncol. 2016 Oct;34(10):432. May 27. 6. Miyamoto H, Izumi K, Yao JL, Li Y, Yang Q, McMahon LA, Gonzalez- Roibon N, Hicks DG, Tacha D, Netto GJ. GATA binding protein 3 is down-regulated in bladder cancer yet strong expression is an independent predictor of poor prognosis in invasive tumor. Hum Pathol. 2012 Nov;43(11):2033-40. 7. Leivo MZ, Elson PJ, Tacha DE, Delahunt B, Hansel DE. A combination of p40, GATA-3 and uroplakin II shows utility in the diagnosis and prognosis of muscle-invasive urothelial carcinoma. Pathology. 2016 Oct;48(6):543-9. 8. Hoang LL, Tacha D, Bremer RE, Haas TS, Cheng L. Uroplakin II (UPII), GATA3, and p40 are Highly Sensitive Markers for the Differential Diagnosis of Invasive Urothelial Carcinoma. Appl Immunohistochem Mol Morphol. 2015 Nov-Dec;23(10):711-6.