

**Supplemental Data Table 1A.** Relative mRNA expression levels of the uPA system members in tissue of PCa patients

|                        | No. of patients | Median <sup>1</sup>     | Range        |
|------------------------|-----------------|-------------------------|--------------|
| <b>uPA</b>             |                 | <b><i>P</i> = 0.004</b> |              |
| Malignant tissue       | 132             | 0.38                    | 0.08 – 11.5  |
| Non- malignant tissue  | 125             | 0.51                    | 0.12 – 2.39  |
| <b>uPAR</b>            |                 | <i>P</i> = 0.604        |              |
| Malignant tissue       | 132             | 0.47                    | 0.04 – 8.61  |
| Non- malignant tissue  | 125             | 0.54                    | 0.00 - 25.8  |
| <b>PAI-1</b>           |                 | <i>P</i> = 0.261        |              |
| Malignant tissue       | 132             | 1.75                    | 0.09 – 121.7 |
| Non- malignant tissue  | 125             | 1.31                    | 0.09 – 37.4  |
| <b>Ratio uPA/PAI-1</b> |                 | <i>P</i> = 0.036*       |              |
| Malignant tissue       | 132             | 0.21                    | 0.01 – 3.81  |
| Non- malignant tissue  | 125             | 0.33                    | 0.03 – 3.15  |

mRNA expression levels of the uPA system members are normalized to *TATA box binding protein (TBP)* gene expression. The Bonferroni-adjusted threshold for significance is at  $\alpha=0.0125$ . <sup>1</sup> Mann-Whitney test, \* Wilcoxon rank test.

**Supplemental Data Table 1B.** Antigen concentrations of the uPA system members in serum of PCa and BPH patients

|              | No. of patients | Median <sup>1</sup>        | Range          |
|--------------|-----------------|----------------------------|----------------|
| <b>uPA</b>   |                 | <i>P</i> = 0.303           |                |
| PCa serum    | 81              | 0.68                       | 0.43 – 1.88    |
| BPH serum    | 36              | 0.68                       | 0.51 – 2.21    |
| <b>uPAR</b>  |                 | <i>P</i> = 0.692           |                |
| PCa serum    | 81              | 0,76                       | 0,20 – 26,2    |
| BPH serum    | 36              | 0.79                       | 0.05 – 1.46    |
| <b>PAI-1</b> |                 | <i>P</i> = 0.310           |                |
| PCa serum    | 81              | 1347,9                     | 557,5 – 2714,0 |
| BPH serum    | 36              | 1385.5                     | 940.9 – 5930.2 |
| <b>PSA</b>   |                 | <b><i>P</i> &lt; 0.001</b> |                |
| PCa serum    | 81              | 9.21                       | 1.29 – 51.9    |
| BPH serum    | 36              | 1.78                       | 0.22 – 17.5    |

Antigen concentration in serum is given in ng/ml; The Bonferroni-adjusted threshold for significance is at  $\alpha=0.0125$ . <sup>1</sup> Mann-Whitney-Test.

**Supplemental Data Table 2.** Overview of literature including the present study: Association of tissue RNA or protein levels of uPA gene family members with clinicopathological parameters in prostate cancer.

| Factor                                  | Number of patients  | Method                               | Significant association / Remarks   | Reference                   |
|---|---|--------------------------------------|---|-----------------------------|
| <b>Tissue RNA</b>                       |   |                                      |   |                             |
| <i>uPA</i>                              | 13 locally recurrent hormone refractory PCa<br>PCa cell lines: PC-3, LNCaP, DU145 | qPCR;<br>Southern hybridization      | <i>uPA</i> mRNA with <i>uPA</i> gene amplification in refractory PCa<br>PC-3 with gene amplification more sensitive to uPA inhibitor  | Helenius <i>et al.</i> 2001 |
| <i>uPA</i> , <i>uPAR</i>                | 25 high grade PCa   | <i>in situ</i> hybridization;<br>IHC | <i>uPA</i> and <i>uPAR</i> expression in PCa and BPH;<br><i>uPA</i> and <i>uPAR</i> expression predominantly in adenocarcinoma cells of high grade PCa;<br>Stromal cells were mostly negative for both <i>uPA</i> & <i>uPAR</i>   | Gavrilov <i>et al.</i> 2001 |
| <i>uPA</i> , <i>uPAR</i> , <i>PAI-1</i> | 44 PCa,<br>23 BPH   | qPCR                                 | Increased expression of <i>uPA</i> and <i>PAI-1</i> in malignant compared with non-malignant prostate tissue;<br><i>uPAR</i> and <i>PAI-1</i> with higher GS  | Riddick <i>et al.</i> 2005  |
| <i>uPAR</i> , <i>PAI-1</i>              | stromal cell cultures   |                                      | <i>uPAR</i> and <i>PAI-1</i> were primarily expressed by stromal cells  | Riddick <i>et al.</i> 2005  |
| <i>uPA</i> , <i>uPAR</i> , <i>PAI-1</i> | 16 PCa ,<br>9 BPH   | <i>in situ</i> hybridization; IHC    | <i>uPA</i> , <i>uPAR</i> and <i>PAI-1</i> expression in both PCa and BPH;<br><i>uPA</i> and <i>uPAR</i> expression predominantly in macrophages,<br><i>PAI-1</i> expression mostly in scattered fibroblast-like cells, few in macrophages;<br>No association between <i>uPA</i> , <i>uPAR</i> or <i>PAI-1</i> expression and GS | Usher <i>et al.</i> 2005    |
| <i>uPA</i> , <i>uPAR</i> , <i>PAI-1</i> | 132 PCa   | qPCR                                 | Strong correlation between expression levels of all three <i>uPA</i> system members;<br><i>uPA</i> with higher GS   | Present study               |
| <b>Tissue Protein</b>                   |   |                                      |   |                             |
| <i>uPA</i> , <i>uPAR</i>                | 120 clinically localized PCa  | IHC                                  | <i>uPA</i> and <i>uPAR</i> with GS, tumor stage, surgical margin status;<br><i>uPA</i> with lymph node status   | Cozzi <i>et al.</i> 2006    |
| <i>uPA</i> , <i>PAI-1</i> , <i>uPAR</i> | 230 clinically localized PCa  | IHC                                  | Combined <i>uPA/PAI-1</i> values with extraprostatic extension and seminal vesicle involvement;<br><i>uPA</i> and <i>PAI-1</i> with biochemical RFS and aggressive disease recurrence; combined <i>uPA/PAI-1</i> values independent predictor   | Gupta <i>et al.</i> 2008    |

|                            |   |                |   |                     |
|----------------------------|---|----------------|---|---------------------|
|                            |   |                | for biochemical RFS and aggressive disease  |                     |
| uPA, PAI-1, uPAR           | 153 PCa with organ-confined disease   | IHC            | uPA and uPAR with tumor stage, GS, lymphatic invasion, surgical margin status, and lymph node metastasis; PAI-1 with tumor stage and surgical margin status; uPA, uPAR and PAI-1 with shorter biochemical RFS; uPA independent predictor for biochemical RFS  | Kumano et al. 2009  |
| <b>Blood-based Protein</b> |   |                |   |                     |
| uPA, suPAR                 | 72 PCa (65% metastatic), 62 BPH, 54 healthy donors  | EIA (Serum)    | Increased uPA and uPAR levels in PCa compared to BPH patients; uPA and uPAR with tumor stage and metastasis; Either uPA or uPAR or both with OS   | Miyake et al. 1999  |
| uPA, suPAR                 | 429 clinically localized PCa, 19 PCa with lymph node metastasis, 10 PCa with bone metastases, 44 healthy donors | EIA (Plasma)   | uPA and uPAR with tumor stage, GS, lymph node metastasis and lymphatic invasion; uPA and uPAR with features of biologically aggressive PCa, disease progression after radical prostatectomy and metastasis; uPA and uPAR in PC patients with bone metastasis>PCa with lymph node metastasis> localized PCa> healthy men | Shariat et al. 2007 |
| uPA, suPAR, PAI-1          | 423 clinically localized PCa  | EIA (Serum)    | uPA and uPAR with biochemical RFS   | Shariat et al. 2008 |
| suPAR                      | 131 metastatic PCa  | TR-FIA (Serum) | Each of the suPAR forms with shorter OS   | Almasi et al. 2011  |
| uPA, suPAR, PAI-1          | 81 PCa, 36 BPH  | EIA (Serum)    | uPAR with shorter OS  | Present study       |

Table was modified according to Schmitt et al. 2010; if not indicated otherwise, high marker levels were associated with clinical parameters;

Abbreviations: PCa: Prostate Cancer; BPH: benign prostatic hyperplasia; qPCR: quantitative PCR; EIA: Enzyme-linked immunosorbent assay; TR-FIA: Time-resolved fluorescence immunoassay; IHC: immunohistochemistry; GS: Gleason score; OS: Overall survival; RFS: recurrence-free survival