SUPPLEMENTARY MATERIALS AND METHODS

Patients and tumor specimens

This study was approved by the institutional review board (IRB10302015) of Chi Mei Medical Center. Informed consent has been obtained for those enrolled into BioBank. For imunohistochemical study and statistical analysis, we retrieved urothelial carcinoma cases from the archives of Chi Mei Medical Center between 1996 and 2004. A total of 635 consecutively treated well-characterized urothelial carcinomas, not otherwise specified, were enrolled including 340 tumors originating from the upper urinary tract and 295 arising from the urinary bladder. Other histological variants were excluded. All patients were treated initially by surgical intervention with curative intent. All patients with UTUC received nephroureterectomy or segmental ureterectomy and excision of bladder cuff with or without regional lymph node dissection. No patient received kidney-sparing surgery for his or her UTUC. For patients with superficial UBUC (pTa and pT1), transurethral resection of bladder tumor (TURBT) with or without intravesical BCG was undergone. Patients with muscle-invasive UBUC were treated with radical cystectomy with bilateral pelvic lymphadenectomy. As a rule, patients with urinary bladder urothalial carcinoma (UBUC) with pT3 or pT4 tumors or with nodal involvement received cisplatin-based adjuvant chemotherapy. However, only 29 of 106 pT3 or pT4 and nodal positive patients with upper tract urothelial carcinoma (UTUC) received cisplatin-based adjuvant chemotherapy. Neo-adjuvant chemotherapy was not introduced to the patients with either UBUC or UTUC in our cohort. The criteria for clinicopathological evaluation were essentially identical to those in our previous works [22]. Two pathologists (IWC & CFL) re-evaluated hematoxylin-eosin sections of all cases. Briefly speaking, the evaluation of histological grade was based on 2004 World Health Organization/International Society of Urological Pathology (WHO/ISUP) classification.[1] Vascular and perineural invasion was evaluated directly on H&E slides, where tumor thrombi in vascular channels or tumor nests around the nerve bundles were seen. The mitotic rate was assessed by calculation of mitotic figures per 10 high-power fields (HPFs; 400x magnification level of light microscope). Mitotic rate less than 10 per 10 HPFs was defined as low mitotic activity, and 10 or more was defined as high mitotic activity.

SUPPLEMENTARY FIGURE

Figure S1. By subdividing 93 cases from GSE31684 into *NDN* high-expression (n=37) and low-expression (n=56) clusters, its expression level significantly predicts disease-specific survival (p=0.0059).