

**Supplementary table S1. Survival analysis with Cox regression of clinical parameters**

| Outcome | Variable  | Univariate analysis |         | Multivariable analysis |         |
|---------|-----------|---------------------|---------|------------------------|---------|
|         |           | HR (95% CI)         | P value | HR (95% CI)            | P value |
| Relapse | Age       | 1.00 (0.97, 1.03)   | 0.97    | 1.00 (0.97, 1.03)      | 0.86    |
|         | ISUP      | 1.55 (1.10, 2.17)   | 0.01    | 1.51 (1.07, 2.14)      | 0.02    |
|         | serum PSA | 1.08 (0.96, 1.22)   | 0.19    | 1.05 (0.93, 1.19)      | 0.44    |
| Death   | Age       | 1.02 (0.99, 1.06)   | 0.2     | 1.02 (0.99, 1.06)      | 0.22    |
|         | ISUP      | 1.41 (0.97, 2.06)   | 0.08    | 1.44 (0.97, 2.13)      | 0.07    |
|         | serum PSA | 1.07 (0.94, 1.22)   | 0.33    | 1.02 (0.89, 1.17)      | 0.78    |

**Supplementary table S2. Distribution of cases in quartiles of staining scores**

|                  | Ki67        |             |             |          |
|------------------|-------------|-------------|-------------|----------|
|                  | Q4          | Q3          | Q2          | Q1       |
| PSA              | 32.9 - 71.2 | 19.1 - 32.9 | 11.2 - 19.1 | 1 - 11.2 |
| Q1<br>0 - 5.62   | 11          | 7           | 2           | 4        |
| Q2<br>5.62 - 9.4 | 5           | 10          | 5           | 5        |
| Q3<br>9.4-11     | 3           | 3           | 10          | 7        |
| Q4<br>11-12      | 2           | 3           | 8           | 7        |

Table S3a. Genes associated with Ki67 Score

| SYMBOL    | logFC | adj. P-value | Overlapping with |              |
|-----------|-------|--------------|------------------|--------------|
|           |       |              | PSA              | Ki67/PSA (-) |
| UBE2T     | 0.48  | 9.55E-11     | x                | x            |
| ANLN      | 0.35  | 2.19E-10     | x                | x            |
| MK        | 0.35  | 7.36E-10     | x                | x            |
| PVT1      | 0.44  | 4.27E-09     | x                | x            |
| HIST1H2BM | 0.44  | 2.34E-08     | x                | x            |
| CKAP2L    | 0.33  | 9.07E-08     | x                | x            |
| E2F7      | 0.23  | 1.31E-07     | x                | x            |
| PTTG1     | 0.18  | 6.64E-07     | x                | x            |
| TOP2A     | 0.39  | 7.45E-06     | x                | x            |
| NUSAP1    | 0.21  | 7.77E-06     | x                | x            |
| DLGAP5    | 0.19  | 1.12E-05     | x                | x            |
| CENPF     | 0.23  | 1.21E-05     | x                | x            |
| MIR1206   | 0.44  | 1.49E-05     | x                | x            |
| KIF20A    | 0.23  | 1.92E-05     | x                | x            |
| CKS2      | 0.34  | 3.06E-05     | x                | x            |
| PPA1      | 0.23  | 3.06E-05     | x                | x            |
| PLK1      | 0.19  | 3.06E-05     | x                | x            |
| HIST1H4C  | 0.20  | 3.46E-05     | x                | x            |
| Y_RNA     | 0.33  | 3.74E-05     | x                | x            |
| PARBP1    | 0.23  | 4.97E-05     | x                | x            |
| PRC1      | 0.27  | 5.12E-05     | x                | x            |
| PRR11     | 0.31  | 6.73E-05     | x                | x            |
| HIST2H4A  | 0.34  | 6.73E-05     | x                | x            |
| TPX2      | 0.23  | 7.54E-05     | x                | x            |
| HJURP     | 0.28  | 7.72E-05     | x                | x            |
| NCAPG     | 0.21  | 8.79E-05     | x                | x            |
| KIF23     | 0.16  | 8.79E-05     | x                | x            |
| HIST1H2AG | 0.25  | 1.03E-04     | x                | x            |
| EZH2      | 0.30  | 1.05E-04     | x                | x            |
| HIST2H4B  | 0.32  | 2.12E-04     | x                | x            |
| PTDSS1    | 0.25  | 3.12E-04     |                  |              |
| ATAD2     | 0.20  | 4.14E-04     |                  | x            |
| TACC3     | 0.17  | 5.32E-04     |                  | x            |
| CDKN3     | 0.28  | 5.62E-04     | x                | x            |
| SHCBP1    | 0.25  | 5.62E-04     |                  | x            |
| STMN1     | 0.31  | 6.39E-04     | x                | x            |
| ARHGAP11B | 0.18  | 6.44E-04     | x                | x            |
| POLQ      | 0.18  | 6.44E-04     |                  | x            |
| HIST1H4H  | 0.16  | 1.45E-03     | x                | x            |
| SNRPE     | 0.23  | 1.48E-03     | x                | x            |
| HMGB2     | 0.22  | 1.77E-03     | x                | x            |
| C7orf73   | 0.16  | 1.79E-03     | x                | x            |
| RPS17P2   | 0.12  | 2.18E-03     |                  | x            |
| TAF1D     | 0.22  | 2.32E-03     |                  | x            |
| CLSPN     | 0.15  | 2.75E-03     | x                | x            |
| PBK       | 0.10  | 3.19E-03     | x                | x            |
| AGO2      | 0.19  | 3.32E-03     | x                | x            |
| LDHA      | 0.22  | 3.72E-03     | x                | x            |
| MYC       | 0.23  | 4.31E-03     |                  | x            |
| KNTC1     | 0.18  | 4.49E-03     | x                | x            |

Top 50 genes (ranked on p-value) associated with immunoreactivity score for Ki67. Unnotated transcripts and transcripts identified by AceView are omitted

Table S3b. Genes negatively associated with Ki67 Score

| SYMBOL        | logFC | adj. P-value | Overlapping with |              |
|---------------|-------|--------------|------------------|--------------|
|               |       |              | PSA              | Ki67/PSA (-) |
| HMG2P46       | -0.51 | 4.85E-03     | x                | x            |
| MATN2         | -0.28 | 2.32E-02     |                  | x            |
| CACNA1D       | -0.27 | 3.85E-02     |                  |              |
| FAIM2         | -0.23 | 4.02E-03     |                  | x            |
| MLPH          | -0.23 | 3.26E-03     | x                | x            |
| RGS17         | -0.21 | 8.16E-03     |                  | x            |
| ABCA8         | -0.21 | 0.0395       |                  | x            |
| CTA-280A3.1   | -0.21 | 0.0247       |                  |              |
| TXNRD2        | -0.17 | 0.0242       | x                | x            |
| LOC728730     | -0.17 | 0.0187       |                  |              |
| PHOSPHO2      | -0.17 | 0.0329       |                  | x            |
| ANXA3         | -0.17 | 0.0407       | x                | x            |
| RNU6-321P     | -0.16 | 0.0479       |                  | x            |
| ATXN1         | -0.14 | 0.0178       |                  |              |
| ASAP3         | -0.16 | 0.0178       |                  |              |
| JAG1          | -0.16 | 0.0349       |                  | x            |
| TBC1D8B       | -0.15 | 0.0083       | x                | x            |
| TNK2-AS1      | -0.13 | 0.0245       |                  | x            |
| PTPRN2        | -0.13 | 0.0242       |                  | x            |
| RP5-1057120.5 | -0.10 | 0.0287       |                  | x            |
| MAGEE1        | -0.13 | 0.0242       |                  | x            |
| FAM19A2       | -0.12 | 0.0460       |                  |              |
| SNORA11       | -0.08 | 0.0216       |                  | x            |
| ITGA9-AS1     | -0.11 | 0.0479       | x                | x            |

Table S4a. Genes associated with PSA Score

| SYMBOL       | logFC | adj. P-value | Overlapping with |              |
|--------------|-------|--------------|------------------|--------------|
|              |       |              | Ki67 (-)         | Ki67/PSA (-) |
| HMGN2P46     | 1.09  | 6.34E-09     | x                | x            |
| KLK3         | 0.58  | 1.39E-05     |                  | x            |
| RN7SL674P    | 0.53  | 3.02E-05     |                  | x            |
| SLC30A4      | 0.66  | 3.82E-05     |                  | x            |
| C8orf34-AS1  | 0.27  | 3.31E-04     |                  |              |
| MLPH         | 0.36  | 3.87E-04     | x                | x            |
| GREB1        | 0.41  | 4.16E-04     |                  | x            |
| FOLH1B       | 0.88  | 4.58E-04     |                  | x            |
| FAM13C       | 0.35  | 5.74E-04     |                  | x            |
| KLK2         | 0.44  | 9.56E-04     |                  | x            |
| TRPM8        | 0.63  | 1.15E-03     |                  | x            |
| OR51C1P      | 0.91  | 1.70E-03     |                  | x            |
| HSPE1P25     | 0.17  | 1.73E-03     |                  | x            |
| PTPN13       | 0.31  | 1.73E-03     |                  |              |
| OR51E2       | 0.83  | 2.42E-03     |                  | x            |
| PCA3_1       | 1.08  | 3.14E-03     |                  |              |
| RDH11        | 0.42  | 3.63E-03     |                  | x            |
| FOLH1        | 0.80  | 4.08E-03     |                  | x            |
| TSPAN1       | 0.45  | 4.51E-03     |                  |              |
| ANXA3        | 0.27  | 5.74E-03     | x                | x            |
| GLMP         | 0.29  | 5.80E-03     |                  | x            |
| ACSM1        | 0.57  | 5.96E-03     |                  | x            |
| POTEH-AS1    | 0.47  | 5.96E-03     |                  |              |
| LOC101927752 | 0.27  | 5.96E-03     |                  |              |
| LIFR         | 0.41  | 7.89E-03     |                  |              |
| PHKB         | 0.24  | 8.98E-03     |                  |              |
| PCA3         | 0.54  | 0.0109       |                  |              |
| CIB1         | 0.23  | 0.0114       |                  |              |
| H2AFJ        | 0.23  | 0.0114       |                  | x            |
| SEMA4A       | 0.15  | 0.0115       |                  |              |
| PHF12        | 0.19  | 0.0115       |                  | x            |
| TTC6         | 0.38  | 0.0123       |                  |              |
| TSTD3        | 0.30  | 0.0129       |                  |              |
| NRG4         | 0.64  | 0.0134       |                  | x            |
| RANBP3L      | 0.38  | 0.0147       |                  |              |
| RNF14        | 0.18  | 0.0152       |                  |              |
| ITGA9-AS1    | 0.16  | 0.0156       | x                | x            |
| LTBP4        | 0.31  | 0.0158       |                  |              |
| SESN1        | 0.30  | 0.0161       |                  |              |
| EPHX2        | 0.21  | 0.0163       |                  |              |
| ERICH5       | 0.16  | 0.0167       |                  |              |
| ARHGAP29     | 0.32  | 0.0177       |                  | x            |
| MAN1C1       | 0.24  | 0.0182       |                  |              |
| ELK4         | 0.41  | 0.0203       |                  |              |
| SLC45A3      | 0.32  | 0.0228       |                  |              |
| SEPT14P17    | 0.21  | 0.0245       |                  |              |
| ADGRL2       | 0.35  | 0.0247       |                  |              |
| C15orf48     | 0.35  | 0.0249       |                  |              |
| HSF4         | 0.15  | 0.0257       |                  |              |
| CPLX3        | 0.28  | 0.0270       |                  | x            |

Table S4b. Genes negatively associated with PSA Score

| SYMBOL    | logFC | adj. P-value | Overlapping with |          |
|-----------|-------|--------------|------------------|----------|
|           |       |              | Ki67             | Ki67/PSA |
| PARPBP    | -0.41 | 6.34E-09     | x                | x        |
| E2F8      | -0.44 | 2.42E-08     | x                | x        |
| CKAP2L    | -0.47 | 2.28E-07     | x                | x        |
| KIF23     | -0.27 | 3.08E-07     | x                | x        |
| HIST1H3B  | -0.58 | 5.78E-07     | x                | x        |
| PTTG1     | -0.26 | 1.19E-06     | x                | x        |
| KIF18A    | -0.22 | 2.30E-06     | x                | x        |
| UBE2T     | -0.56 | 8.57E-06     | x                | x        |
| PRR11     | -0.48 | 1.36E-05     | x                | x        |
| TTK       | -0.41 | 1.59E-05     | x                | x        |
| HIST1H1E  | -0.27 | 1.77E-05     | x                | x        |
| CENPF     | -0.32 | 3.02E-05     | x                | x        |
| PPA1      | -0.33 | 3.19E-05     | x                | x        |
| NCAPG     | -0.31 | 5.50E-05     | x                | x        |
| HIST1H2AI | -0.30 | 5.50E-05     | x                | x        |
| TOP2A     | -0.53 | 6.43E-05     | x                | x        |
| SUPV3L1   | -0.23 | 7.45E-05     |                  |          |
| E2F7      | -0.28 | 7.68E-05     |                  | x        |
| DGAT2     | -0.27 | 7.68E-05     | x                | x        |
| STMN1     | -0.47 | 9.40E-05     | x                | x        |
| KIAA1524  | -0.21 | 9.70E-05     | x                | x        |
| HIST1H4A  | -0.48 | 1.13E-04     |                  | x        |
| DLGAP5    | -0.25 | 1.16E-04     | x                | x        |
| HIST1H3I  | -0.40 | 1.65E-04     |                  | x        |
| CHEK1     | -0.25 | 1.75E-04     |                  | x        |
| ARHGAP11B | -0.27 | 3.31E-04     | x                | x        |
| NUSAP1    | -0.27 | 3.58E-04     | x                | x        |
| HIST2H2AB | -0.28 | 3.73E-04     | x                | x        |
| ANLN      | -0.37 | 3.76E-04     | x                | x        |
| MK        | -0.37 | 4.58E-04     | x                | x        |
| HIST2H4B  | -0.44 | 4.93E-04     | x                | x        |
| HIST2H4A  | -0.45 | 5.01E-04     | x                | x        |
| SMC4      | -0.30 | 5.05E-04     | x                | x        |
| TUBBP6    | -0.16 | 5.22E-04     |                  |          |
| E2F3      | -0.27 | 5.33E-04     |                  |          |
| HIST1H2AG | -0.34 | 6.22E-04     | x                | x        |
| LDHA      | -0.33 | 6.22E-04     | x                | x        |
| HIST1H3A  | -0.27 | 7.28E-04     |                  | x        |
| PSMD14    | -0.20 | 7.42E-04     |                  | x        |
| MIR1206   | -0.54 | 9.98E-04     | x                | x        |
| CCNB2     | -0.27 | 9.98E-04     |                  | x        |
| HIST1H4C  | -0.25 | 9.98E-04     | x                | x        |
| TUBA1C    | -0.22 | 1.05E-03     | x                | x        |
| DBF4      | -0.22 | 1.15E-03     | x                | x        |
| HIST1H2BJ | -0.27 | 1.21E-03     | x                | x        |
| PRC1      | -0.34 | 1.26E-03     | x                | x        |
| CDKN3     | -0.38 | 1.45E-03     | x                | x        |
| PNP       | -0.26 | 1.50E-03     |                  | x        |
| C3orf67   | -0.28 | 1.69E-03     | x                | x        |
| PLK1      | -0.23 | 1.71E-03     | x                | x        |

Top 50 genes (ranked on p-value) associated with immunoreactivity score for PSA. Unnotated transcripts and transcripts identified by AceView are omitted

**Table S5a. Genes associated with Ki67/PSA**

| SYMBOL    | logFC | adj. P-value | Overlapping with<br>PSA (-) Ki67 |   |
|-----------|-------|--------------|----------------------------------|---|
| UBE2T     | 0.35  | 2.00E-13     | x                                | x |
| CKAP2L    | 0.25  | 6.36E-12     | x                                | x |
| ANLN      | 0.24  | 2.14E-11     | x                                | x |
| MK        | 0.25  | 6.64E-11     | x                                | x |
| PTTG1     | 0.14  | 9.82E-11     | x                                | x |
| PARPBP    | 0.20  | 4.26E-10     | x                                | x |
| E2F7      | 0.17  | 5.77E-10     | x                                | x |
| KIF23     | 0.13  | 8.42E-09     | x                                | x |
| PVT1      | 0.29  | 8.81E-09     | x                                | x |
| HIST1H2BM | 0.30  | 1.20E-08     | x                                | x |
| TOP2A     | 0.30  | 1.20E-08     | x                                | x |
| CENPF     | 0.18  | 1.20E-08     | x                                | x |
| PPA1      | 0.18  | 3.06E-08     | x                                | x |
| DLGAP5    | 0.14  | 3.06E-08     | x                                | x |
| PRR11     | 0.25  | 3.49E-08     | x                                | x |
| NUSAP1    | 0.16  | 4.43E-08     | x                                | x |
| NCAPG     | 0.17  | 1.34E-07     | x                                | x |
| MIR1206   | 0.32  | 2.22E-07     | x                                | x |
| HIST2H4A  | 0.26  | 4.98E-07     | x                                | x |
| HIST1H4C  | 0.15  | 4.98E-07     | x                                | x |
| KIF20A    | 0.17  | 5.53E-07     | x                                | x |
| PLK1      | 0.14  | 6.23E-07     | x                                | x |
| Y_RNA     | 0.24  | 6.74E-07     | x                                | x |
| PRC1      | 0.20  | 7.77E-07     | x                                | x |
| HIST1H2AG | 0.19  | 8.79E-07     | x                                | x |
| STMN1     | 0.25  | 1.01E-06     | x                                | x |
| E2F8      | 0.19  | 1.07E-06     | x                                | x |
| HIST2H4B  | 0.24  | 1.10E-06     | x                                | x |
| HIST1H3B  | 0.26  | 1.19E-06     | x                                | x |
| EZH2      | 0.23  | 1.84E-06     | x                                | x |
| ARHGAP11B | 0.14  | 2.10E-06     | x                                | x |
| HJURP     | 0.20  | 4.33E-06     | x                                | x |
| CDKN3     | 0.21  | 6.16E-06     | x                                | x |
| CKS2      | 0.23  | 9.44E-06     | x                                | x |
| TPX2      | 0.16  | 1.10E-05     | x                                | x |
| HIST1H1E  | 0.13  | 1.10E-05     | x                                | x |
| TTK       | 0.19  | 1.32E-05     | x                                | x |
| KIF18A    | 0.10  | 1.32E-05     | x                                | x |
| LDHA      | 0.17  | 1.86E-05     | x                                | x |
| KIAA1524  | 0.10  | 3.44E-05     | x                                | x |
| AGO2      | 0.15  | 3.63E-05     | x                                | x |
| TUBA1C    | 0.12  | 4.24E-05     | x                                | x |
| DBF4      | 0.12  | 4.24E-05     | x                                | x |
| HMGB2     | 0.17  | 4.46E-05     | x                                | x |
| HIST1H2AI | 0.14  | 5.47E-05     | x                                | x |
| HIST2H2AB | 0.13  | 8.43E-05     | x                                | x |
| SNRPE     | 0.17  | 8.57E-05     | x                                | x |
| PLK4      | 0.12  | 8.57E-05     | x                                | x |
| SMC4      | 0.15  | 9.05E-05     | x                                | x |
| HIST1H4H  | 0.12  | 9.05E-05     | x                                | x |

**Table S5b. Genes negatively associated with Ki67/PSA**

| SYMBOL        | logFC | adj. P-value | Overlapping with<br>PSA Ki67 (-) |   |
|---------------|-------|--------------|----------------------------------|---|
| HMGN2P46      | -0.48 | 6.06E-08     | x                                | x |
| MLPH          | -0.19 | 1.11E-05     | x                                | x |
| SLC30A4       | -0.28 | 2.86E-04     | x                                |   |
| FOLH1B        | -0.40 | 7.11E-04     | x                                |   |
| TBC1D8B       | -0.11 | 7.49E-04     | x                                | x |
| ANXA3         | -0.14 | 9.81E-04     | x                                | x |
| FAIM2         | -0.16 | 1.12E-03     |                                  | x |
| RN7SL674P     | -0.21 | 1.16E-03     |                                  |   |
| RDH11         | -0.20 | 1.46E-03     | x                                |   |
| KLK3          | -0.22 | 2.14E-03     | x                                |   |
| ITGA9-AS1     | -0.09 | 2.14E-03     | x                                | x |
| TXNRD2        | -0.13 | 2.42E-03     | x                                | x |
| OR51E2        | -0.38 | 2.43E-03     | x                                |   |
| GREB1         | -0.17 | 2.47E-03     | x                                |   |
| GLMP          | -0.14 | 2.93E-03     | x                                |   |
| RNU6-321P     | -0.13 | 3.00E-03     |                                  | x |
| TRPM8         | -0.27 | 3.00E-03     | x                                |   |
| LTBP4         | -0.16 | 3.19E-03     |                                  |   |
| MATN2         | -0.21 | 3.55E-03     |                                  | x |
| ARHGAP29      | -0.16 | 4.16E-03     | x                                |   |
| SERHL         | -0.29 | 4.17E-03     |                                  |   |
| OR51C1P       | -0.40 | 4.24E-03     | x                                |   |
| MAGEE1        | -0.09 | 4.38E-03     |                                  | x |
| ZNF577        | -0.16 | 5.84E-03     |                                  |   |
| ABCA8         | -0.16 | 7.96E-03     |                                  | x |
| TNK2-AS1      | -0.09 | 8.11E-03     |                                  | x |
| ACPP          | -0.29 | 8.62E-03     |                                  |   |
| KLK2          | -0.18 | 9.14E-03     | x                                |   |
| PHF12         | -0.09 | 9.95E-03     | x                                |   |
| PTPRN2        | -0.09 | 9.97E-03     |                                  | x |
| CPNE4         | -0.27 | 0.0114       |                                  |   |
| CPLX3         | -0.14 | 0.0118       | x                                |   |
| FOLH1         | -0.34 | 0.0128       | x                                |   |
| RN7SL564P     | -0.06 | 0.0147       | x                                |   |
| GHR           | -0.15 | 0.0148       |                                  |   |
| COG3          | -0.07 | 0.0187       | x                                |   |
| RGMB-AS1      | -0.16 | 0.0200       |                                  |   |
| ACSM1         | -0.24 | 0.0203       | x                                |   |
| ZNF432        | -0.10 | 0.0224       |                                  |   |
| RP5-1057I20.5 | -0.06 | 0.0245       |                                  | x |
| ZNF613        | -0.14 | 0.0254       |                                  |   |
| PHOSPHO2      | -0.11 | 0.0254       |                                  | x |
| SNORA11       | -0.05 | 0.0258       |                                  | x |
| C7            | -0.10 | 0.0268       |                                  |   |
| ARHGEF38      | -0.20 | 0.0290       | x                                |   |
| SERP2         | -0.10 | 0.0299       |                                  |   |
| HSPE1P25      | -0.07 | 0.0333       | x                                |   |
| CIB1          | -0.10 | 0.0336       | x                                |   |
| RGS17         | -0.12 | 0.0339       |                                  | x |
| Y_RNA         | -0.21 | 0.0347       |                                  |   |

Top 50 genes (ranked on p-value) associated with the Ki67/PSA ratio. Unnotated transcripts and transcripts identified by AceView are omitted