Increased angiogenesis is associated with a 32-gene expression signature and 6p21 amplification in aggressive endometrial cancer

Supplementary Material

**Figure 1**: Validation of the 32-gene signature in relation to A: histologic subtype, B: histologic grade, C: FIGO stage in the primary series and correspondingly (D-F) in an external dataset *(NCBI GEO: GSE2109).*
Figure 2: The 32-gene angiogenesis signature and correlation to recurrence-free survival in a validation series according to the Kaplan-Meier method. Number of cases/number of events in parenthesis.
Table S1: Genes differentially expressed between tumors with high versus low vascular proliferation.

| Gene name | Systematic name | Description                                                                 | Fold Change |
|-----------|-----------------|------------------------------------------------------------------------------|-------------|
| **Upregulated genes** |                 |                                                                              |             |
| NFIL3     | NM_005384       | Homo sapiens nuclear factor, interleukin 3 regulated                         | 1.5         |
| FSTL3     | NM_002600       | Homo sapiens follistatin-like 3 (secreted glycoprotein)                      | 1.5         |
| TPM1      | NM_003866       | Homo sapiens tropomyosin 1 (alpha)                                          | 1.5         |
| PDGFb     | NM_002008       | Homo sapiens platelet-derived growth factor beta polypeptide (simian sarcoma viral (v-sis) oncogene homolog) | 1.4         |
| FHL3      | NM_004468       | Homo sapiens four and a half LIM domains 3                                   | 1.4         |
| SERPINH1  | NM_001235       | Homo sapiens serpin peptidase inhibitor, clade H (heat shock protein 47), member 1, | 1.4         |
| ITGB3     | ST3548          | Homo sapiens integrin beta 3 mRNA                                            | 1.3         |
| ARFRP1    | NM_003224       | Homo sapiens ADP-ribosylation factor related protein 1                       | 1.2         |
| RNASE2    | NM_002934       | Homo sapiens ribonuclease, RNase A family, 2 (liver, eosinophil-derived neurotoxin) | 1.2         |
| THCG2740750 | THCG2740750  | Unknown                                                                      | 1.2         |
| KCNQ2     | NM_004516       | Homo sapiens potassium voltage-gated channel, KQT-like subfamily, member 3 | 1.2         |
| SERPINB5  | NM_002639       | Homo sapiens serpin peptidase inhibitor, clade B (ovalbumen), member 5      | 1.2         |
| RNF169    | ENST00000296563 | RING finger protein 169, [Source:Uniprot:SWISSPROT;Acc:Q9NCN4]               | 1.2         |
| HIST1H2BJ | BC014312        | Homo sapiens histone cluster 1, H2bj, mRNA (cDNA clone MGC:22655 IMAGE:4048288) | 1.2         |
| **Downregulated genes** |                 |                                                                              |             |
| FLJ21736  | NM_024922       | Homo sapiens esterase 31                                                    | -1.5        |
| FHT       | NM_002012       | Homo sapiens fragile histidine triad gene                                   | -1.5        |
| ZNF75     | NM_007131       | Homo sapiens zinc finger protein 75 (D8C6) (ZNF75), mRNA [NM_007131]         | -1.5        |
| PGPEP1    | NM_017712       | Homo sapiens pyroglutamyl-peptidase I                                      | -1.4        |
| C20orf74  | NM_020343       | Homo sapiens chromosome 20 open reading frame 74                           | -1.4        |
| DXK17     | NM_006386       | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 17                      | -1.3        |
| ITPK1     | NM_014216       | Homo sapiens inositol 1,3,4-triphosphate 5/6 kinase                         | -1.3        |
| FUK       | NM_145059       | Homo sapiens fusokinase                                                     | -1.3        |
| RBM5      | AF107485        | Homo sapiens LUCA-15 protein                                                | -1.3        |
| LOC442288 | XR_016052       | Homo sapiens similar to 90S ribosomal protein L7a                          | -1.3        |
| RPL7A     | NM_000972       | Homo sapiens ribosomal protein L7a                                          | -1.2        |
| ERBB2IP   | NM_018965       | Homo sapiens erbB2 interacting protein                                      | -1.2        |
| ABHD17A   | NM_031213       | abhydrolase domain containing 17A                                          | -1.2        |
| NPCRD1    | AF159973        | Homo sapiens nasopharyngeal carcinoma down-regulated protein                | -1.2        |
| BC011455  | BC011455        | Homo sapiens cDNA clone IMAGE:4177309, partial cds. [BC011455]              | -1.2        |
| SESN3     | NM_144685       | sestrin 3                                                                   | -1.2        |
| AA609749  | AA609749        | TR-G004804 G004804 Hypothetical 4.7 kD Protein; mRNA sequence [AA609749]     | -1.2        |
| AA399656  | AA399656        | Ovarian granulosa cell 13.0 kD protein HGR74 (Human); mRNA sequence [AA399656] | -1.1        |

*SAM; significance analysis of microarray; FDR <25%.
Table S2. Association between the 32-gene angiogenesis signature and other selected gene expression signatures, related to vascular biology, epithelial-mesenchymal transition and stemness.

| Signature                                      | Spearman’s rho | P-value |
|------------------------------------------------|----------------|---------|
| VEGF signature [1]                             | 0.44           | 0.001   |
| Vascular invasion signature [2]                | 0.19           | 0.10    |
| Wound response signature [3]                   | 0.33           | 0.003   |
| Hypoxia gene signature [4]                     | 0.21           | 0.071   |
| TGFβ gene-response signature [5]               | 0.55           | <0.001  |
| BMI-1 driven signature [6]                     | 0.31           | 0.008   |
REFERENCES TO SUPPLEMENTARY TABLE 2

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