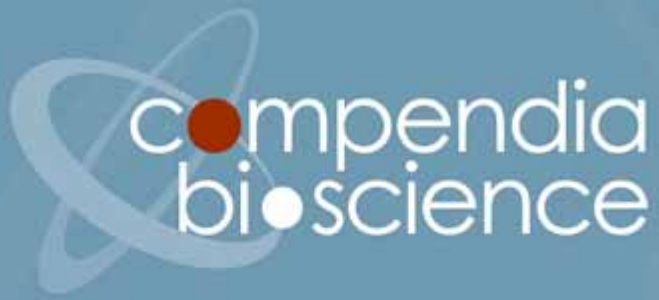
# Angiogenesis signatures in cancer gene expression data

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# Agenda

- Background
- Angiogenesis Signatures
- Tumor populations
- Q & A

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# Background

- Angiogenesis
  - The normal process of forming new blood vessels, such as during development
- Tumor Angiogenesis
  - The process of establishing blood supply to a tumor
- Angiogenesis inhibitors
  - VEGF (Avastin) – Metastatic colon, breast ca., NSCLC, relapsed glioblastoma
  - VEGFRs (Sutent) – Metastatic RCC, GIST
  - Does clinical benefit vary by angiogenic activity?

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# Angiogenesis pathway

- Tumor secretes pro-angiogenic factors
- Receptors on endothelium signal
- Stimulates blood vessel growth and recruitment to tumor

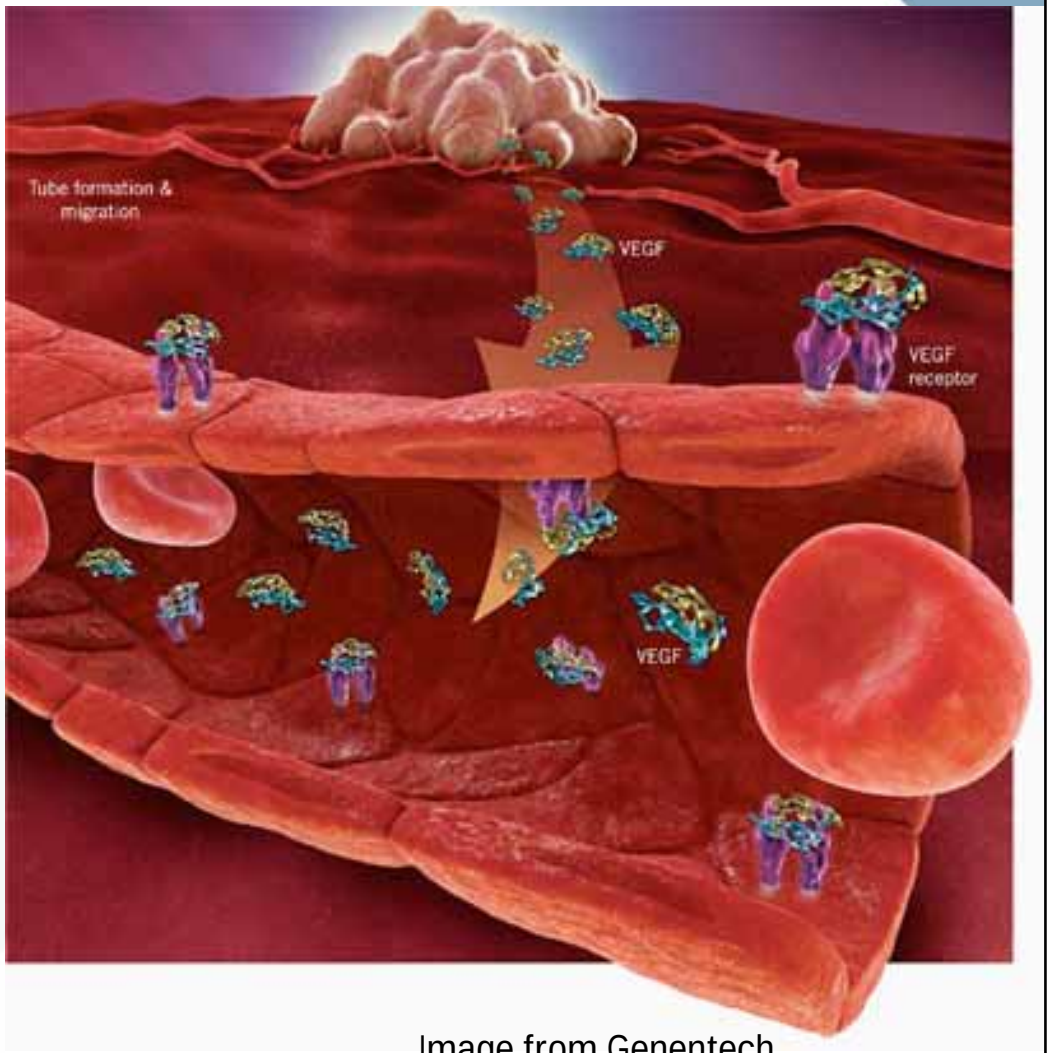


Image from Genentech BioOncology.com

# Hypothesis

- Tumors with increased angiogenic signaling are more susceptible to angiogenesis inhibitors
- A gene expression readout for angiogenic signaling can identify such tumors
- An angiogenesis signature should identify known indications and predict new indications
- Genes / pathways in the signature may represent new targets
- An angiogensis signature could provide a tool to identify individual patients likely to benefit

# Oncomine

- Global collection of published microarray data
  - 33,000+ experiments
  - Tumors & cell lines
  - mRNA & DNA
- Standardized metadata
  - Clinical, pathology, molecular & experimental
- Pre-computed analysis
  - Differential expression, co-expression, outlier analysis, pathway analysis, molecular concepts

# Angiogenesis signatures

- Gene expression readout
  - VEGF expression ( & correlates)
  - Angiogenesis pathway
  - Hypoxic response
- Correlated expression in tumors
  - Co-regulation suggests representation of biological pathway in tumors

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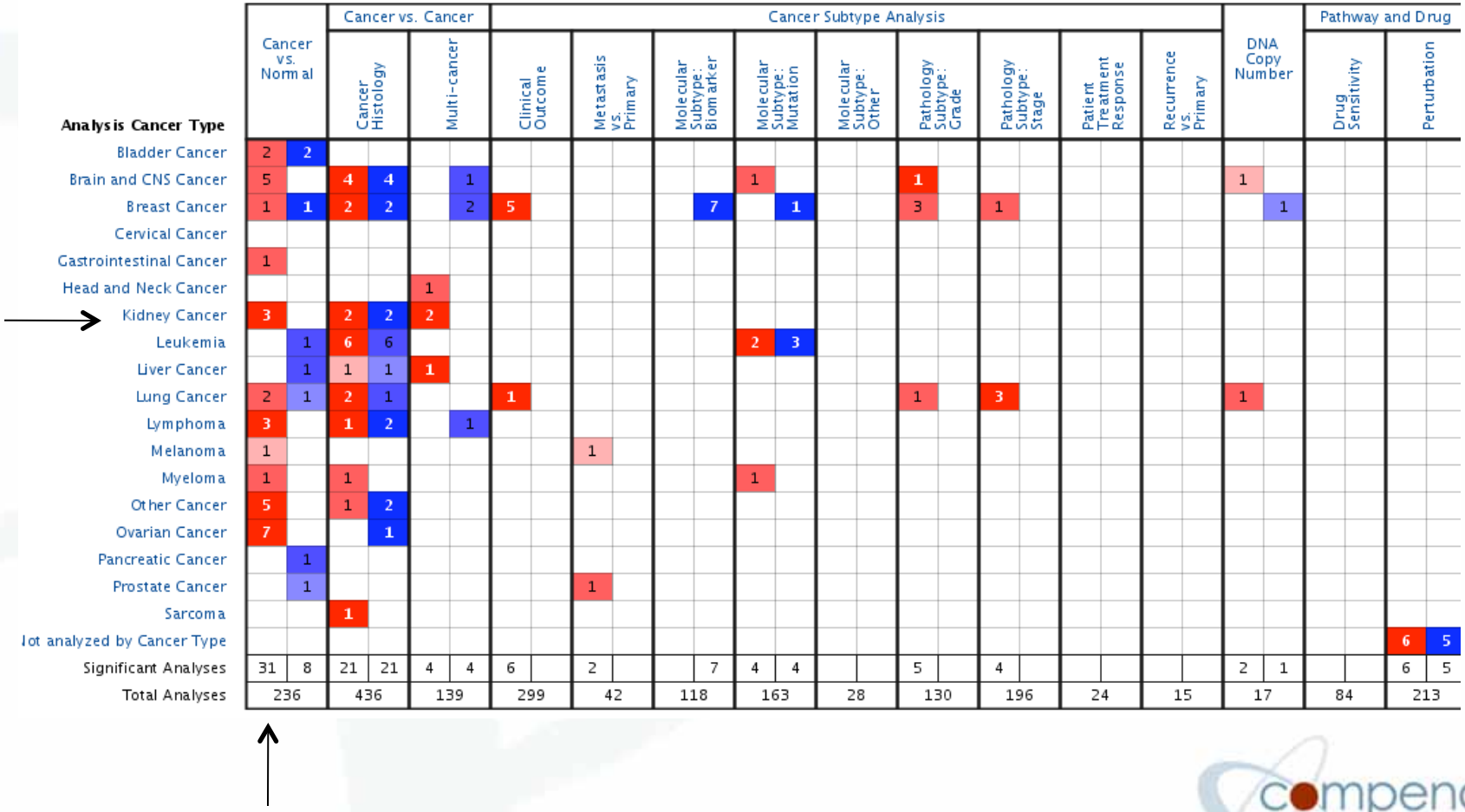
# VEGFA expression in Oncomine

**Disease Summary for VEGFA**



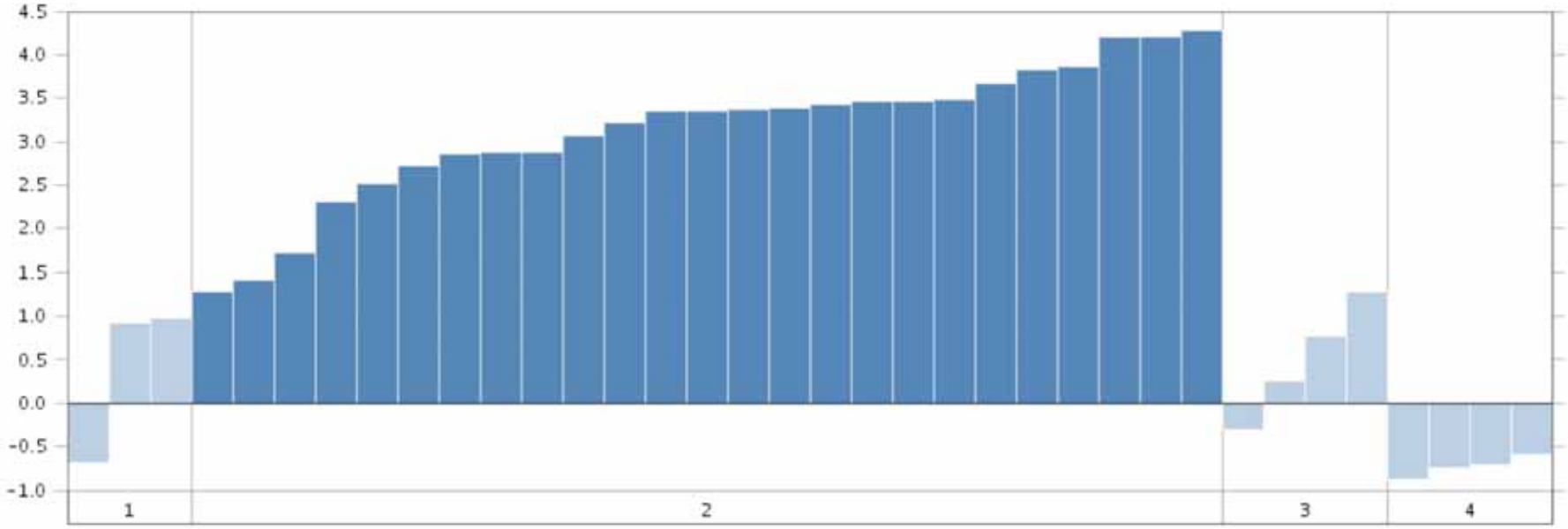
| Analysis Cancer Type | Cancer vs. Normal | | Cancer vs. Cancer | | | | Cancer Subtype Analysis | | | | | | | | | | | | DNA Copy Number | | Pathway and Drug | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Cancer Histology | | Multi-cancer | | Clinical Outcome | | Metastasis vs. Primary | | Molecular Subtype: Biomarker | | Molecular Subtype: Mutation | | Molecular Subtype: Other | | Pathology Subtype: Grade | | Pathology Subtype: Stage | | Patient Treatment Response | | Recurrence vs. Primary | | | | Drug Sensitivity | | Perturbation | |
| Bladder Cancer | 2 | 2 | | | | | | | | | | | | | | | | | | | | | | |
| Brain and CNS Cancer | 5 | | 4 | 4 | | 1 | | | | | | | 1 | | | | 1 | | | | | | 1 | | | | | |
| Breast Cancer | 1 | 1 | 2 | 2 | | 2 | 5 | | | | | 7 | | 1 | | | 3 | | 1 | | | | | 1 | | | | |
| Cervical Cancer | | | | | | | | | | | | | | | | | | | | | | | | |
| Gastrointestinal Cancer | 1 | | | | | | | | | | | | | | | | | | | | | | | |
| Head and Neck Cancer | | | | | 1 | | | | | | | | | | | | | | | | | | | |
| Kidney Cancer | 3 | | 2 | 2 | 2 | | | | | | | | | | | | | | | | | | | |
| Leukemia | | 1 | 6 | 6 | | | | | | | | | 2 | 3 | | | | | | | | | | |
| Liver Cancer | | 1 | 1 | 1 | 1 | | | | | | | | | | | | | | | | | | | |
| Lung Cancer | 2 | 1 | 2 | 1 | | | 1 | | | | | | | | | | 1 | | 3 | | | | 1 | |
| Lymphoma | 3 | | 1 | 2 | | 1 | | | | | | | | | | | | | | | | | | |
| Melanoma | 1 | | | | | | | | 1 | | | | | | | | | | | | | | | |
| Myeloma | 1 | | 1 | | | | | | | | | | 1 | | | | | | | | | | | |
| Other Cancer | 5 | | 1 | 2 | | | | | | | | | | | | | | | | | | | | |
| Ovarian Cancer | 7 | | | 1 | | | | | | | | | | | | | | | | | | | | |
| Pancreatic Cancer | | 1 | | | | | | | | | | | | | | | | | | | | | | |
| Prostate Cancer | | 1 | | | | | | | 1 | | | | | | | | | | | | | | | |
| Sarcoma | | | 1 | | | | | | | | | | | | | | | | | | | | | |
| Not analyzed by Cancer Type | | | | | | | | | | | | | | | | | | | | | | | 6 | 5 |
| Significant Analyses | 31 | 8 | 21 | 21 | 4 | 4 | 6 | | 2 | | | 7 | 4 | 4 | | | 5 | | 4 | | | | 2 | 1 | | | 6 | 5 |
| Total Analyses | 236 | | 436 | | 139 | | 299 | | 42 | | 118 | | 163 | | 28 | | 130 | | 196 | | 24 | | 15 | | 17 | | 84 | | 213 | |

# VEGFA Expression in Higgins Renal

Renal Cell Carcinoma Type: Clear Cell Renal Cell Carcinoma

*(normalized expression units)*

| | | | |
|---|---|---|---|
| **Over-expression Gene Rank:** | 34 (in top 1%) | **P-value:** | 1.52E-9 |
| **Reporter:** | IMAGE:34778 | **t-Test:** | 10.478 |




## Legend

1. Chromophobe Renal Cell Carcinoma (3) **2. Clear Cell Renal Cell Carcinoma (25)** 3. Granular Renal Cell Carcinoma (4) 4. Papillary Renal Cell Carcinoma (4)

## Higgins Renal

| | |
|---|---|
| Am J Pathol 2003/03/01 | 44 samples |
| mRNA | 5,794 measured genes |
| Platform not pre-defined in Oncomine | |

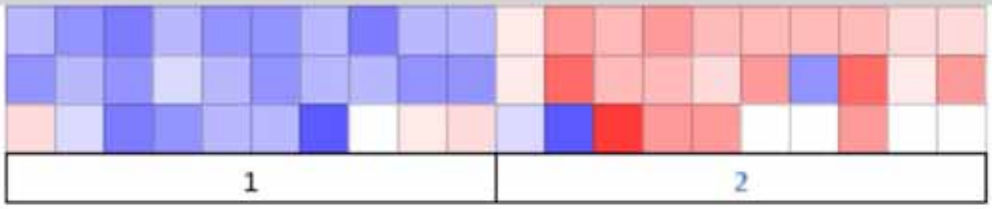


•Oncomine Source: https://qa6.oncomine.com:443/resource/main.html#a:717;cv:detail;d:82;dso:geneOverex;dt:predefinedClass;ec:[2];epv:150001,150829;et:over;f:432451;g:7422;p:200000550;pg:1;pvf:39129,150014,150817;scr:datasets;ss:analysis;th:g10.0,p1.00E-4;v:5

# •Comparison of PGF, VEGFA and VEGFC in Gumz Renal

•Over-expression in Clear Cell Renal Cell Carcinoma vs. Normal

| Rank | P-value | Gene | Reporter | Gene |
|---|---|---|---|---|
| 14 | 3.47E-11 | VEGFA | 210512_s_at | VEGFA |
| 741 | 4.38E-5 | PGF | 209652_s_at | PGF |
| 3369 | 0.045 | VEGFC | 209946_at | VEGFC |




**•Legend**

•1. Kidney (10) **2. Clear Cell Renal Cell Carcinoma (10)**

**•Gumz Renal**

| | |
|---|---|
| Clin Cancer Res 2007/08/15 | 20 samples |
| mRNA | 12,427 measured genes |
| Human Genome U133A Array | |


•Note: Colors are z-score normalized to depict relative expression levels within rows. They cannot be used to compare gene expression values between rows.



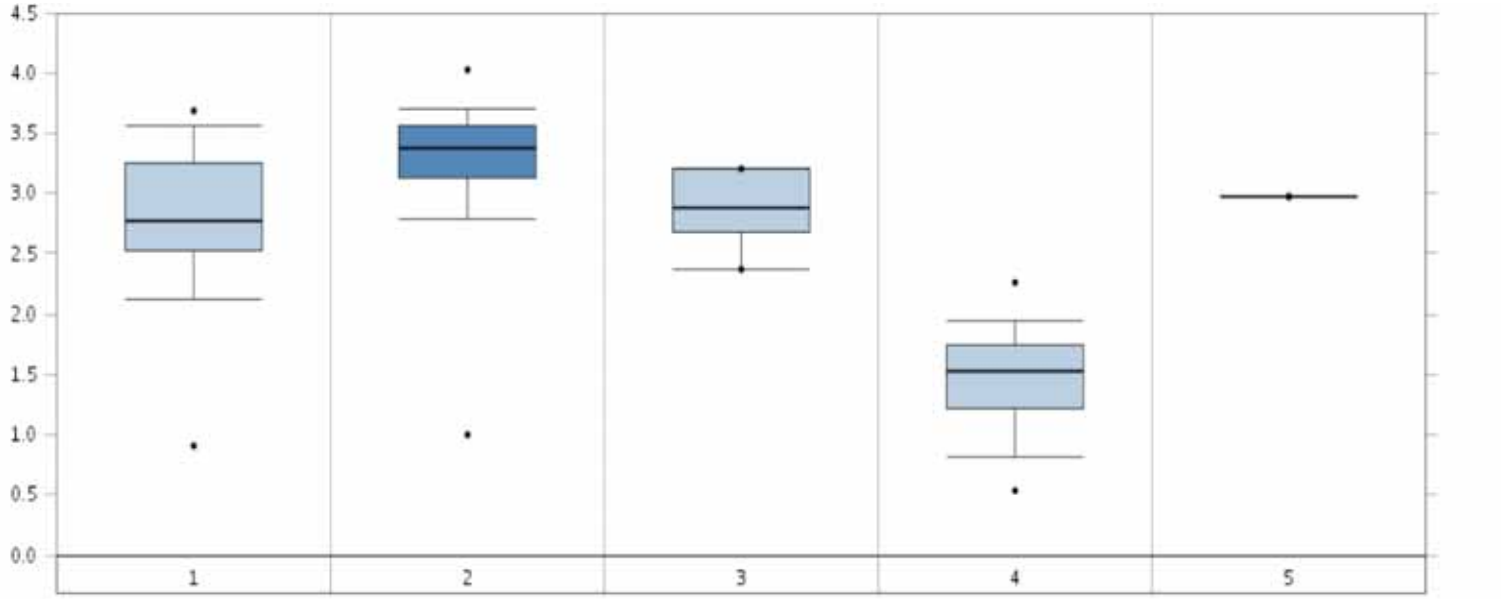
•Oncomine Source: https://qa6.oncomine.com:443/resource/main.html#a:1846;cv:detail;d:67367807;dso:geneOverex;dt:predefinedClass;ec:[2];epv:150001,150829;et:over;f:546247;g:7422;p:200001292;pg:1;pvf:31379,39129,39131,150004,150817;scr:datasets;ss:analysis;th:g10.0,p1.00E-4;v:5

# •VEGFA Expression in Bittner Renal

•Renal Cell Carcinoma Type: Clear Cell Renal Cell Carcinoma

•*(normalized expression units)*

| | | | |
|---|---|---|---|
| **Over-expression Gene Rank:** | 134 (in top 1%) | **P-value:** | 2.01E-11 |
| **Reporter:** | 210512_s_at | **t-Test:** | 8.544 |




## •Legend

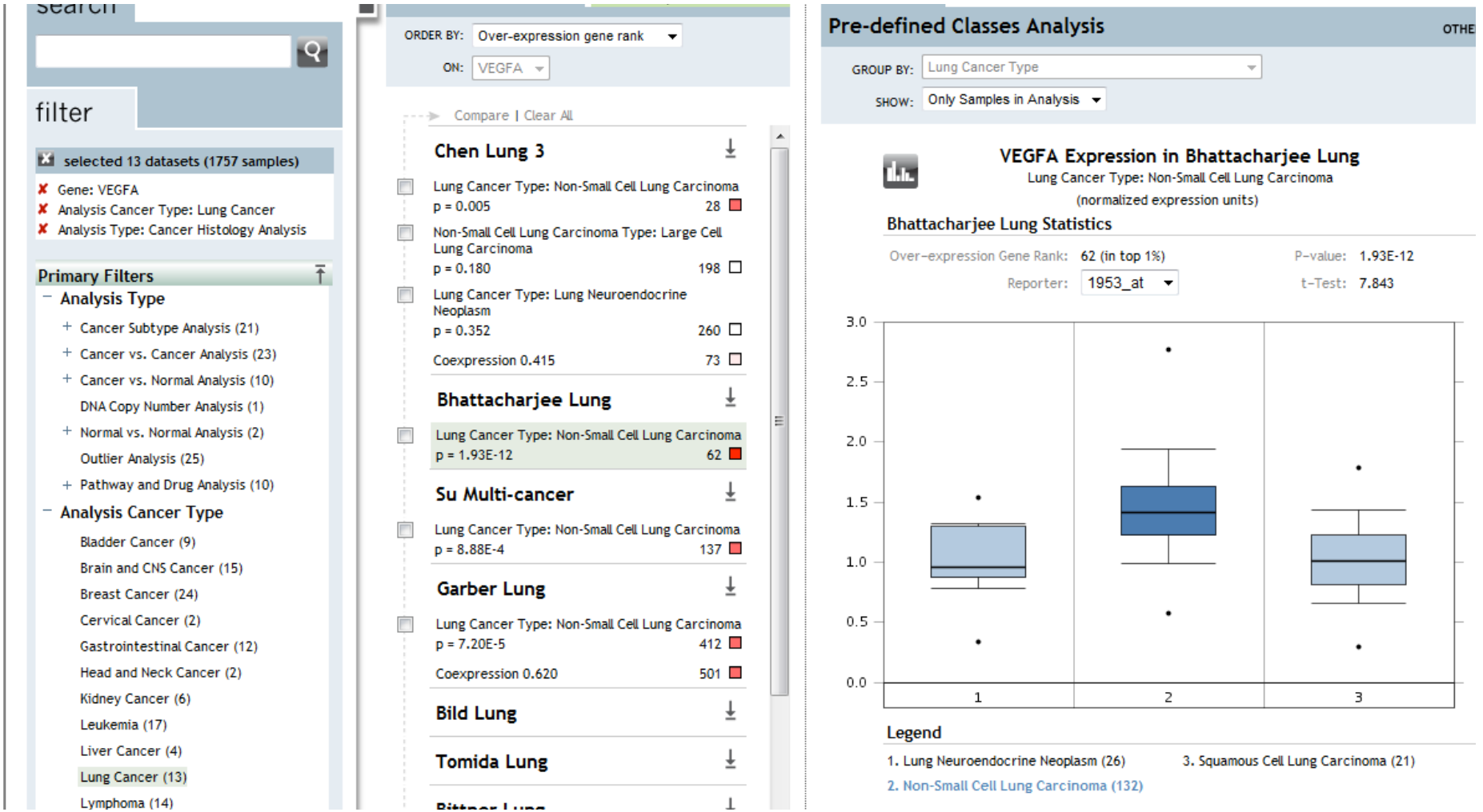
•1. Chromophobe Renal Cell Carcinoma (16) **2. Clear Cell Renal Cell Carcinoma (184)** 3. Granular Renal Cell Carcinoma (5) 4. Papillary Renal Cell Carcinoma (21) 5. Sarcomatoid Renal Cell Carcinoma (1)

## •Bittner Renal

| | |
|---|---|
| Not Published 2005/01/15 | 256 samples |
| mRNA | 19,079 measured genes |
| Human Genome U133 Plus 2.0 Array | |

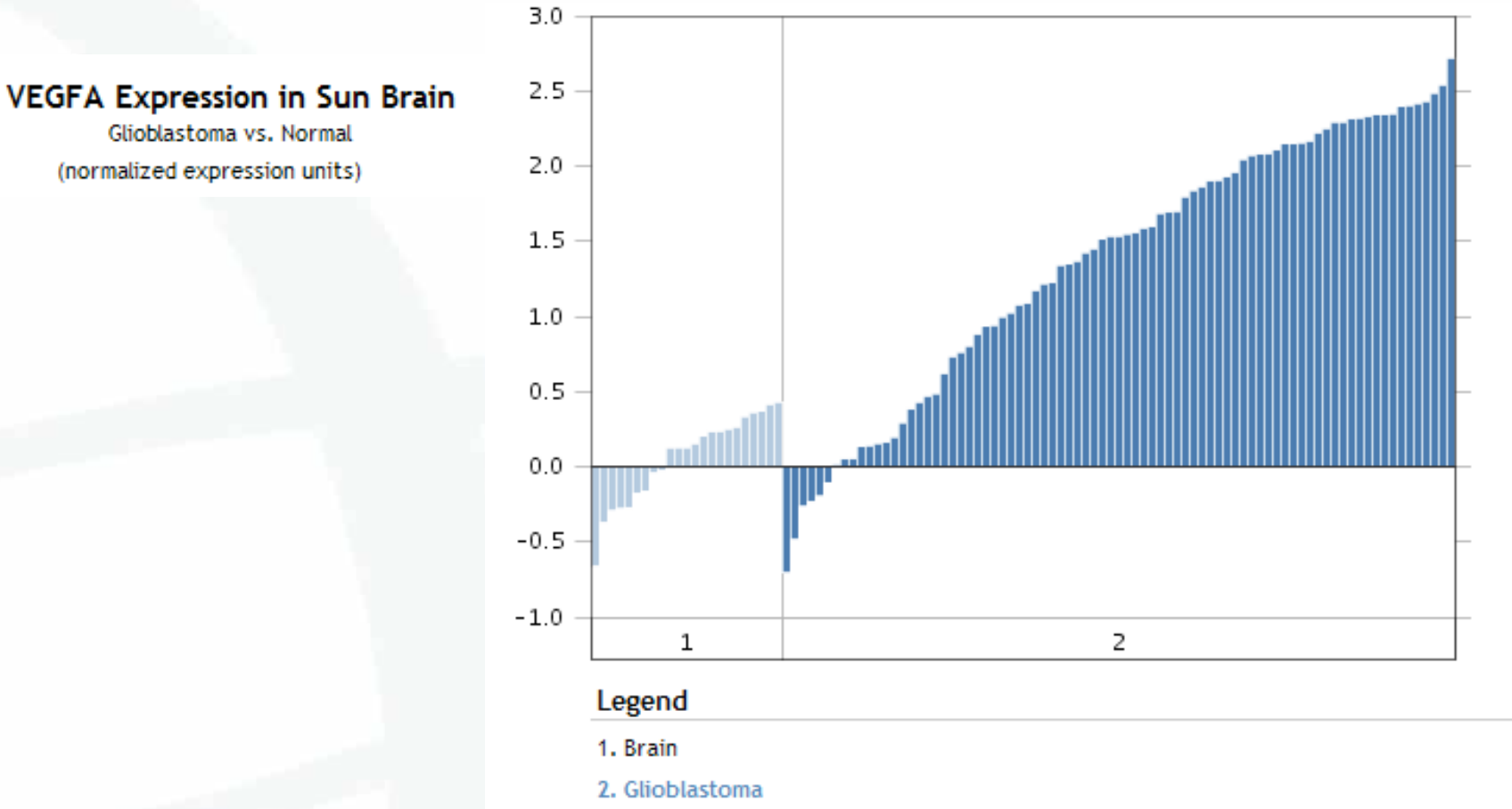


•Oncomine Source: https://qa6.oncomine.com:443/resource/main.html#a:224;cv:detail;d:97370307;dso:geneOverex;dt:predefinedClass;ec:[2];epv:150001,150829;et:over;f:1905655;g:7422;gt:boxplot;p:200000163;pg:1;pvf:39129,150014,150817;scr:datasets;ss:analysis;th:g10.0,p1.00E-4;v:5


filter
selected 13 datasets (1757 samples)
Gene: VEGFA
Analysis Cancer Type: Lung Cancer
Analysis Type: Cancer Histology Analysis
Primary Filters
Analysis Type
Cancer Subtype Analysis (21)
Cancer vs. Cancer Analysis (23)
Cancer vs. Normal Analysis (10)
DNA Copy Number Analysis (1)
Normal vs. Normal Analysis (2)
Outlier Analysis (25)
Pathway and Drug Analysis (10)
Analysis Cancer Type
Bladder Cancer (9)
Brain and CNS Cancer (15)
Breast Cancer (24)
Cervical Cancer (2)
Gastrointestinal Cancer (12)
Head and Neck Cancer (2)
Kidney Cancer (6)
Leukemia (17)
Liver Cancer (4)
Lung Cancer (13)
Lymphoma (14)
ORDER BY: Over-expression gene rank
ON: VEGFA
Compare | Clear All
Chen Lung 3
Lung Cancer Type: Non-Small Cell Lung Carcinoma
p = 0.005 28
Non-Small Cell Lung Carcinoma Type: Large Cell Lung Carcinoma
p = 0.180 198
Lung Cancer Type: Lung Neuroendocrine Neoplasm
p = 0.352 260
Coexpression 0.415 73
Bhattacharjee Lung
Lung Cancer Type: Non-Small Cell Lung Carcinoma
p = 1.93E-12 62
Su Multi-cancer
Lung Cancer Type: Non-Small Cell Lung Carcinoma
p = 8.88E-4 137
Garber Lung
Lung Cancer Type: Non-Small Cell Lung Carcinoma
p = 7.20E-5 412
Coexpression 0.620 501
Bild Lung
Tomida Lung
Pre-defined Classes Analysis
OTHE
GROUP BY: Lung Cancer Type
SHOW: Only Samples in Analysis
VEGFA Expression in Bhattacharjee Lung
Lung Cancer Type: Non-Small Cell Lung Carcinoma
(normalized expression units)
Bhattacharjee Lung Statistics
Over-expression Gene Rank: 62 (in top 1%)
P-value: 1.93E-12
Reporter: 1953_at
t-Test: 7.843
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1
2
3
Legend
1. Lung Neuroendocrine Neoplasm (26)
2. Non-Small Cell Lung Carcinoma (132)
3. Squamous Cell Lung Carcinoma (21)

# Is VEGF expression high in normal brain tissues?

VEGFA expression is low in normal brain tissue, but high in glioblastoma



# VEGFA Cluster from Sun_Brain

search

filter

selected 1 datasets (81 samples)

- Gene: VEGFA (Search: vegf)
- Cancer Type: Glioblastoma
- Concept Type: Oncomine Clusters
- Dataset Name: Sun Brain

Primary Filters

- Analysis Type
  - Cancer Types Analysis (1)
  - Cancer vs. Normal Analysis (1)
- Cancer Type

Sample Filters

Dataset Filters

Concept Filters

datasets | concepts

*Select a primary concept to compare with other concepts.*

Sun Brain - cluster ID n3808 [214]
Oncomine Clusters

visualize

**Concept Details**

OTHER VIEWS:

EXPORT:

**Concept:**

Name: Sun Brain - cluster ID n3808
Concept Type: Oncomine Clusters
Size: 214 genes
Null List: Human Genome U133 Plus 2.0 Array (19079)

**Gene List: (214)**

| | |
|---|---|
| ABCC3 | ATP-binding cassette, sub-family C (CFTR/MRP), member 3 |
| ACTN1 | actinin, alpha 1 |
| ADAM12 | ADAM metallopeptidase domain 12 (meltrin alpha) |
| ADFP | adipose differentiation-related protein |
| ADM | adrenomedullin |
| AEBP1 | AE binding protein 1 |
| AFAP1L1 | actin filament associated protein 1-like 1 |
| ALPK3 | alpha-kinase 3 |
| ANGPT2 | angiopoietin 2 |
| ANTXR1 | anthrax toxin receptor 1 |
| ANXA1 | annexin A1 |

Selected Genes in Sun Brain

Comparison of Selected Genes in Nutt Brain

Over-expression in Glioblastoma Dead at 3 Years

| P-value | Gene |
|---|---|
| 8.48E-6 | ADM |
| 1.09E-4 | C1S |
| 1.36E-4 | CHI3L2 |
| 2.74E-4 | PHLDA2 |
| 3.65E-4 | FZD2 |
| 4.83E-4 | ANGPT2 |
| 0.001 | COL1A2 |
| 0.002 | ADFP |
| 0.003 | PBEF1 |
| 0.003 | COL6A3 |
| 0.003 | FLNA |
| 0.003 | C8F1 |
| 0.004 | MTMP11 |
| 0.004 | CA12 |
| 0.004 | MYL9 |
| 0.004 | COL3A1 |
| 0.004 | ABCC3 |
| 0.004 | AEBP1 |
| 0.005 | ANXA1 |
| 0.006 | C1R |

egend

. Glioblastoma - Alive at 3 Years

. Glioblastoma - Dead at 3 Years

Comparison of Selected Genes in Bild CellLine

Over-expression in HRAS Transfection (Human Mammary Epithelial Cells)

| P-value | Gene |
|---|---|
| 3.40E-20 | FOSL1 |
| 1.04E-17 | TCIF1 |
| 5.82E-16 | VEGFA |
| 7.71E-16 | PTX3 |
| 1.80E-15 | PBEF1 |
| 1.27E-14 | EPHA2 |
| 1.51E-13 | ANXA1 |
| 3.04E-13 | TIMP1 |
| 3.67E-13 | MFAP2 |
| 4.23E-13 | LIF |
| 4.42E-13 | ABCC3 |
| 1.05E-12 | TNFRSF12A |
| 1.22E-12 | MMP14 |
| 2.33E-12 | S100A10 |
| 3.63E-12 | PRBP1 |
| 3.68E-12 | FBUM1 |
| 3.71E-12 | TUBB6 |
| 6.20E-12 | CA12 |
| 8.41E-12 | CLIC1 |
| 8.86E-12 | KIAA0040 |

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. GFP Transfection Control (Human Mammary Epithelial Cells)

. HRAS Transfection (Human Mammary Epithelial Cells)

# Genes Co-expressed with VEGFA

datasets | concepts

ORDER BY: Over-expression gene rank

ON: VEGFA

Compare | Clear All

**Sun Brain**

- Glioblastoma — p = 8.14E-11 — 1
- Glioblastoma vs. Normal — p = 1.06E-19 — 246
- Outlier 90th% — 86
- Coexpression 0.719 — 743

**Nutt Brain**

- Anaplastic Oligodendroglioma Dead at 3 Years — p = 0.004 — 13
- Glioblastoma Dead at 3 Years — p = 0.011 — 191
- Anaplastic Oligodendroglioma Dead at 1 Year — p = 0.035 — 275
- Coexpression 0.761 — 318

**Shai Brain**

- Glioblastoma — p = 2.42E-5 — 55
- Glioblastoma vs. Normal — p = 2.13E-5 — 332
- Coexpression 0.630 — 2190

**Mischel Brain**

visualize

**Co-expression Analysis**

GROUP BY: Cancer and Normal Type

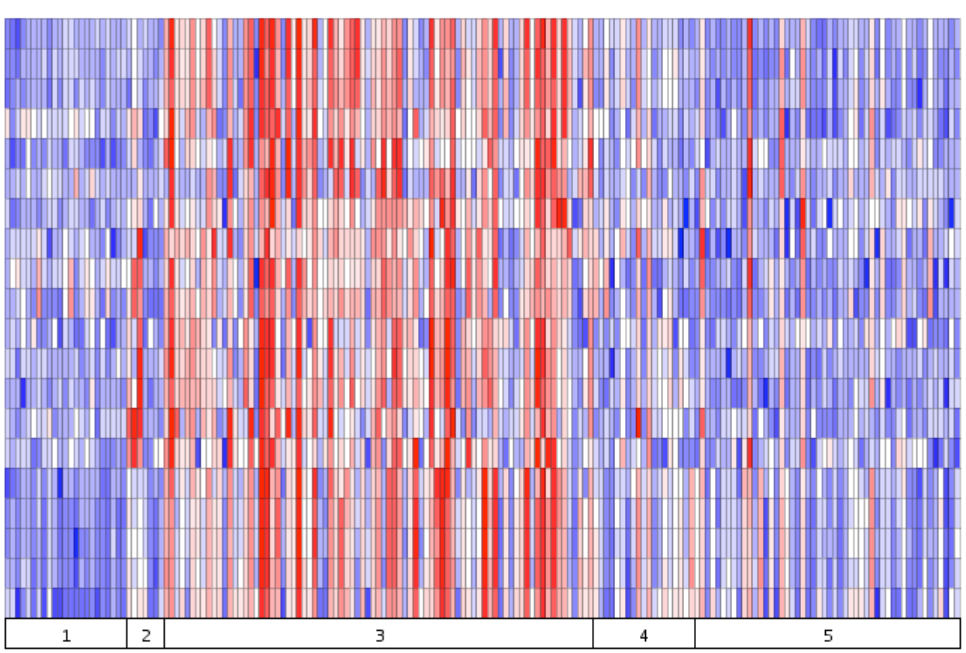
SHOW: All Samples in Dataset

1 | 2 | 3 | 4 | 5 »

**Genes Co-expressed with VEGFA in Sun Brain**

Grouped by Cancer and Normal Type

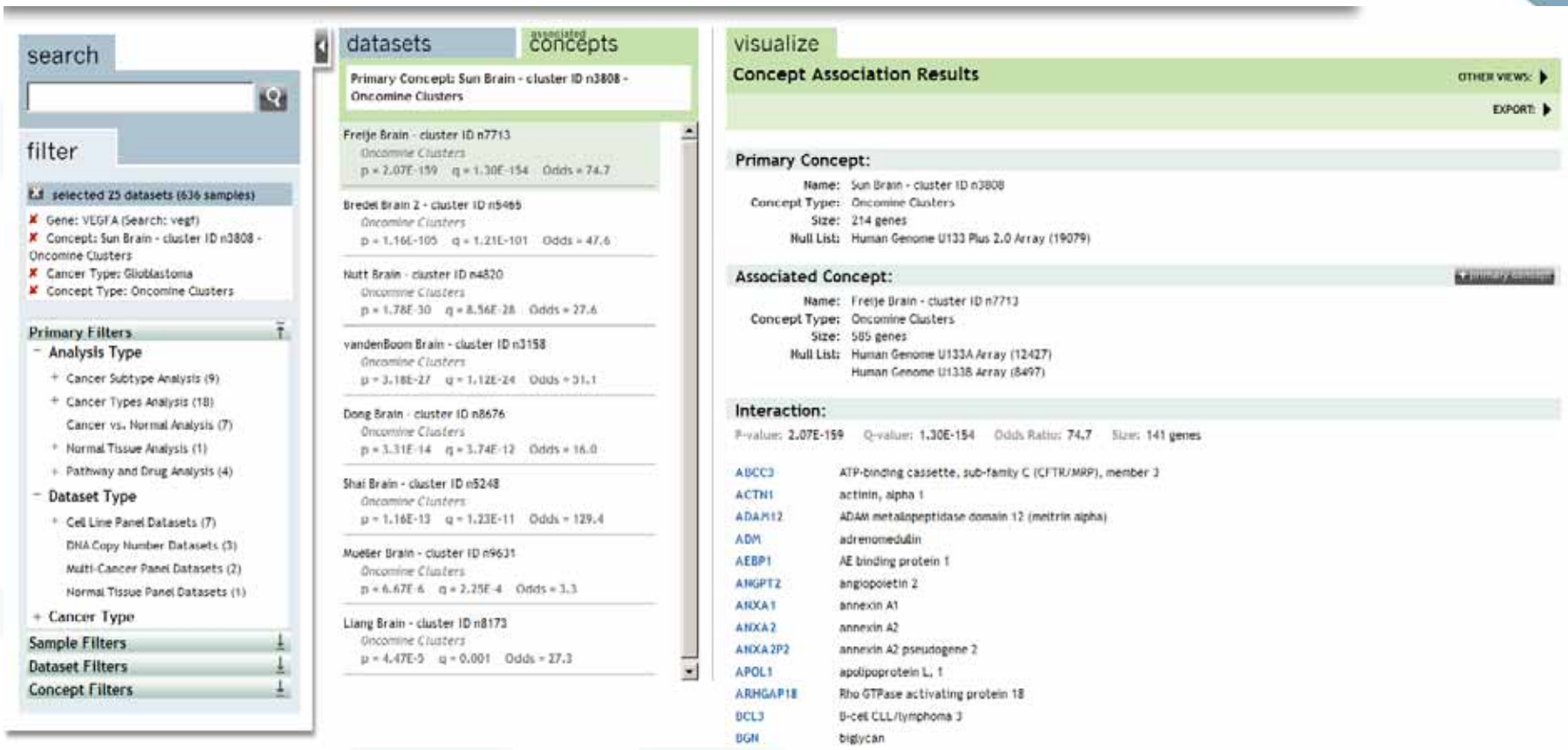
| Correlation | Gene | Reporter |
|---|---|---|
| 1.000 | VEGFA | 210512_s_at |
| 0.948 | VEGFA | 210513_s_at |
| 0.948 | VEGFA | 212171_x_at |
| 0.948 | VEGFA | 211527_x_at |
| 0.855 | ADM | 202912_at |
| 0.797 | HIG2 | 1554452_a_at |
| 0.767 | - | 230710_at |
| 0.727 | - | 227868_at |
| 0.719 | ESM1 | 208394_x_at |
| 0.719 | - | 230746_s_at |
| 0.719 | STC1 | 204597_x_at |
| 0.704 | LOX | 213640_s_at |
| 0.704 | LOX | 204298_s_at |
| 0.704 | - | 215446_s_at |
| 0.673 | ADFP | 209122_at |
| 0.658 | TREM1 | 219434_at |
| 0.656 | CA12 | 210735_s_at |
| 0.656 | - | 215867_x_at |
| 0.656 | CA12 | 214164_x_at |
| 0.656 | CA12 | 203963_at |
| 0.656 | CA12 | 204508_s_at |




**Legend**

1. Brain
2. Diffuse Astrocytoma
3. Glioblastoma
4. Anaplastic Astrocytoma
5. Oligodendroglioma

# Concepts Associated with VEGFA

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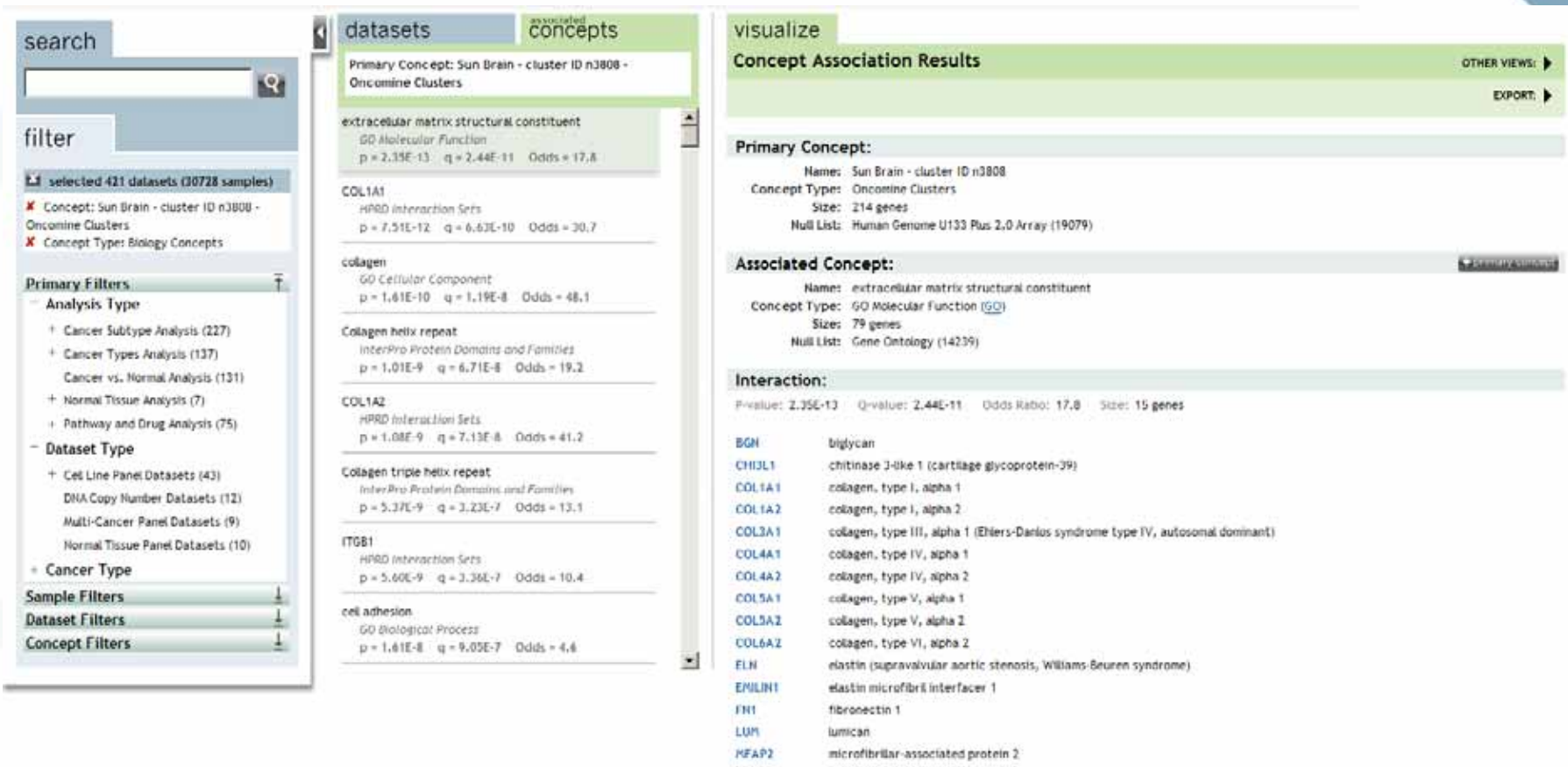
# ECM Concept Associated with VEGFA

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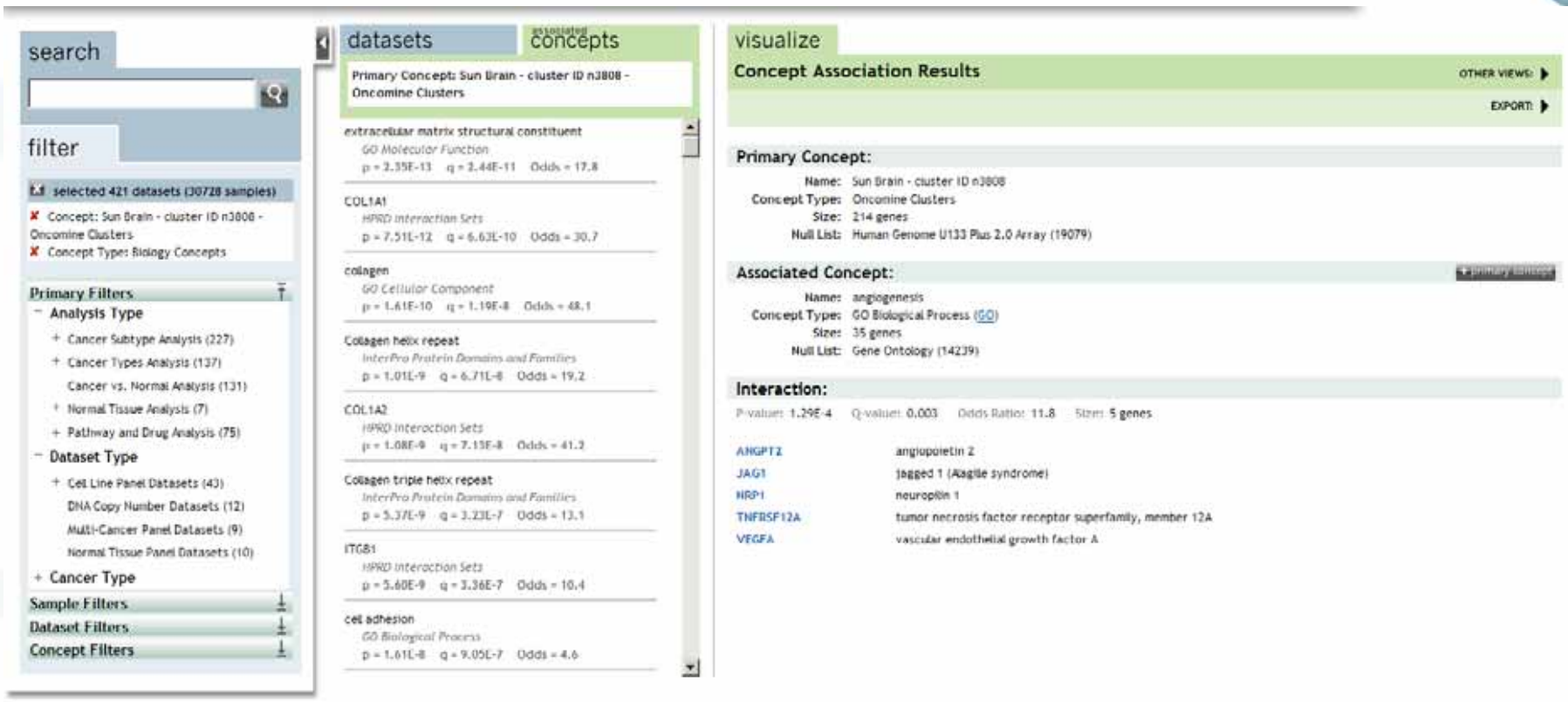
# Angiogenesis Associated with VEGFA

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# Angiogenesis Pathway

## Concept Information

**Concept:**

| | |
|---|---|
| **Name:** | angiogenesis |
| **Concept Type:** | GO Biological Process (GO) |
| **Size:** | 35 genes |
| **Null List:** | Gene Ontology (14239) |

- Growth factors, receptors

| | |
|---|---|
| AGGF1 | angiogenic factor with G patch and FHA domains 1 |
| ANG | angiogenin, ribonuclease, RNase A family, 5 |
| ANGPT1 | angiopoietin 1 |
| ANGPT2 | angiopoietin 2 |
| ANPEP | alanyl (membrane) aminopeptidase (aminopeptidase N, aminopeptidase M, micro aminopeptidase, CD13, p150) |
| ECGF1 | endothelial cell growth factor 1 (platelet-derived) |
| EGFL7 | EGF-like-domain, multiple 7 |
| EPAS1 | endothelial PAS domain protein 1 |
| EREG | epiregulin |
| FGF1 | fibroblast growth factor 1 (acidic) |
| FGF2 | fibroblast growth factor 2 (basic) |
| FGF6 | fibroblast growth factor 6 |
| FIGF | c-fos induced growth factor (vascular endothelial growth factor D) |
| FLT1 | fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular perm factor receptor) |
| HAND2 | heart and neural crest derivatives expressed 2 |
| IL18 | interleukin 18 (interferon-gamma-inducing factor) |
| IL8 | interleukin 8 |
| JAG1 | jagged 1 (Alagille syndrome) |
| KDR | kinase insert domain receptor (a type III receptor tyrosine kinase) |
| MMP19 | matrix metallopeptidase 19 |
| NARG1 | NMDA receptor regulated 1 |
| NRP1 | neuropilin 1 |
| NRP2 | neuropilin 2 |
| PGF | placental growth factor, vascular endothelial growth factor-related protein |
| PLXDC1 | plexin domain containing 1 |
| PROK2 | prokineticin 2 |
| RHOB | ras homolog gene family, member B |
| ROBO4 | roundabout homolog 4, magic roundabout (Drosophila) |
| SH2D2A | SH2 domain protein 2A |
| TMPRSS6 | transmembrane protease, serine 6 |
| TNFAIP2 | tumor necrosis factor, alpha-induced protein 2 |
| TNFRSF12A | tumor necrosis factor receptor superfamily, member 12A |
| TNFSF12 | tumor necrosis factor (ligand) superfamily, member 12 |
| VEGFA | vascular endothelial growth factor A |
| VEGFC | vascular endothelial growth factor C |

# Angiogenesis pathway associations

| Oncomine Signatures | # | Avg (OR) |
|---|---|---|
| Cancer Type: Kidney Cancer | 4 | 7.0 |
| Sarcoma Type: Liposarcoma | 3 | 7.3 |
| Acute Leukemia Type: Acute Myeloid Leukemia | 2 | 5.0 |
| Acute Myeloid Leukemia - CBFB-MYH11 Gene Fusion | 2 | 6.0 |
| Brain and CNS Cancer Type: Glioblastoma | 2 | 7.5 |
| Ductal Breast Carcinoma Type: Invasive Ductal Breast Carcinoma | 2 | 7.5 |
| Lymphoma Type: Diffuse Large B-Cell Lymphoma | 2 | 5.5 |
| Mature B-Cell Non-Hodgkin's Lymphoma Type: Diffuse Large B-Cell Lymphoma | 2 | 5.5 |
| Renal Cell Carcinoma Type: Clear Cell Renal Cell Carcinoma | 2 | 8.0 |

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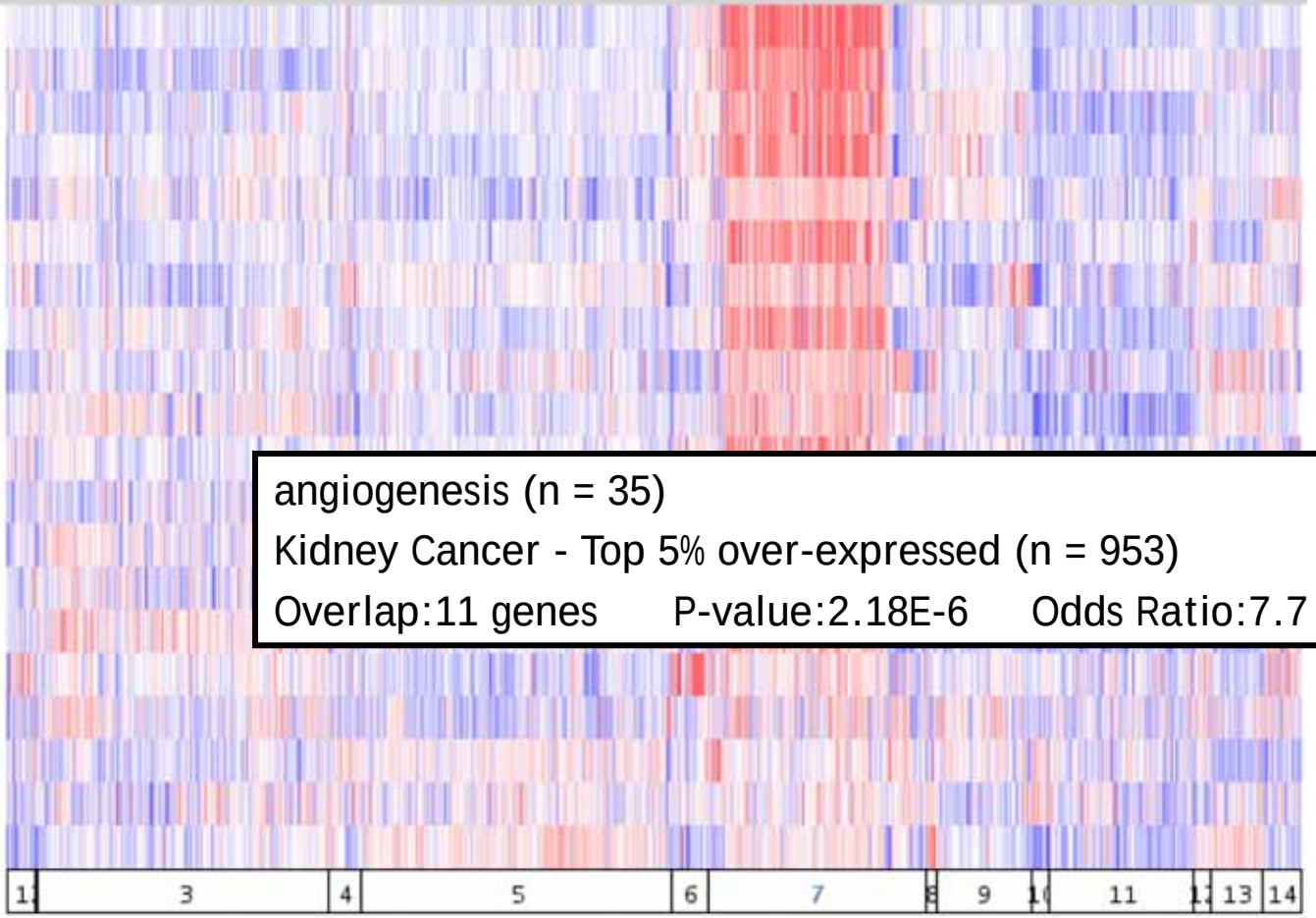
# Angiogenesis genes

## Over-expression in Cancer Type: Kidney Cancer

| Rank | P-value | Gene |
|---|---|---|
| 223 | 4.73E-59 | FLT1 |
| 251 | 7.90E-57 | VEGFA |
| 259 | 9.85E-56 | EPAS1 |
| 498 | 2.87E-41 | KDR |
| 606 | 8.15E-37 | NRP1 |
| 616 | 1.69E-36 | ANGPT2 |
| 686 | 2.12E-34 | JAG1 |
| 690 | 2.88E-34 | ROBO4 |
| 765 | 2.49E-32 | ANPEP |
| 807 | 5.38E-31 | RHOB |
| 878 | 1.74E-29 | PGF |
| 1505 | 2.56E-18 | ANGPT1 |
| 1620 | 7.54E-17 | EGFL7 |
| 1839 | 1.95E-14 | FGF2 |
| 1909 | 7.20E-14 | PLXDC1 |
| 2441 | 3.20E-10 | VEGFC |
| 2711 | 9.06E-9 | TNFSF12 |
| 2824 | 2.52E-8 | IL18 |
| 3133 | 3.87E-7 | AGGF1 |
| 4192 | 1.45E-4 | ANG |




**Legend**

1. Bladder Cancer (32) 2. Brain and CNS Cancer (4) 3. Breast Cancer (328) 4. Cervical Cancer (35) 5. Gastrointestinal Cancer (350) 6. Head and Neck Cancer (41) **7. Kidney Cancer (246)** 8. Liver Cancer (11) 9. Lung Cancer (107) 10. Lymphoma (19) 11. Ovarian Cancer (164) 12. Pancreatic Cancer (19) 13. Prostate Cancer (59) 14. Sarcoma (42)

**Bittner Multi-cancer**

Not Published 2006/01/01

1,911 samples

mRNA

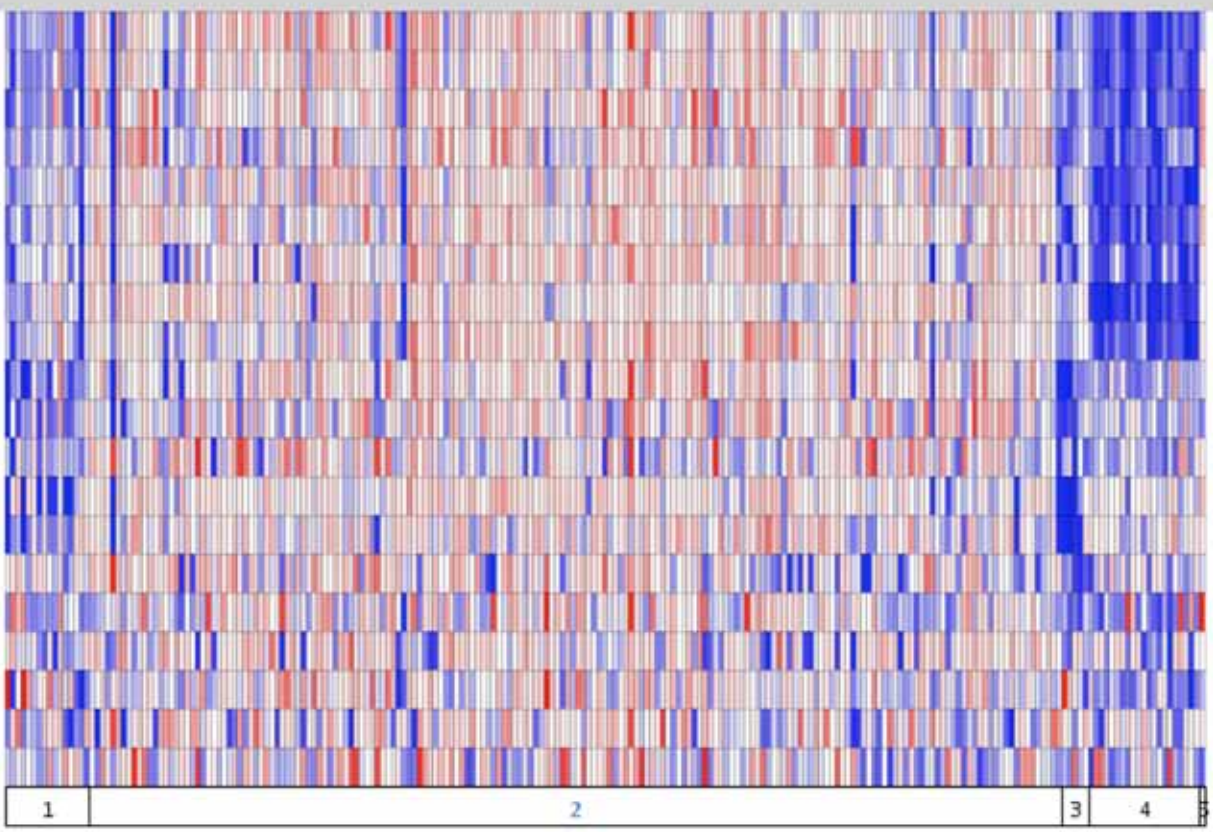
19,079 measured genes

Human Genome U133 Plus 2.0 Array

# Angiogenesis genes

Over-expression in Renal Cell Carcinoma Type: Clear Cell Renal Cell Carcinoma

| Rank | P-value | Gene |
|---|---|---|
| 2 | 2.52E-17 | EPAS1 |
| 4 | 3.90E-16 | ROBO4 |
| 63 | 2.46E-13 | PLXDC1 |
| 82 | 1.38E-12 | PGF |
| 84 | 1.43E-12 | FLT1 |
| 107 | 4.79E-12 | ANGPT2 |
| 133 | 1.91E-11 | EGFL7 |
| 134 | 2.01E-11 | VEGFA |
| 183 | 2.20E-10 | KDR |
| 217 | 7.74E-10 | JAG1 |
| 609 | 1.19E-6 | RHOB |
| 831 | 1.02E-5 | NRP2 |
| 1503 | 3.79E-4 | NRP1 |
| 1677 | 6.63E-4 | ANG |
| 2107 | 0.002 | MMP19 |
| 2256 | 0.003 | VEGFC |
| 2307 | 0.003 | NARG1 |
| 3118 | 0.014 | ANGPT1 |
| 3862 | 0.031 | SH2D2A |
| 4669 | 0.062 | ANPEP |




**Legend**

1. Chromophobe Renal Cell Carcinoma (16) **2. Clear Cell Renal Cell Carcinoma (184)** 3. Granular Renal Cell Carcinoma (5) 4. Papillary Renal Cell Carcinoma (21) 5. Sarcomatoid Renal Cell Carcinoma (1)

**Bittner Renal**

| | |
|---|---|
| Not Published 2005/01/15 | 256 samples |
| mRNA | 19,079 measured genes |

.

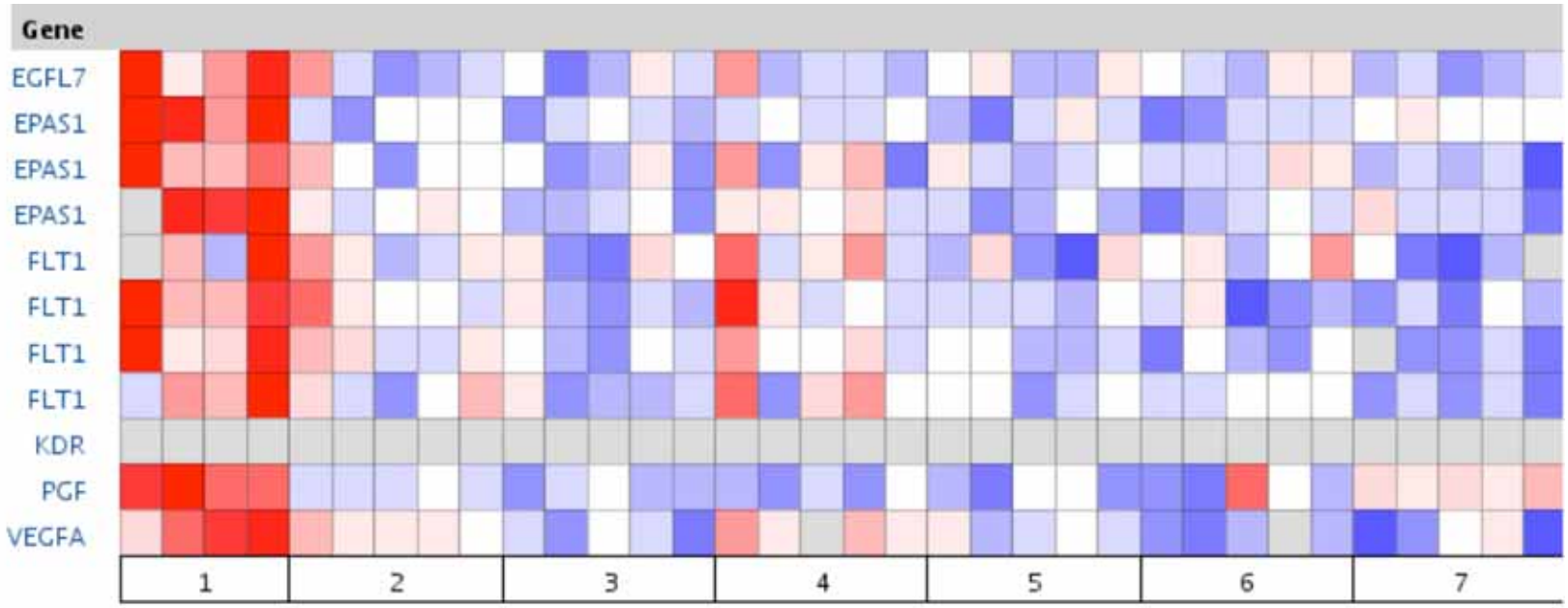
angiogenesis (n = 35)

Clear Cell Renal Cell Carcinoma - Top 1% over-expressed (n = 190)

Overlap: 9 genes P-value:1.97E-10 Odds Ratio:30.6

# Comparison of Selected Genes in Higgins Normal

## Grouped by Kidney Structure




**Legend**

1. Glomeruli (4) 2. Inner Cortex (5) 3. Inner Medulla (5) 4. Outer Cortex (5) 5. Outer Medulla (5) 6. Papillary Tips (5) 7. Pelvis (5)

**Higgins Normal**

Mol Biol Cell 2004/02/01

34 samples

mRNA

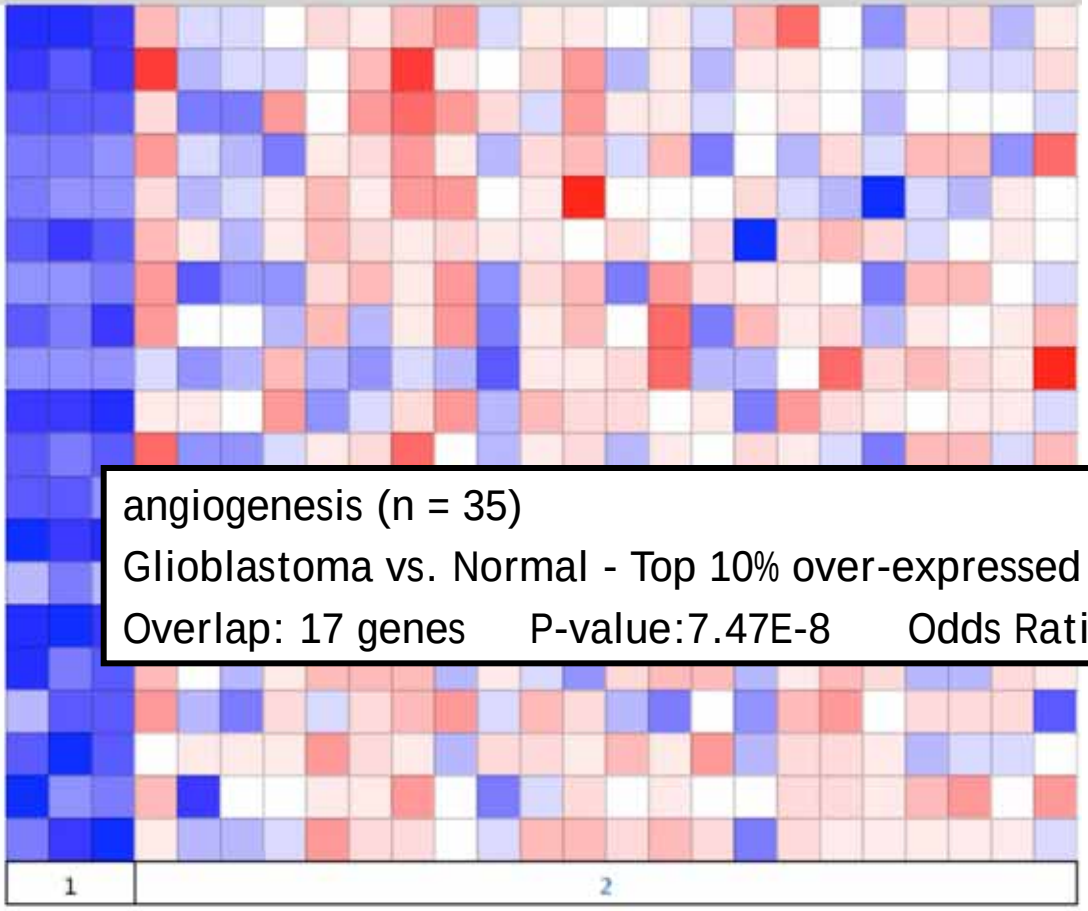
13,016 measured genes

Platform not pre-defined in Oncomine

# Angiogenesis genes

## Over-expression in Glioblastoma vs. Normal

| Rank | P-value | Gene |
|---|---|---|
| 97 | 1.32E-11 | ANG |
| 158 | 5.91E-10 | TNFAIP2 |
| 192 | 2.83E-9 | FGF1 |
| 414 | 4.60E-7 | ECGF1 |
| 491 | 1.66E-6 | FGF2 |
| 497 | 1.78E-6 | PGF |
| 521 | 2.40E-6 | MMP19 |
| 754 | 2.45E-5 | ANGPT1 |
| 837 | 4.78E-5 | TNFRSF12A |
| 960 | 1.12E-4 | EPAS1 |
| 982 | 1.26E-4 | IL8 |
| 1160 | 3.44E-4 | PLXDC1 |
| 1169 | 3.65E-4 | ANGPT2 |
| 1279 | 6.33E-4 | NARG1 |
| 1386 | 9.59E-4 | ROBO4 |
| 1523 | 0.002 | EGFL7 |
| 1742 | 0.003 | VEGFA |
| 2392 | 0.011 | KDR |
| 2803 | 0.020 | TNFSF12 |
| 2814 | 0.021 | FLT1 |




angiogenesis (n = 35)
Glioblastoma vs. Normal - Top 10% over-expressed (n = 1907)
Overlap: 17 genes P-value:7.47E-8 Odds Ratio:7.2

**Legend**

1. Neural Stem Cell (3) **2. Glioblastoma (22)**

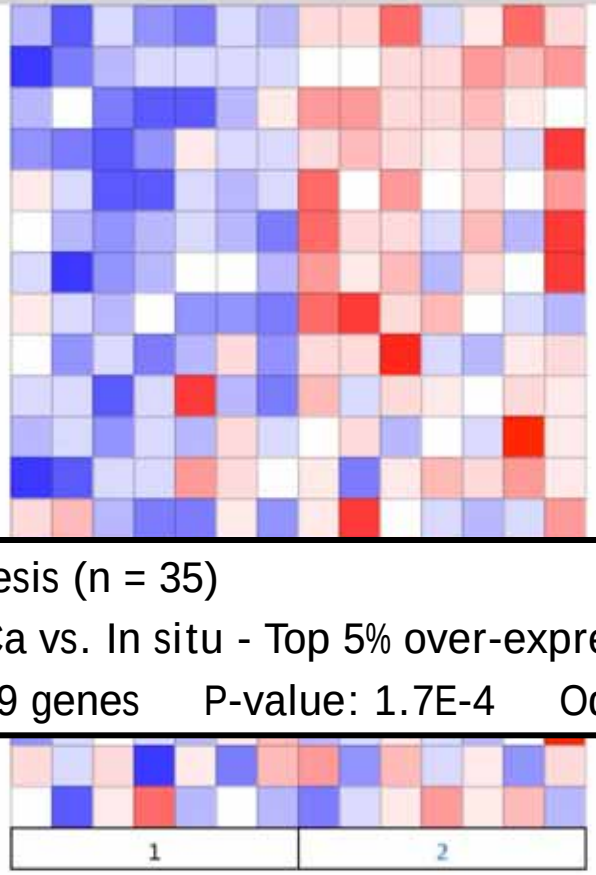
**Lee Brain**

Cancer Cell 2006/05/15
101 samples
mRNA
19,079 measured genes
Human Genome U133 Plus 2.0 Array

# Angiogenesis Genes

## Over-expression in Ductal Breast Carcinoma Type: Invasive Ductal Breast Carcinoma

| Rank | P-value | Gene |
|---|---|---|
| 39 | 1.66E-4 | NRP2 |
| 86 | 4.56E-4 | SH2D2A |
| 111 | 6.18E-4 | ANGPT2 |
| 200 | 0.001 | KDR |
| 285 | 0.003 | PLXDC1 |
| 327 | 0.003 | MMP19 |
| 401 | 0.005 | FLT1 |
| 747 | 0.016 | IL18 |
| 892 | 0.021 | ROBO4 |
| 1816 | 0.069 | NRP1 |
| 2019 | 0.081 | ANGPT1 |
| 2435 | 0.104 | EPAS1 |
| 2491 | 0.107 | VEGFC |
| 3381 | 0 | |
| 3555 | 0 | |
| 4250 | 0 | |
| 4866 | 0 | |
| 5710 | 0 | |
| 6104 | 0.295 | ANG |
| 6376 | 0.307 | ECGF1 |




angiogenesis (n = 35)

Ductal BCa vs. In situ - Top 5% over-expressed (n = 953)

Overlap: 9 genes  P-value: 1.7E-4  Odds Ratio: 5.7

**Legend**

1. Ductal Breast Carcinoma in Situ (7) **2. Invasive Ductal Breast Carcinoma (7)**

**Schuetz Breast 2**

Cancer Res 2006/05/18

mRNA

Human Genome U133 Plus 2.0 Array

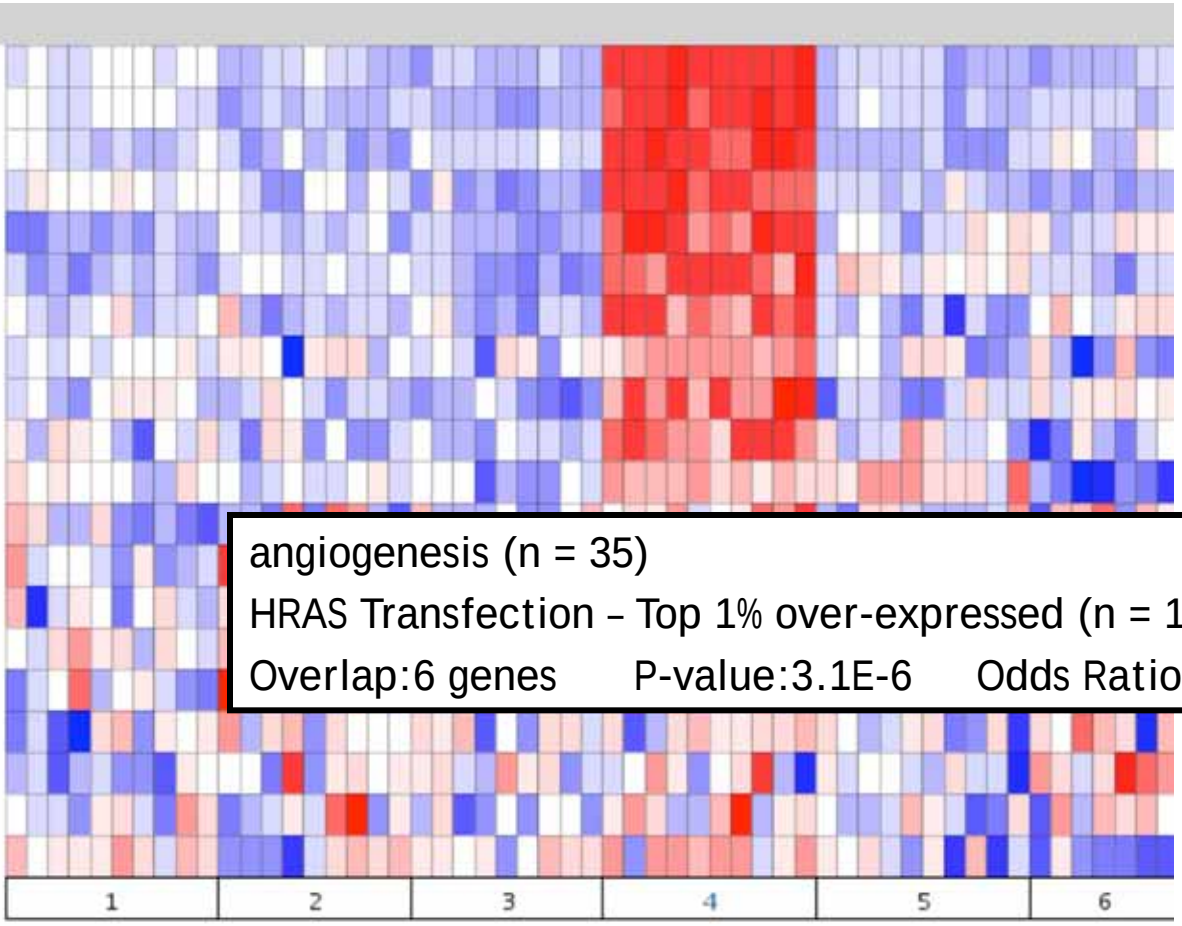
14 samples

19,079 measured genes

# Angiogenesis genes

Over-expression in HRAS Transfection - Human Mammary Epithelial Cells

| Rank | P-value | Gene |
|---|---|---|
| 20 | 1.63E-17 | EREG |
| 42 | 5.82E-16 | VEGFA |
| 79 | 1.05E-14 | EPAS1 |
| 125 | 1.45E-13 | IL8 |
| 179 | 1.05E-12 | TNFRSF12A |
| 188 | 1.56E-12 | NRP2 |
| 668 | 7.46E-9 | FGF2 |
| 787 | 2.56E-8 | ROBO4 |
| 1064 | 2.31E-7 | JAG1 |
| 1561 | 5.34E-6 | RHOB |
| 2069 | 4.71E-5 | NARG1 |
| 3928 | 0.003 | ANGPT2 |
| 4587 | 0.006 | ANPEP |
| 6401 | 0.030 | PLXDC1 |
| 6784 | 0.038 | ECGF1 |
| 7403 | 0.057 | MMP19 |
| 7696 | 0.068 | PGF |
| 7897 | 0.075 | AGGF1 |
| 8327 | 0.094 | TNFSF12 |
| 9757 | 0.182 | NRP1 |




angiogenesis (n = 35)
HRAS Transfection – Top 1% over-expressed (n = 190)
Overlap:6 genes P-value:3.1E-6 Odds Ratio:17.8

**Legend**

1. GFP Transfection Control (10) 2. CTNNB1 Transfection (9) 3. E2F3 Transfection (9) **4. HRAS Transfection (10)** 5. MYC Transfection (10) 6. SRC Transfection (7)

**Bild CellLine**

Nature 2005/11/07
mRNA
Human Genome U133 Plus 2.0 Array
55 samples
19,079 measured genes

# Correlation of angiogensis pathway

- Does angiogenesis pathway genes show correlation in particular cancer types?
- Identify individual tumors
- Approach
  - Oncomine clusters
  - Sets of correlated genes (>0.50)

| Tissue | # | Avg (OR) |
|---|---|---|
| Brain | 8 | 24.5 |
| Renal | 7 | 23.3 |
| Breast | 6 | 29.9 |
| Melanoma | 6 | 10.7 |
| Bladder | 5 | 9.6 |
| Leukemia | 5 | 13.0 |
| Lung | 4 | 4.8 |
| Lymphoma | 4 | 20.0 |
| Prostate | 4 | 8.7 |
| Sarcoma | 4 | 29.5 |
| Colon | 2 | 16.5 |

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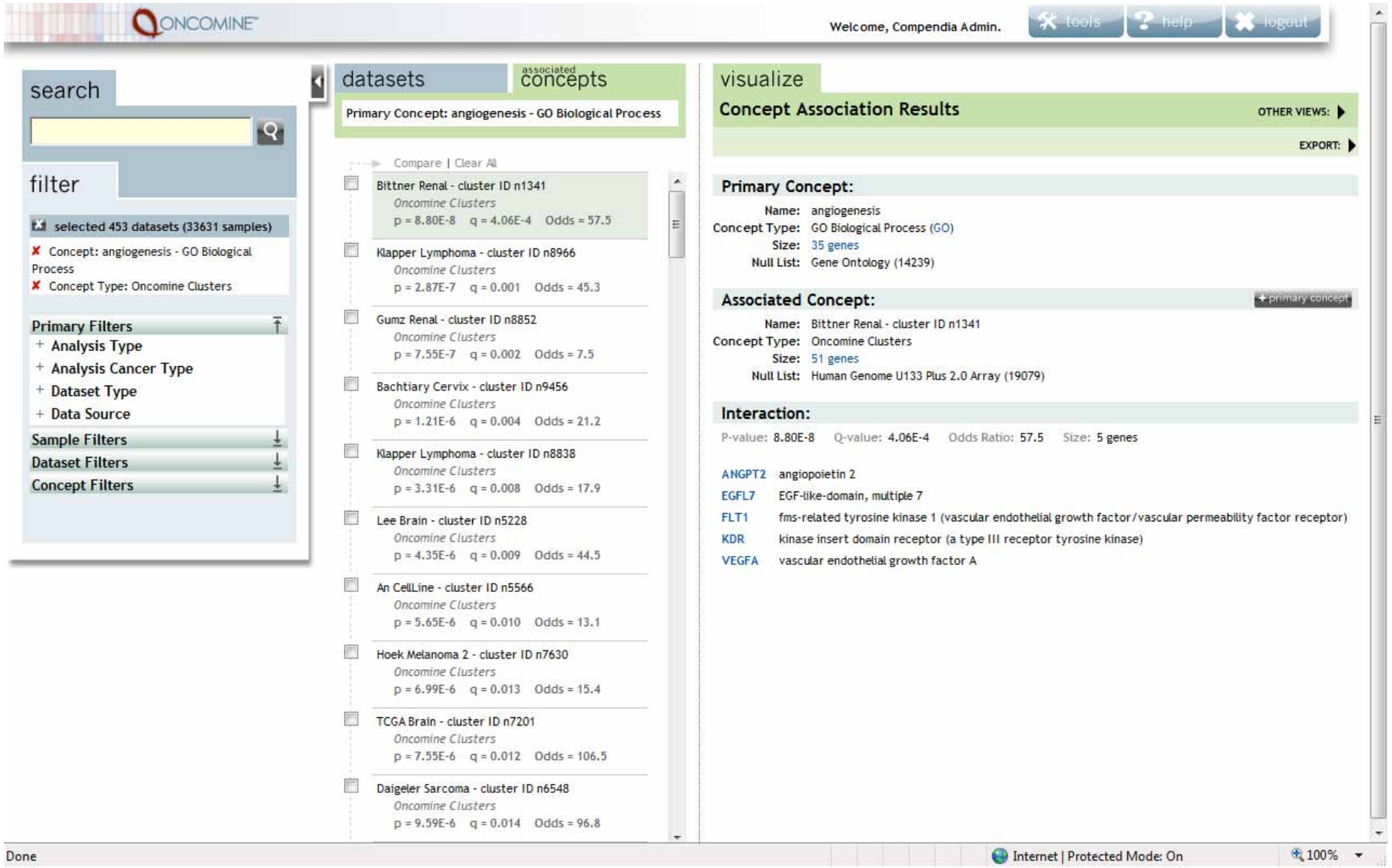
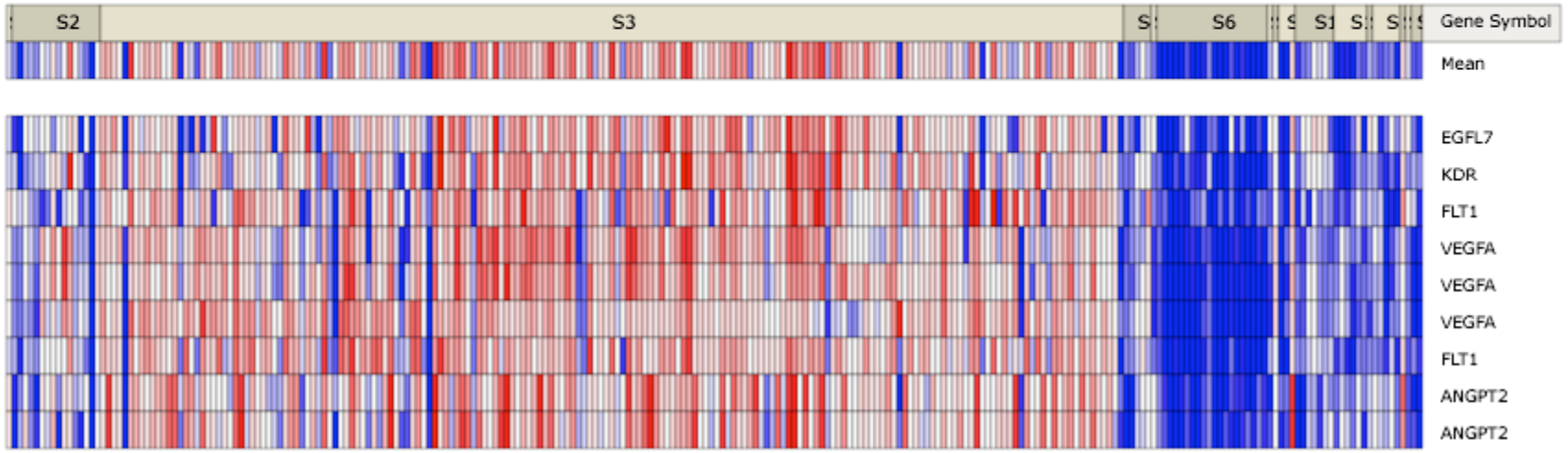

ONCOMINE
Welcome, Compendia Admin.
tools
help
logout
search
filter
selected 453 datasets (33631 samples)
Concept: angiogenesis - GO Biological Process
Concept Type: Oncomine Clusters
Primary Filters
Analysis Type
Analysis Cancer Type
Dataset Type
Data Source
Sample Filters
Dataset Filters
Concept Filters
datasets
associated concepts
Primary Concept: angiogenesis - GO Biological Process
Compare | Clear All
Bittner Renal - cluster ID n1341
Oncomine Clusters
p = 8.80E-8 q = 4.06E-4 Odds = 57.5
Klapper Lymphoma - cluster ID n8966
Oncomine Clusters
p = 2.87E-7 q = 0.001 Odds = 45.3
Gumz Renal - cluster ID n8852
Oncomine Clusters
p = 7.55E-7 q = 0.002 Odds = 7.5
Bachtiary Cervix - cluster ID n9456
Oncomine Clusters
p = 1.21E-6 q = 0.004 Odds = 21.2
Klapper Lymphoma - cluster ID n8838
Oncomine Clusters
p = 3.31E-6 q = 0.008 Odds = 17.9
Lee Brain - cluster ID n5228
Oncomine Clusters
p = 4.35E-6 q = 0.009 Odds = 44.5
An CellLine - cluster ID n5566
Oncomine Clusters
p = 5.65E-6 q = 0.010 Odds = 13.1
Hoek Melanoma 2 - cluster ID n7630
Oncomine Clusters
p = 6.99E-6 q = 0.013 Odds = 15.4
TCGA Brain - cluster ID n7201
Oncomine Clusters
p = 7.55E-6 q = 0.012 Odds = 106.5
Daigeler Sarcoma - cluster ID n6548
Oncomine Clusters
p = 9.59E-6 q = 0.014 Odds = 96.8
visualize
Concept Association Results
OTHER VIEWS:
EXPORT:
Primary Concept:
Name: angiogenesis
Concept Type: GO Biological Process (GO)
Size: 35 genes
Null List: Gene Ontology (14239)
Associated Concept:
+ primary concept
Name: Bittner Renal - cluster ID n1341
Concept Type: Oncomine Clusters
Size: 51 genes
Null List: Human Genome U133 Plus 2.0 Array (19079)
Interaction:
P-value: 8.80E-8 Q-value: 4.06E-4 Odds Ratio: 57.5 Size: 5 genes
ANGPT2 angiopoietin 2
EGFL7 EGF-like-domain, multiple 7
FLT1 fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)
KDR kinase insert domain receptor (a type III receptor tyrosine kinase)
VEGFA vascular endothelial growth factor A
Done
Internet | Protected Mode: On
100%

# Angiogenesis signature in RCC

| Navigation | Width | Contrast | Map Type | Sub Class |
|---|---|---|---|---|
| Next 20 | ◀◀ ◀ ◆ ▶ ▶▶ | ◀◀ ◀ ◆ ▶ ▶▶ | Heat | Renal Carcinoma - Type |

**Study:** Bittner_Renal
**Experiment Type:** mRNA
**Tissue:** Carcinoma of the Collecting Ducts of Bellini (1), Chromophobe Renal Cell Carcinoma (16), Clear Cell Renal Cell Carcinoma (185), Granular Renal Cell Carcinoma (5), Infiltrating Renal Pelvis Urothelial Carcinoma, Sarcomatoid Variant (1), Papillary Renal Cell Carcinoma (20), Renal Angiomyolipoma (1), Renal Carcinoma (1), Renal Cell Carcinoma (3), Renal Oncocytoma (7), Renal Pelvis Papillary Urothelial Carcinoma (6), Renal Pelvis Squamous Cell Carcinoma (1), Renal Pelvis Urothelial Carcinoma (5)

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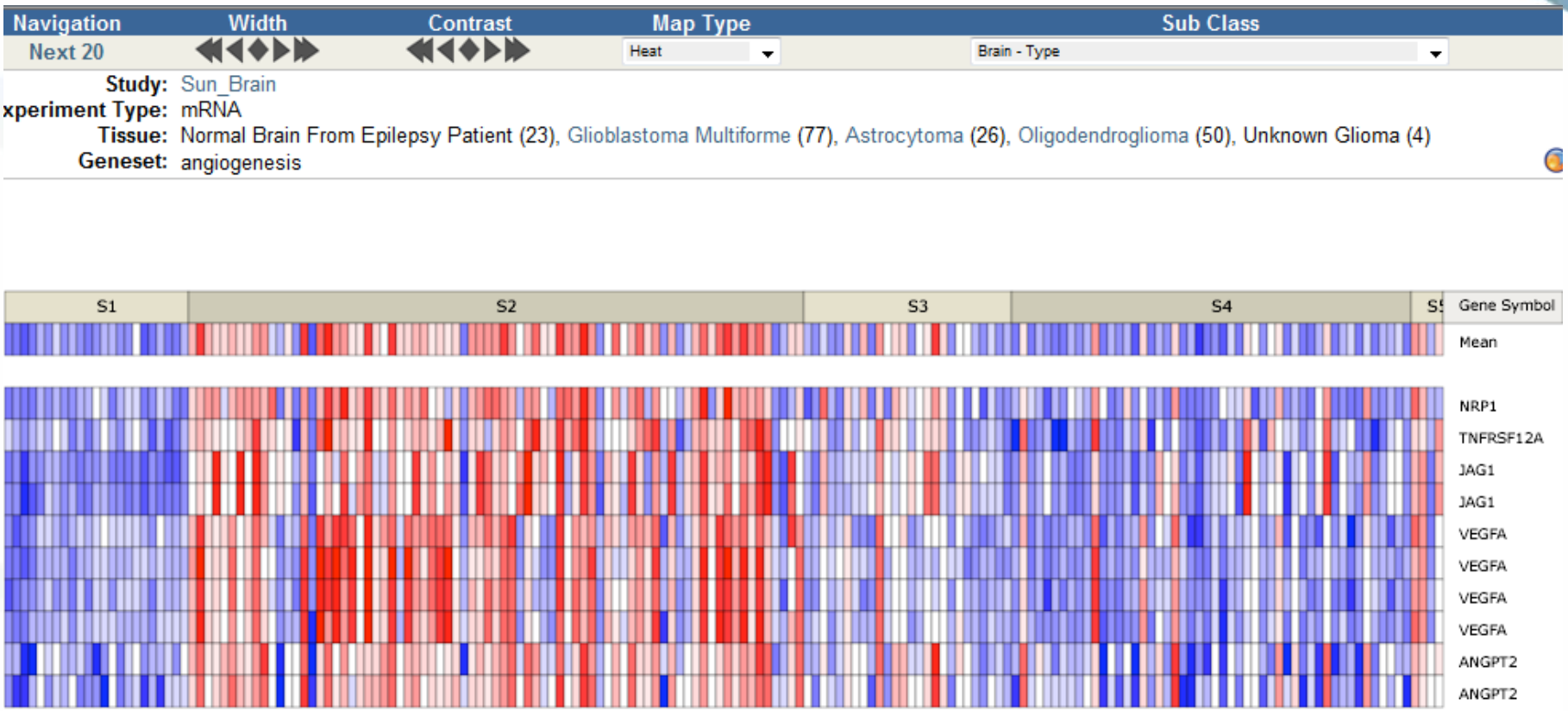
# Angiogenesis signature in glioblastoma

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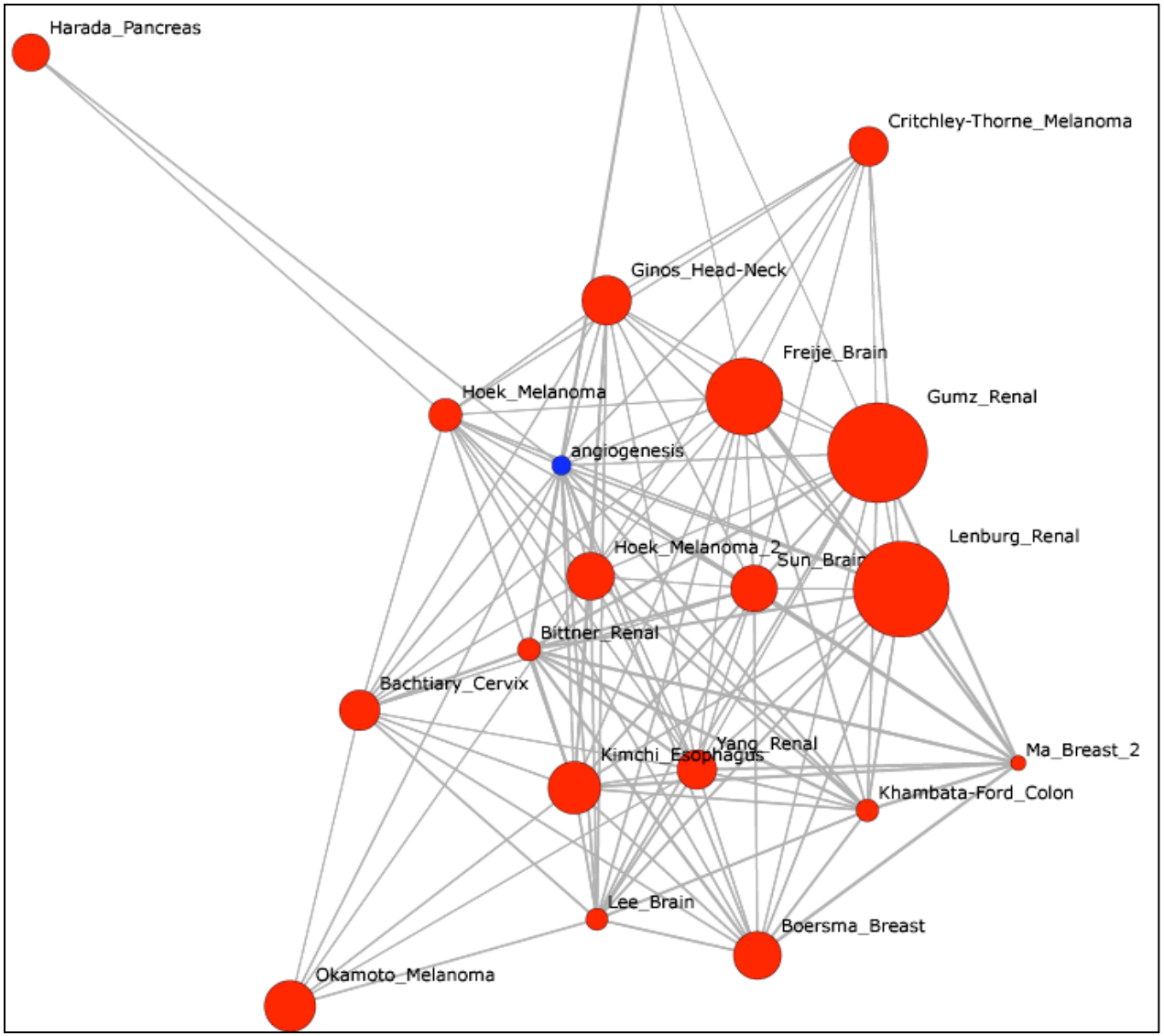
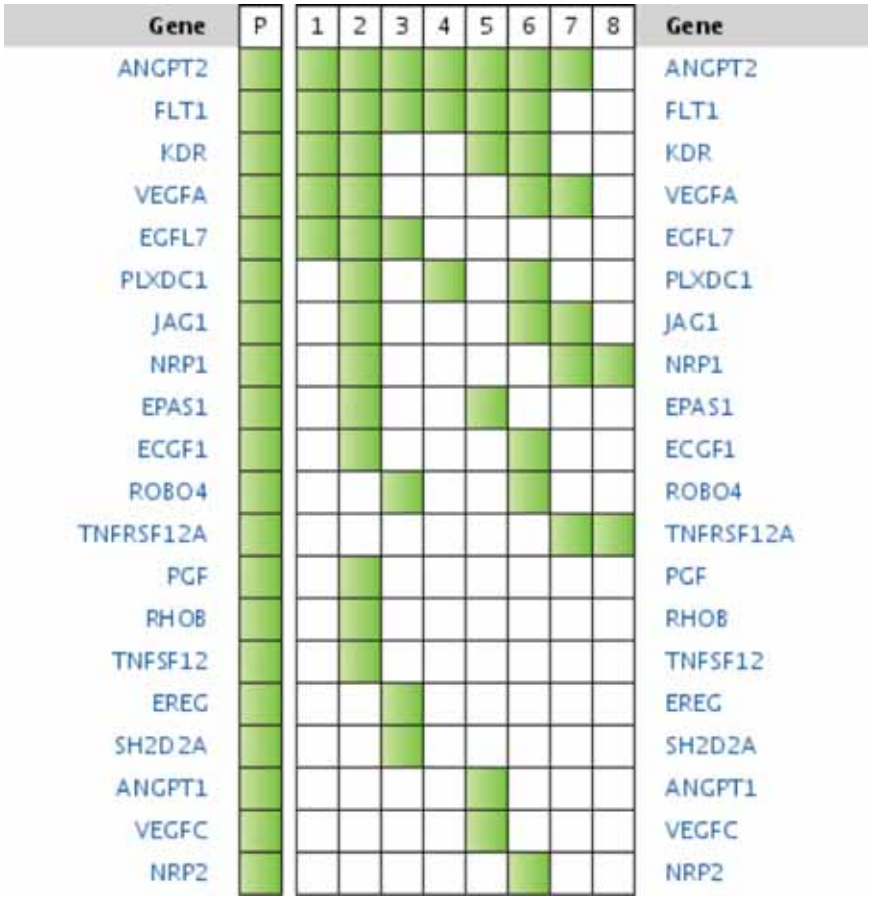


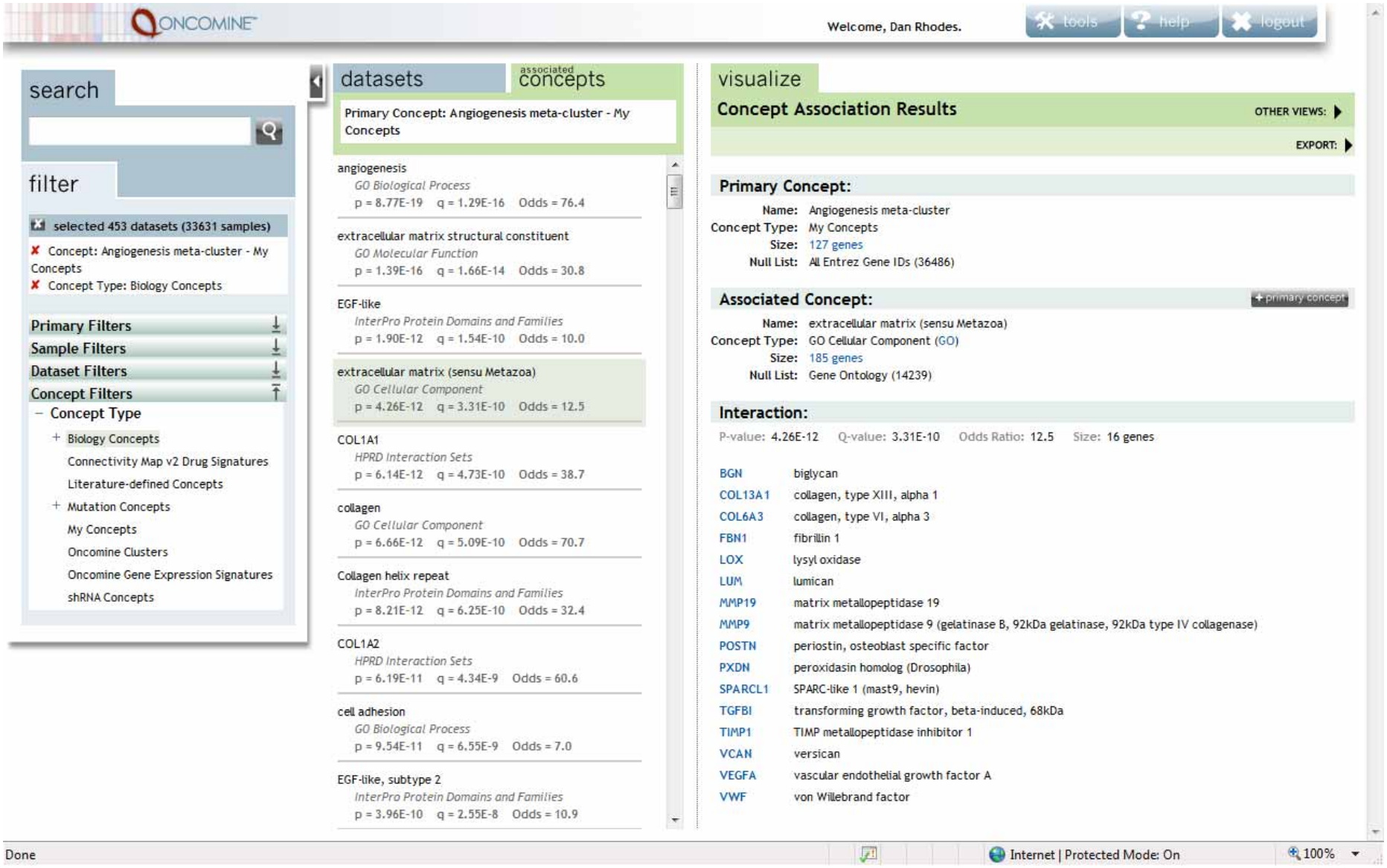

•P-value: <1E-3 Odds Ratio: >4

# Angiogenesis genes across 8 tumor clusters




**Legend**

P. angiogenesis
*GO Biological Process*
1. Bittner Renal - cluster ID n1341
*Oncomine Clusters*
2. Gumz Renal - cluster ID n8852
*Oncomine Clusters*
3. Bachtiary Cervix - cluster ID n9456
*Oncomine Clusters*
4. TCGA Brain - cluster ID n7201
*Oncomine Clusters*
5. Boersma Breast - cluster ID n7839
*Oncomine Clusters*
6. Lenburg Renal - cluster ID n9819
*Oncomine Clusters*
7. Sun Brain - cluster ID n3808
*Oncomine Clusters*
8. Hoek Melanoma - cluster ID n5920
*Oncomine Clusters*


ONCOMINE
Welcome, Dan Rhodes.
tools
help
logout
search
filter
selected 453 datasets (33631 samples)
Concept: Angiogenesis meta-cluster - My Concepts
Concept Type: Biology Concepts
Primary Filters
Sample Filters
Dataset Filters
Concept Filters
Concept Type
Biology Concepts
Connectivity Map v2 Drug Signatures
Literature-defined Concepts
Mutation Concepts
My Concepts
Oncomine Clusters
Oncomine Gene Expression Signatures
shRNA Concepts
datasets
associated concepts
Primary Concept: Angiogenesis meta-cluster - My Concepts
angiogenesis
GO Biological Process
p = 8.77E-19 q = 1.29E-16 Odds = 76.4
extracellular matrix structural constituent
GO Molecular Function
p = 1.39E-16 q = 1.66E-14 Odds = 30.8
EGF-like
InterPro Protein Domains and Families
p = 1.90E-12 q = 1.54E-10 Odds = 10.0
extracellular matrix (sensu Metazoa)
GO Cellular Component
p = 4.26E-12 q = 3.31E-10 Odds = 12.5
COL1A1
HPRD Interaction Sets
p = 6.14E-12 q = 4.73E-10 Odds = 38.7
collagen
GO Cellular Component
p = 6.66E-12 q = 5.09E-10 Odds = 70.7
Collagen helix repeat
InterPro Protein Domains and Families
p = 8.21E-12 q = 6.25E-10 Odds = 32.4
COL1A2
HPRD Interaction Sets
p = 6.19E-11 q = 4.34E-9 Odds = 60.6
cell adhesion
GO Biological Process
p = 9.54E-11 q = 6.55E-9 Odds = 7.0
EGF-like, subtype 2
InterPro Protein Domains and Families
p = 3.96E-10 q = 2.55E-8 Odds = 10.9
visualize
Concept Association Results
OTHER VIEWS:
EXPORT:
Primary Concept:
Name: Angiogenesis meta-cluster
Concept Type: My Concepts
Size: 127 genes
Null List: All Entrez Gene IDs (36486)
Associated Concept:
primary concept
Name: extracellular matrix (sensu Metazoa)
Concept Type: GO Cellular Component (GO)
Size: 185 genes
Null List: Gene Ontology (14239)
Interaction:
P-value: 4.26E-12 Q-value: 3.31E-10 Odds Ratio: 12.5 Size: 16 genes
BGN biglycan
COL13A1 collagen, type XIII, alpha 1
COL6A3 collagen, type VI, alpha 3
FBN1 fibrillin 1
LOX lysyl oxidase
LUM lumican
MMP19 matrix metallopeptidase 19
MMP9 matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)
POSTN periostin, osteoblast specific factor
PXDN peroxidasin homolog (Drosophila)
SPARCL1 SPARC-like 1 (mast9, hevin)
TGFBI transforming growth factor, beta-induced, 68kDa
TIMP1 TIMP metallopeptidase inhibitor 1
VCAN versican
VEGFA vascular endothelial growth factor A
VWF von Willebrand factor
Done
Internet | Protected Mode: On
100%

# Hypoxic response signature

- Transcriptional regulation in response to hypoxia and HIF-1 (Manalo et al, Blood, 2005)
  - Areterial endothelial cells cultured under hypoxic conditions
  - Transfected with HIF-1 alpha
  - 191 genes up-regulated by both conditions
- Hypoxic response signature characteristics
  - Cell adhesion, ECM, HIF-1 binding sites
  - VEGFA, VEGFC, PLCG2

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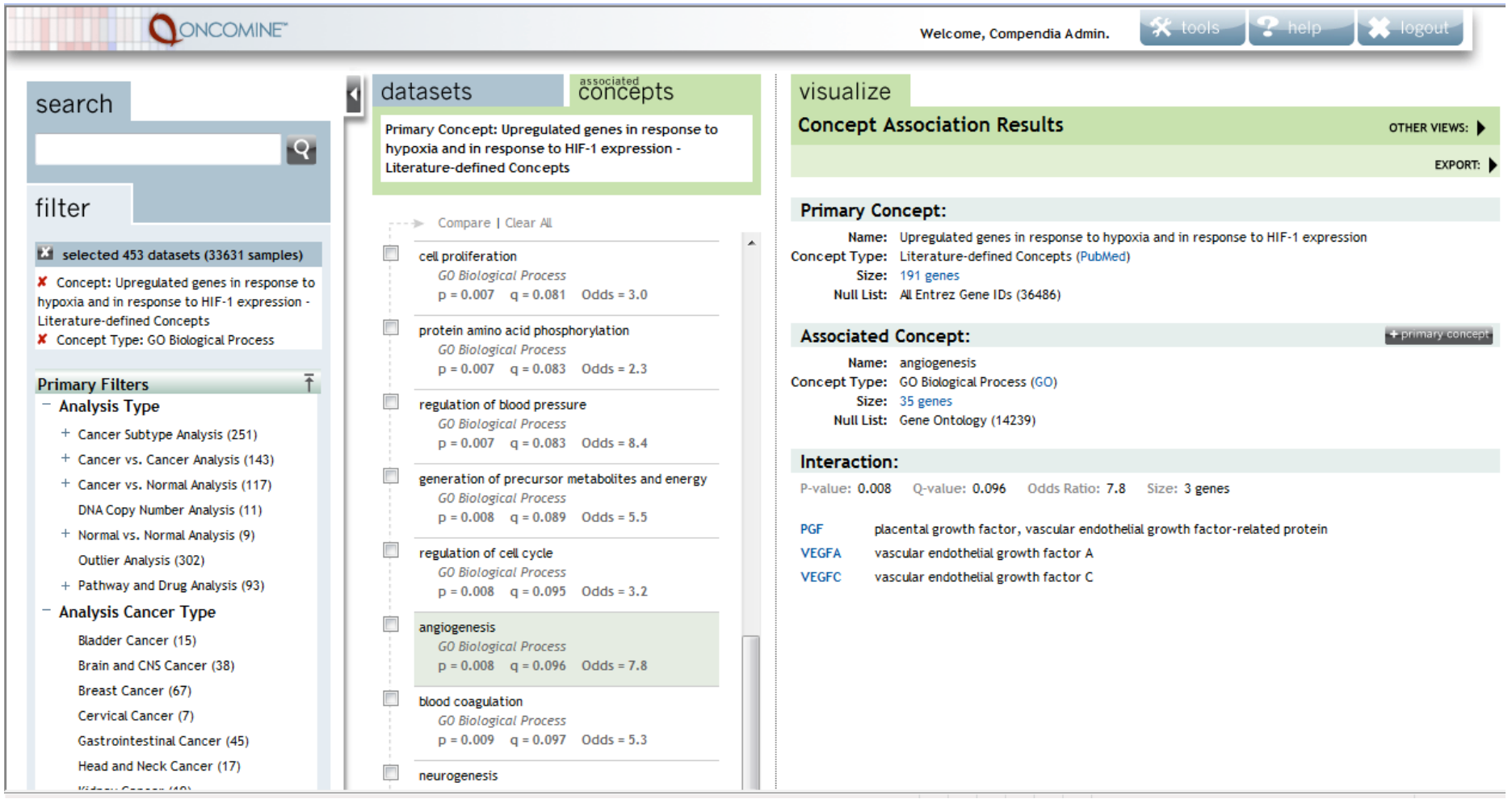
ONCOMINE
Welcome, Compendia Admin.
tools
help
logout
search
filter
selected 453 datasets (33631 samples)
Concept: Upregulated genes in response to hypoxia and in response to HIF-1 expression - Literature-defined Concepts
Concept Type: GO Biological Process
Primary Filters
Analysis Type
Cancer Subtype Analysis (251)
Cancer vs. Cancer Analysis (143)
Cancer vs. Normal Analysis (117)
DNA Copy Number Analysis (11)
Normal vs. Normal Analysis (9)
Outlier Analysis (302)
Pathway and Drug Analysis (93)
Analysis Cancer Type
Bladder Cancer (15)
Brain and CNS Cancer (38)
Breast Cancer (67)
Cervical Cancer (7)
Gastrointestinal Cancer (45)
Head and Neck Cancer (17)
datasets
associated concepts
Primary Concept: Upregulated genes in response to hypoxia and in response to HIF-1 expression - Literature-defined Concepts
Compare | Clear All
cell proliferation
GO Biological Process
p = 0.007 q = 0.081 Odds = 3.0
protein amino acid phosphorylation
GO Biological Process
p = 0.007 q = 0.083 Odds = 2.3
regulation of blood pressure
GO Biological Process
p = 0.007 q = 0.083 Odds = 8.4
generation of precursor metabolites and energy
GO Biological Process
p = 0.008 q = 0.089 Odds = 5.5
regulation of cell cycle
GO Biological Process
p = 0.008 q = 0.095 Odds = 3.2
angiogenesis
GO Biological Process
p = 0.008 q = 0.096 Odds = 7.8
blood coagulation
GO Biological Process
p = 0.009 q = 0.097 Odds = 5.3
neurogenesis
visualize
Concept Association Results
OTHER VIEWS:
EXPORT:
Primary Concept:
Name: Upregulated genes in response to hypoxia and in response to HIF-1 expression
Concept Type: Literature-defined Concepts (PubMed)
Size: 191 genes
Null List: All Entrez Gene IDs (36486)
Associated Concept:
+ primary concept
Name: angiogenesis
Concept Type: GO Biological Process (GO)
Size: 35 genes
Null List: Gene Ontology (14239)
Interaction:
P-value: 0.008 Q-value: 0.096 Odds Ratio: 7.8 Size: 3 genes
PGF placental growth factor, vascular endothelial growth factor-related protein
VEGFA vascular endothelial growth factor A
VEGFC vascular endothelial growth factor C

# Hypoxic response signature associations

| Oncomine Signatures | Count | Avg (OR) |
|---|---|---|
| Cancer Type: Kidney Cancer | 7 | 5.0 |
| Bladder Cancer Type: Bladder Urothelial Carcinoma | 5 | 3.8 |
| Brain and CNS Cancer Type: Glioblastoma | 3 | 4.3 |
| Cancer Type: Brain and CNS Cancer | 3 | 3.6 |
| Clear Cell Renal Cell Carcinoma vs. Normal | 3 | 4.9 |
| Glioblastoma vs. Normal | 3 | 5.0 |
| Organ Type: Lung | 3 | 3.3 |
| Renal Cell Carcinoma Type: Clear Cell Renal Cell Carcinoma | 3 | 7.1 |
| Cancer Type: Pancreatic Cancer | 2 | 3.3 |
| Diffuse Gastric Adenocarcinoma vs. Normal | 2 | 4.6 |
| Ductal Breast Carcinoma - ERBB2 Positive | 2 | 3.4 |
| Ductal Breast Carcinoma Type: Invasive Ductal Breast Carcinoma | 2 | 4.0 |
| Gastric Adenocarcinoma Type: Gastric Mixed Adenocarcinoma | 2 | 3.6 |
| Gastric Mixed Adenocarcinoma vs. Normal | 2 | 3.7 |
| Head and Neck Squamous Cell Carcinoma vs. Normal | 2 | 4.4 |
| Infiltrating Bladder Urothelial Carcinoma - Advanced N Stage | 2 | 4.3 |

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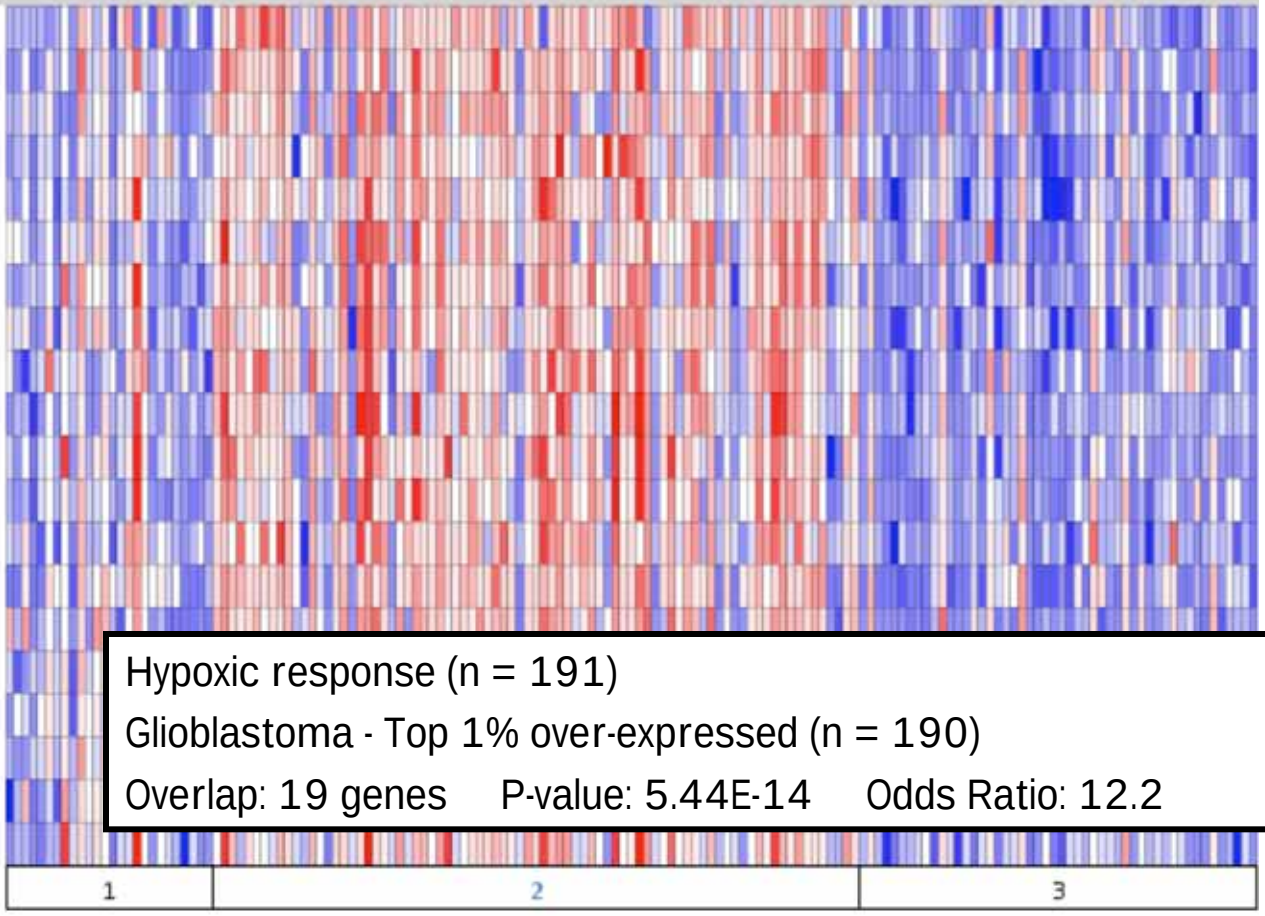
# Upregulated genes in response to hypoxia and in response to HIF-1 expression

Over-expression in Brain and CNS Cancer Type: Glioblastoma

| Rank | P-value | Gene |
|---|---|---|
| 1 | 3.27E-19 | SHOX2 |
| 12 | 1.23E-16 | COL4A2 |
| 14 | 1.62E-16 | VEGFA |
| 17 | 2.36E-16 | FKBP9 |
| 32 | 3.00E-15 | LAMB1 |
| 42 | 6.20E-15 | ADM |
| 43 | 6.49E-15 | FNDC3B |
| 45 | 7.44E-15 | SERPINE1 |
| 63 | 5.52E-14 | C8orf4 |
| 64 | 5.83E-14 | LOX |
| 71 | 8.45E-14 | COL1A2 |
| 75 | 9.93E-14 | LOXL2 |
| 92 | 3.55E-13 | IGFBP3 |
| 100 | 5.69E-13 | COL4A1 |
| 131 | 2.02E-12 | STC1 |
| 145 | 3.02E-12 | PLOD1 |
| 146 | 3.30E-12 | SPAG4 |
| 177 | 6.79E-12 | GBE1 |
| 181 | 7.23E-12 | ARL4C |
| 229 | 2.63E-11 | COL5A1 |




Hypoxic response (n = 191)

Glioblastoma - Top 1% over-expressed (n = 190)

Overlap: 19 genes P-value: 5.44E-14 Odds Ratio: 12.2

**Legend**

1. Astrocytoma (26) **2. Glioblastoma (81)** 3. Oligodendroglial Tumor (50)

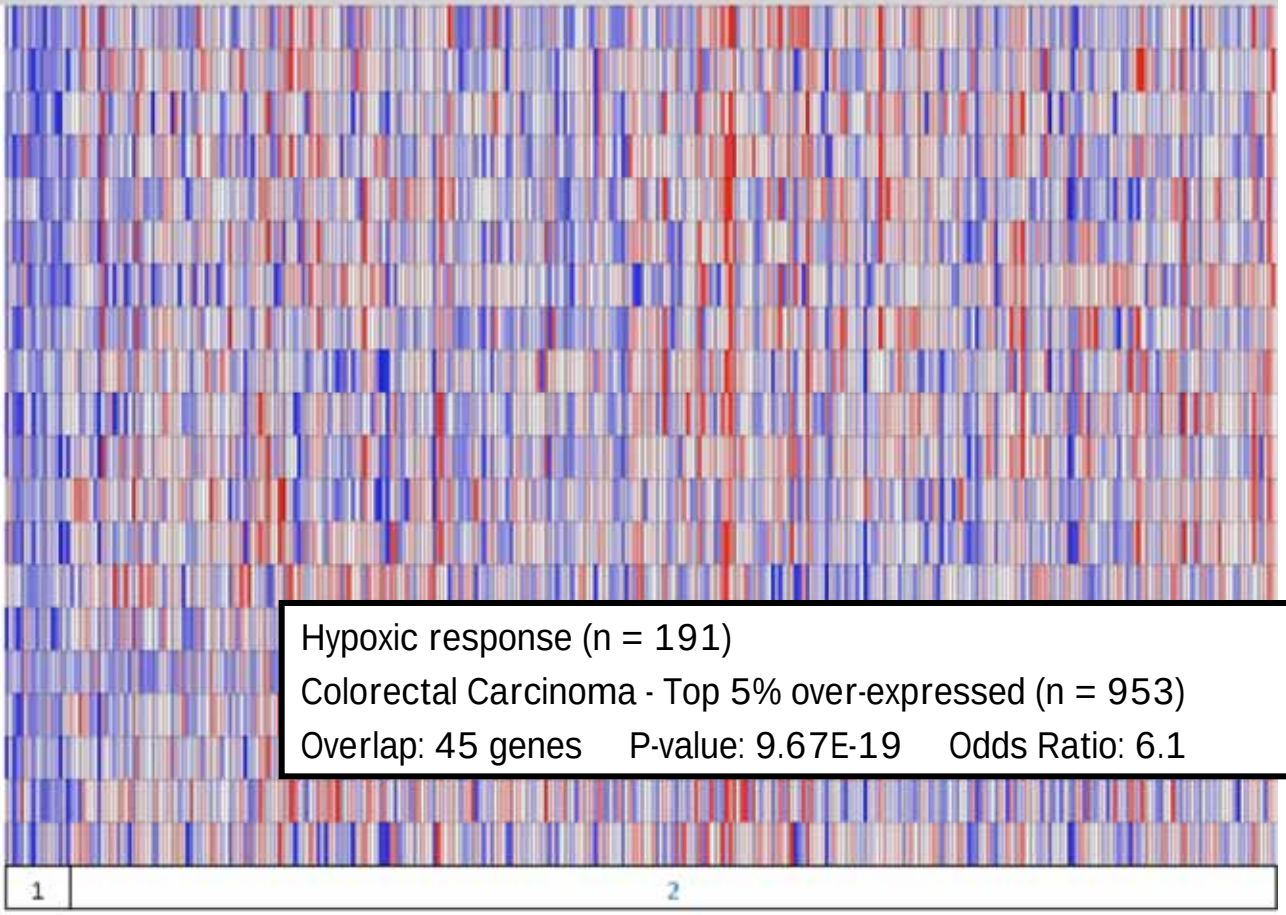
**Sun Brain**

| | |
|---|---|
| Cancer Cell 2006/04/17 | 180 samples |
| mRNA | 19,079 measured genes |
| Human Genome U133 Plus 2.0 Array | |

# Upregulated genes in response to hypoxia and in response to HIF-1 expression

Over-expression in Colorectal Cancer Type: Colorectal Carcinoma

| Rank | P-value | Gene |
|---|---|---|
| 9 | 4.01E-5 | GADD45B |
| 12 | 6.41E-5 | TNFAIP3 |
| 13 | 6.70E-5 | SERPINE1 |
| 22 | 1.42E-4 | SLC2A3 |
| 41 | 4.16E-4 | RGS3 |
| 47 | 5.72E-4 | BGN |
| 48 | 5.77E-4 | NPR1 |
| 49 | 5.82E-4 | NUAK1 |
| 83 | 0.001 | PLOD2 |
| 91 | 0.001 | COL18A1 |
| 99 | 0.001 | COL1A2 |
| 124 | 0.002 | ZEB1 |
| 129 | 0.002 | COL4A2 |
| 130 | 0.002 | IER3 |
| 138 | 0.002 | VEGFC |
| 153 | 0.002 | ANGPTL4 |
| 167 | 0.003 | TNS1 |
| 169 | 0.003 | LOX |
| 197 | 0.003 | ADM |
| 198 | 0.003 | FILIP1L |




Hypoxic response (n = 191)

Colorectal Carcinoma - Top 5% over-expressed (n = 953)

Overlap: 45 genes P-value: 9.67E-19 Odds Ratio: 6.1

**Legend**

1. Colorectal Adenoma (17) **2. Colorectal Carcinoma (313)**

**Bittner Colon**

| | |
|---|---|
| Not Published 2005/01/15 | 373 samples |
| mRNA | 19,079 measured genes |
| Human Genome U133 Plus 2.0 Array | |

# Correlation of signature in tumors

| Tissue | # | Avg (OR) |
|---|---|---|
| Breast | 35 | 9.7 |
| Brain | 19 | 22.7 |
| Lung | 12 | 8.0 |
| Ovarian | 10 | 14.2 |
| Prostate | 10 | 12.0 |
| Sarcoma | 9 | 14.8 |
| Lymphoma | 8 | 10.2 |
| Bladder | 7 | 8.6 |
| Melanoma | 7 | 18.3 |
| Normal | 7 | 10.1 |
| Renal | 7 | 12.7 |
| Colon | 6 | 10.4 |
| Leukemia | 6 | 12.8 |
| Esophagus | 3 | 11.4 |
| Head-Neck | 3 | 12.7 |
| Liver | 3 | 8.2 |
| Neuroblastoma | 3 | 9.8 |
| Pancreas | 3 | 5.0 |
| Skin | 3 | 6.3 |
| Cervix | 2 | 12.4 |
| Multi-cancer | 2 | 12.4 |
| Seminoma | 2 | 22.0 |

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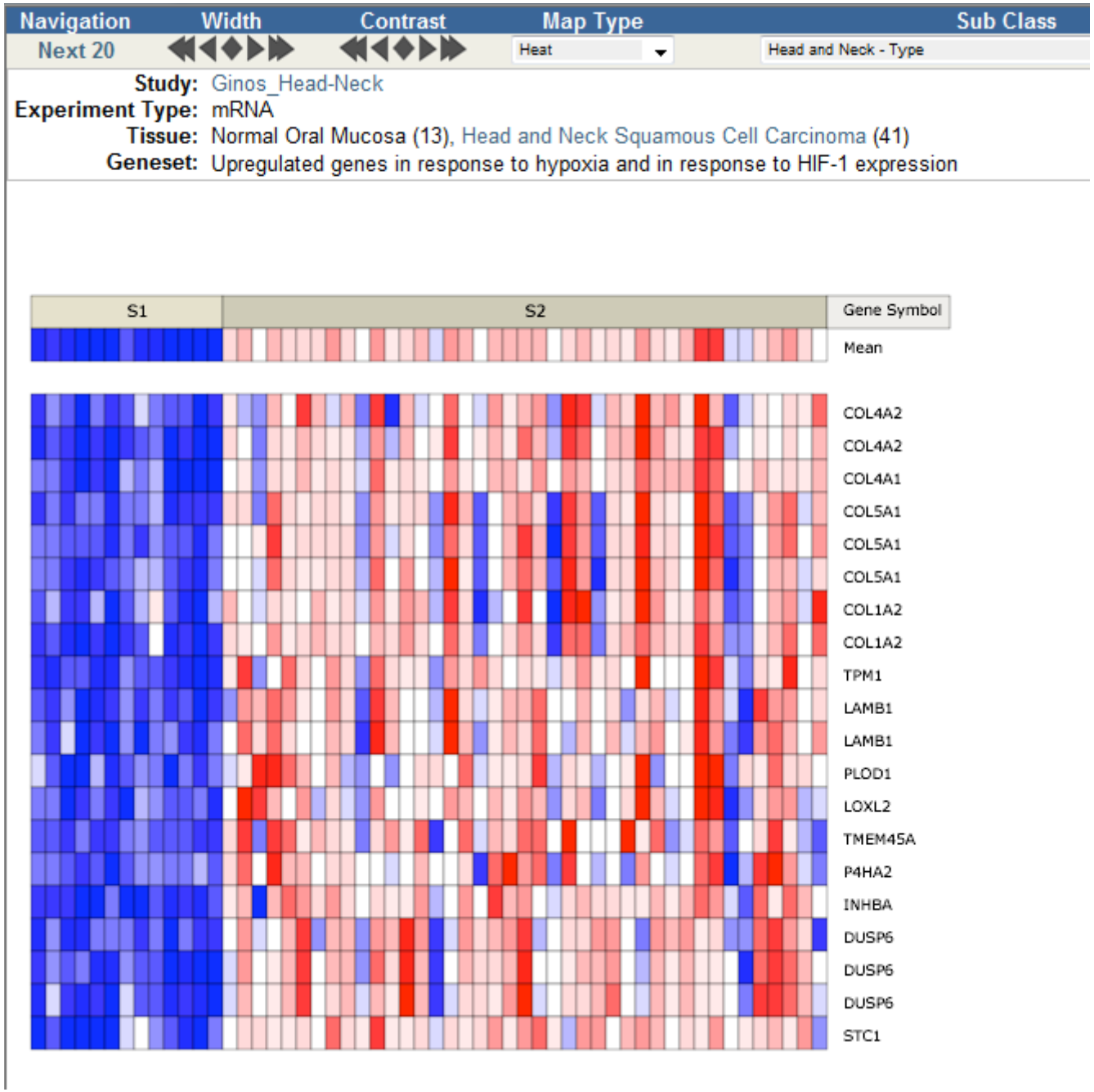
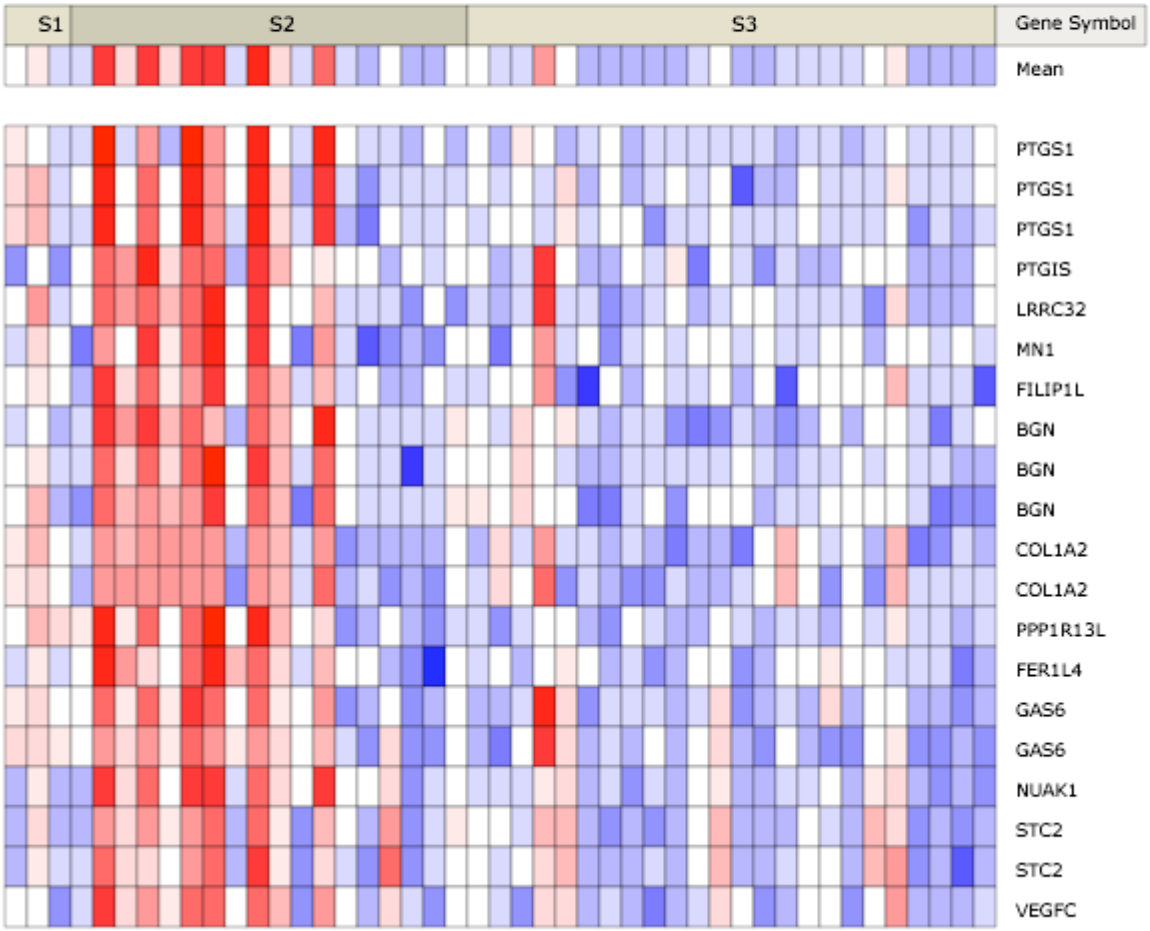

Navigation
Width
Contrast
Map Type
Sub Class
Next 20
Heat
Head and Neck - Type
Study: Ginos_Head-Neck
Experiment Type: mRNA
Tissue: Normal Oral Mucosa (13), Head and Neck Squamous Cell Carcinoma (41)
Geneset: Upregulated genes in response to hypoxia and in response to HIF-1 expression
S1
S2
Gene Symbol
Mean
COL4A2
COL4A2
COL4A1
COL5A1
COL5A1
COL5A1
COL1A2
COL1A2
TPM1
LAMB1
LAMB1
PLOD1
LOXL2
TMEM45A
P4HA2
INHBA
DUSP6
DUSP6
DUSP6
STC1

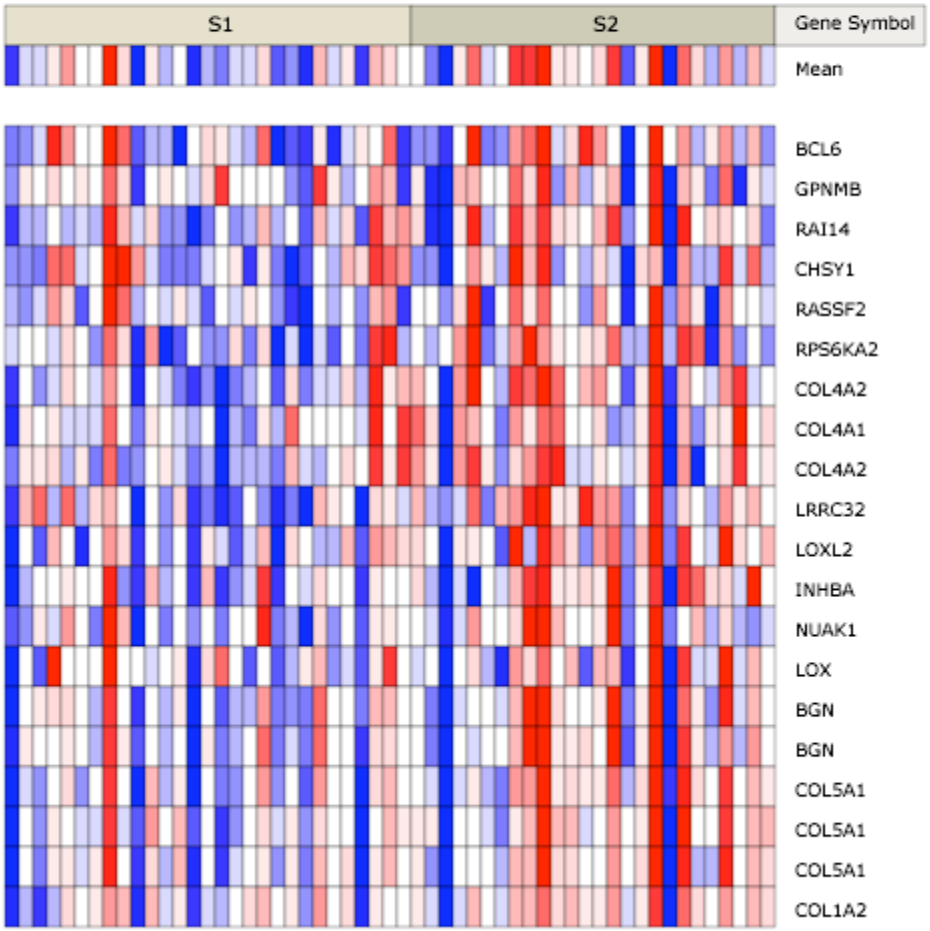
| Navigation | Width | Contrast | Map Type | Sub Class |
|---|---|---|---|---|
| Next 20 | | | Heat | Skin - Type |

**Study:** Hoek_Melanoma
**Experiment Type:** mRNA
**Tissue:** Normal Melanocyte (3), Cutaneous Melanoma (18), Metastasic Melanoma (24)
**Geneset:** Upregulated genes in response to hypoxia and in response to HIF-1 expression



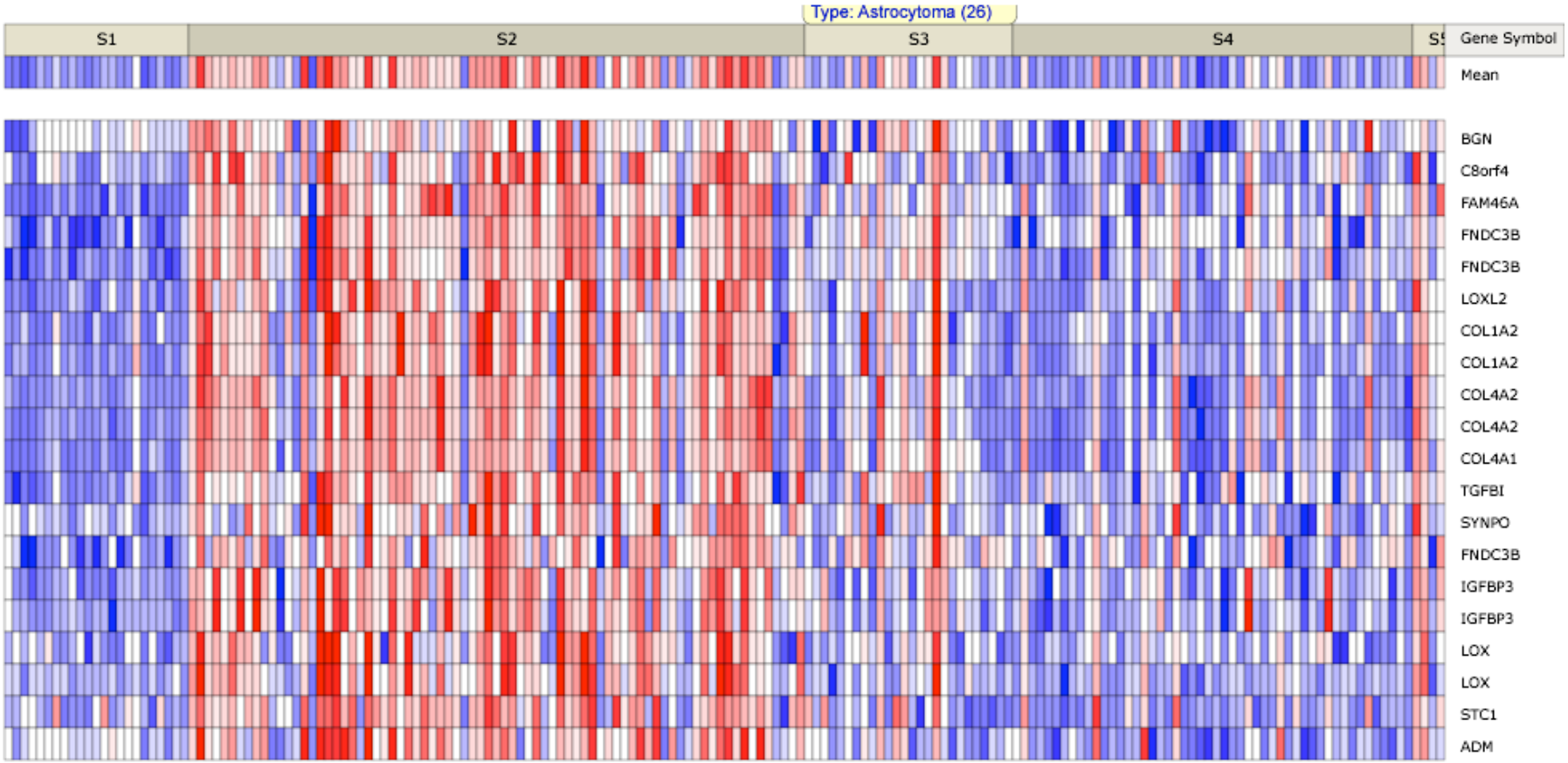
| Navigation | Width | Contrast | Map Type | Sub Class |
|---|---|---|---|---|
| Next 20 | | | Heat | Colorectal Carcinoma - Recurrence - 5 Years |

**Study:** Lin_Colon
**Experiment Type:** mRNA
**Tissue:** Colorectal Carcinoma (55)
**Geneset:** Upregulated genes in response to hypoxia and in response to HIF-1 expression



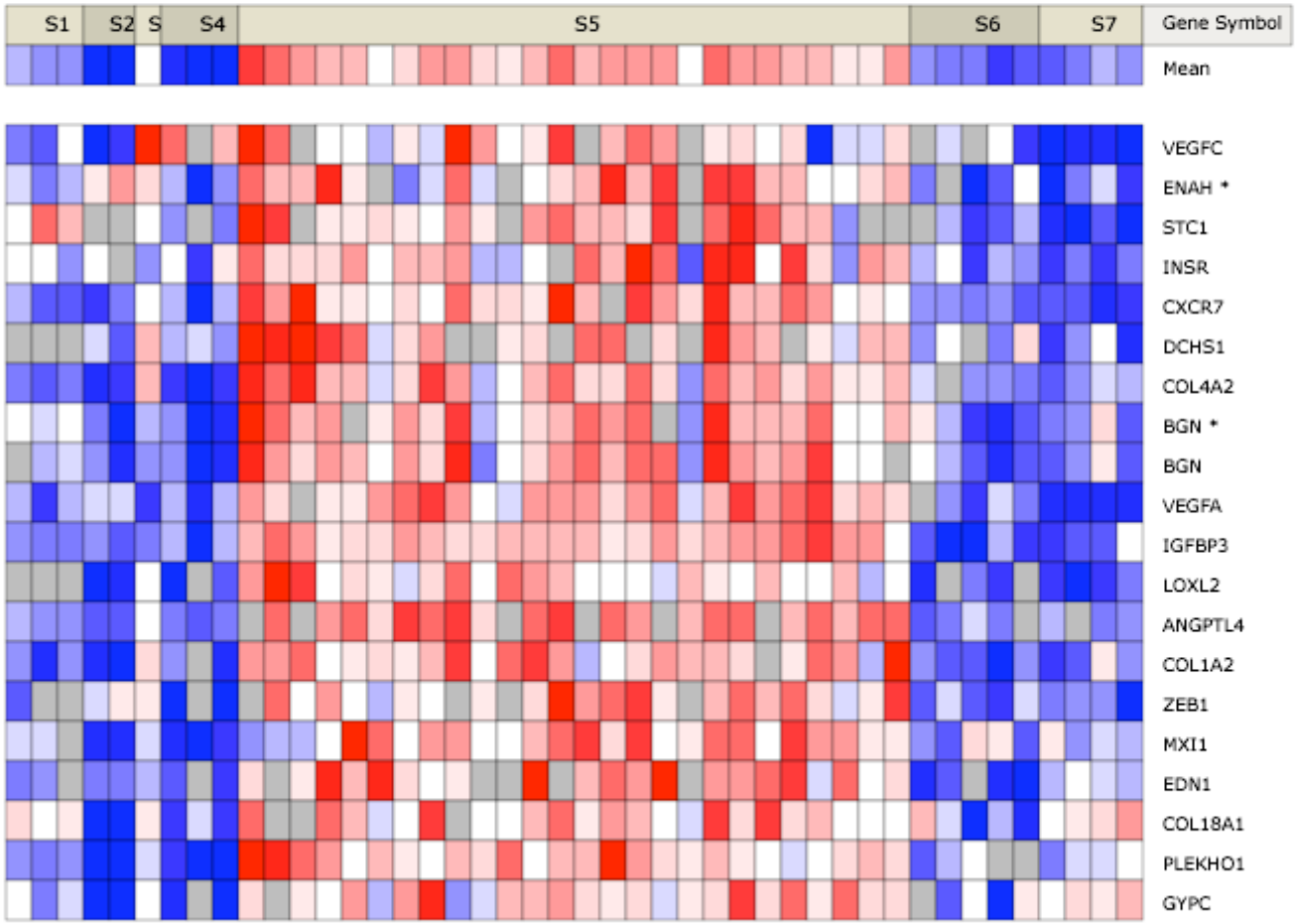
| Navigation | Width | Contrast | Map Type | Sub Class |
|---|---|---|---|---|
| Next 20 | | | Heat | Brain - Type |

**Study:** Sun_Brain
**Experiment Type:** mRNA
**Tissue:** Normal Brain From Epilepsy Patient (23), Glioblastoma Multiforme (77), Astrocytoma (26), Oligodendroglioma (50), Unknown Glioma (4)
**Geneset:** Upregulated genes in response to hypoxia and in response to HIF-1 expression



| Navigation | Width | Contrast | Map Type |
|---|---|---|---|
| Next 20 | ◀◀ ◀ ◆ ▶ ▶▶ | ◀◀ ◀ ◆ ▶ ▶▶ | Heat |

**Study:** Higgins_Renal
**Experiment Type:** mRNA
**Tissue:** Normal Kidney (3), Benign Oncocytoma (2), Angiomyolipoma (1), Chromophobe Renal Cell Carcinoma (3), Clear Renal Cell Carcinoma (26), Granular Renal Cell Carcinoma (5), Papillary Renal Cell Carcinoma (4)
**Geneset:** Upregulated genes in response to hypoxia and in response to HIF-1 expression



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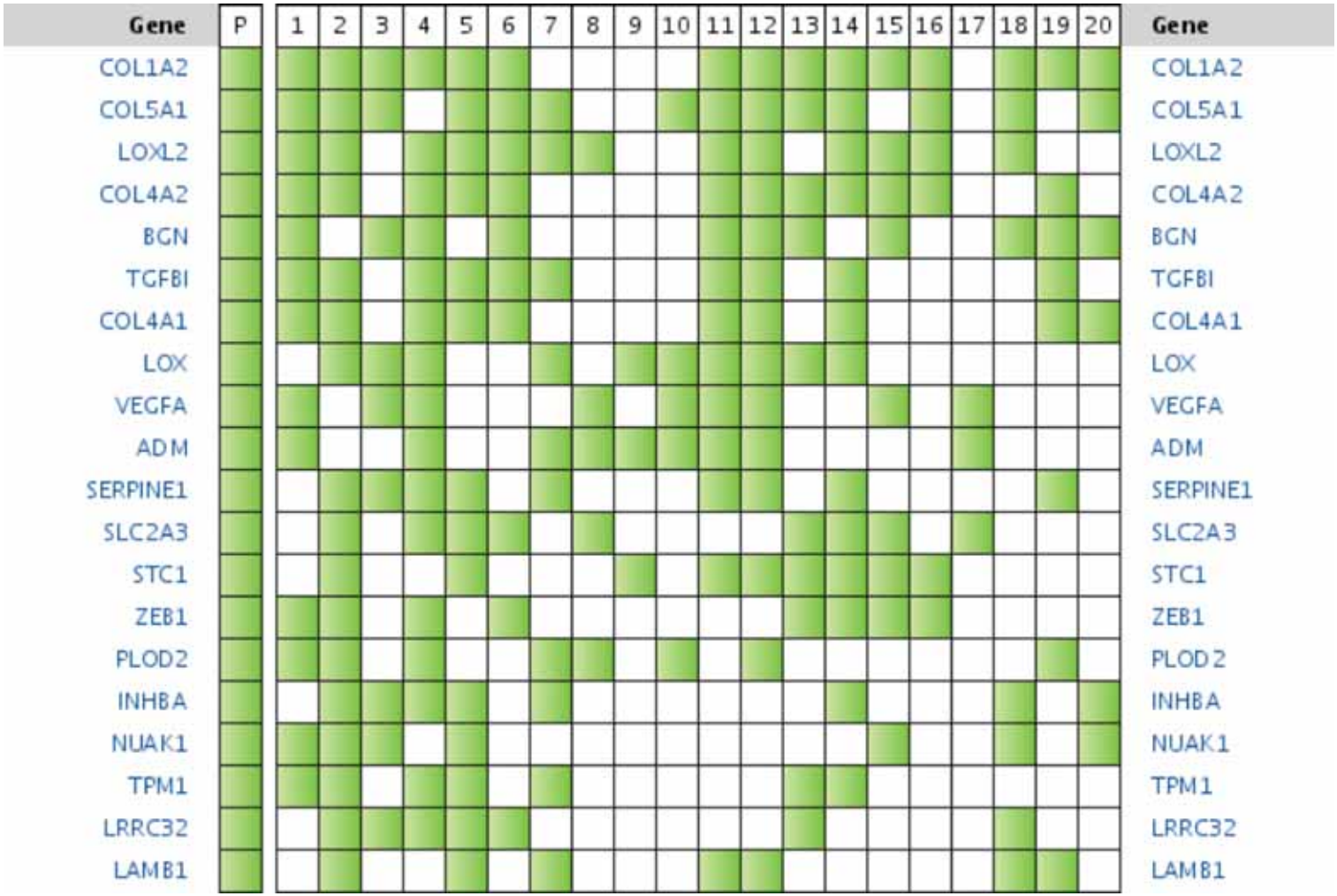
# Hypoxia response co-expressed in solid tumors



# Summary

- Gene expression readout for angiogenesis pathway
  - VEGFA & correlates
  - Angiogenesis pathway
  - Hypoxic response signature
- Tumor populations over-expressing angiogenesis signatures
  - Clear cell RCC (not papillary)
  - Glioblastoma
  - Fraction of other tumor populations (H&N, Colon…)
  - Activated by HRAS / MAPK
- Do signatures predict response to therapy?

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