

OVEREXPRESSION OF CTAG1B IS A POTENTIAL BIOMARKER IN BLADDER CANCER

Siti Farizan Mansor^{1,2}, Radha Kodiappan^{1,9}, Chan Soon Choy³, Mohd. Khairul Anuar Md. Akhir¹, Chin Fee Wai^{1,3}, Shalini Vellasamy⁸, Rozita Rosli^{1,4}, Syahril Abdullah¹, Huzlinda Husin⁶, Fauzah Abd. Ghani⁶, Rosna Yumus⁷, Azad Hassan Abdul Razack⁵, Ong Teng Aik⁵, Abhimanyu Veerakumarasivam^{1,3,4*}

¹Medical Genetics Laboratory, Genetics & Regenerative Medicine Research Centre, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Serdang, Selangor Darul Ehsan.

²Department of Medical Laboratory Technology, Faculty of Health Sciences, Universiti Teknologi MARA, Puncak Alam, Selangor Darul Ehsan.

³Perdana University Graduate School of Medicine, Perdana University, Serdang, Selangor Darul Ehsan.

⁴UPM-MAKNA Cancer Research Laboratory, Institute of Bioscience, Universiti Putra Malaysia, Serdang, Selangor Darul Ehsan.

⁵Department of Surgery, Faculty of Medicine, University of Malaya, Kuala Lumpur, Wilayah Persekutuan.

⁶Department of Pathology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Serdang, Selangor Darul Ehsan.

⁷Department of Pathology, Hospital Kuala Lumpur, Jalan Pahang Kuala Lumpur, Wilayah Persekutuan.

⁸Department of Biomedical Sciences, Faculty of Medicine, Universiti Malaya, Kuala Lumpur, Wilayah Persekutuan.

⁹Perdana University Royal College of Surgeons in Ireland, Perdana University, Serdang, Selangor Darul Ehsan.

*Corresponding author: abhimanyu@upm.edu.my / drabhi@perdanauniversity.edu.my

Urothelial cell carcinoma (UCC) is the most common form of bladder cancer and is associated with the need for life-long surveillance once a patient is diagnosed with a non-invasive disease. Due to the long-term risk of recurrence and the need for life-long routine monitoring and therapy, the cost per UCC patient from diagnosis to death is the highest of all cancers. The development of non-invasive biomarkers of recurrence and progression can increase survival, decrease treatment costs and improve patient quality of life. However, to date, no biomarker(s) have been endorsed for the use in the clinical management of UCC, especially in predicting risk of progression and recurrence. CTAG1B was previously found to be highly expressed in high-stage and grade bladder cancer, albeit in Caucasian cohorts. However, despite its potential as a target for cancer immunotherapy, the effect of expression modulation on cellular phenotypes has never been reported. In this study, we overexpressed CTAG1B in an invasive bladder cancer cell line, EJ28 after we confirmed that this cell line minimally expressed CTAG1B. The cells were transfected with CTAG1B-pcDNA3.1(-) and the level of expression was confirmed by qRT-PCR. Once the expression was confirmed to persist up to 72h post-transfection, the transfected cells were subjected to various phenotypic assays. In addition, the pattern of CTAG1B expression in a cohort of Malaysian bladder cancer paraffin-embedded tissues was also determined using immunohistochemistry. The effect of CTAG1B overexpression on the cell cycle, migratory and proliferative potential was observed. The changes in phenotype were compared with that of untransfected and mock controls. CTAG1B was overexpressed 20 times as compared to the untransfected and mock controls in the transfected cells. CTAG1B overexpression resulted in cells to migrate slower at 24h post-transfection but proliferate significantly faster after 72-96h post-transfection. In addition, CTAG1B was more frequently expressed in advanced bladder cancer stages and grades. The findings from this study contribute to the current knowledge of CTAG1B's role in tumourigenesis. Further functional studies will contribute towards realising the potential of CTAG1B as a biomarker for predicting the risk of progression and recurrence of bladder cancer.