## Supplementary information S4 (table) | Role(s) of BRD-containing proteins in cancer (mutations, expression, translocations)

<table>
<thead>
<tr>
<th>Sub-Family</th>
<th>Protein</th>
<th>Mutations, Expression and Role(s) in Cancer</th>
<th>Ref.</th>
<th>Fusion Partners</th>
<th>Loss of BRD in fusion</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>CECR2</td>
<td>Mutated in paediatric leukemias</td>
<td>(1)</td>
<td>-</td>
<td>-</td>
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<tr>
<td></td>
<td>FALZ/BPTF</td>
<td>Involved in c-MYC transcriptional activity and in vivo tumorigenesis</td>
<td>(2-4)</td>
<td>-</td>
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<td></td>
<td></td>
<td>Increased expression in non-small-cell lung cancer (NSCLC), rectal cancer</td>
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<tr>
<td></td>
<td>GCN5L2</td>
<td>Association of increased expression with ESCC risk in northeast Indian population</td>
<td>(5)</td>
<td>-</td>
<td>-</td>
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<tr>
<td></td>
<td>PCAF</td>
<td>Inhibitor of the mitogenic activity of the adenoviral oncoprotein E1A</td>
<td>(6-8)</td>
<td>-</td>
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<tr>
<td></td>
<td></td>
<td>Regulates b-catenin transcriptional activity</td>
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<td></td>
<td></td>
<td>Over-expressed in paediatric tumours</td>
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<tr>
<td></td>
<td>BRD2</td>
<td>Recurrently mutated in paediatric leukemia</td>
<td>(1, 9, 10)</td>
<td>-</td>
<td>-</td>
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<tr>
<td></td>
<td></td>
<td>Regulates E2F target genes through H2A.Z.2 in melanoma</td>
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<tr>
<td></td>
<td></td>
<td>Highly expressed in melanoma</td>
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<tr>
<td></td>
<td>BRD3</td>
<td>Fusion with NUT in NMC</td>
<td>(11)</td>
<td>NUT</td>
<td>No</td>
<td>(11)</td>
</tr>
<tr>
<td>II</td>
<td>BRD4</td>
<td>Regulates Myc transcription</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td>Contributes to either MYCN or c-MYC over-expression in High-grade serous ovarian carcinoma</td>
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<td></td>
<td></td>
<td>Required for the replication of tumour viruses</td>
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<td></td>
<td></td>
<td>Increased expression in HCC, melanoma, glioblastoma and malignant peripheral nerve sheath tumors (MPNST)</td>
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<td></td>
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<td>BRD4-Twist interaction leads to tumorigenicity in basal-like breast cancer.</td>
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<td>Significantly up-regulated in hepato-cellular carcinoma tissues; primary and metastatic melanoma tissues</td>
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<td>Involved in the androgen receptor-mediated gene transcription in castration-resistant prostate cancer</td>
<td>(10, 12-22)</td>
<td>NUT</td>
<td>No</td>
<td>(23, 24)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Targeting BRD4 and PI3K together, but not alone, inhibits growth of many tumour cells</td>
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<td></td>
<td></td>
<td>Simultaneous inhibition of CDK9 and MYC/BRD4 efficiently induces growth arrest and apoptosis of cancer cells</td>
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<td></td>
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<td>Together with hematopoietic transcription factors and p300/CPB acts to promote transcriptional activation, supporting leukemia maintenance</td>
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<td></td>
<td>BRD4</td>
<td>Highly expressed in non-small-cell lung cancer (NSCLC)</td>
<td>(1, 25)</td>
<td>-</td>
<td>-</td>
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<td></td>
<td></td>
<td>Recurrently mutated in paediatric leukemia</td>
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<td></td>
<td>BAZ1A</td>
<td>Mutated in carcino-sarcomas</td>
<td>(15, 26, 27)</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>
### III

<table>
<thead>
<tr>
<th>Gene</th>
<th>Aberrations and Mutations</th>
<th>Details</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CREBBP</strong></td>
<td>Chromosomal aberrations and mutations detected in AML, follicular lymphoma and ALL</td>
<td>-</td>
<td>(1, 33-44) KAT6A KAT6B MLL SLX4 RHBDF1 No (35, 36, 45-47)</td>
</tr>
<tr>
<td><strong>EP300</strong></td>
<td>Chromosomal aberrations and mutations detected in leukemia, epithelial cancer and cervical carcinoma</td>
<td>Recurrently mutated in paediatric leukemias High frequency of somatic mutations in oesophageal squamous cell cancer (associated with poor survival) Mutations in adenoid cystic carcinomas, squamous cell lung cancers and angioimmunoblastic T-cell lymphomas</td>
<td>(1, 41-43, 48-53) KAT6A ZNF384 MLL No (49, 54) (55)</td>
</tr>
</tbody>
</table>

### IV

<table>
<thead>
<tr>
<th>Gene</th>
<th>Regulates sensitivity to spindle poisons in colon cancer</th>
<th>Details</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BRD8</strong></td>
<td>High expression levels correlate with poor prognosis in some cancers</td>
<td>Transcriptional co-regulator of myc, E2F and ERAlpha Increased expression in hepato-cellular carcinoma tissues, glioblastoma cell lines, gastric cancer and endometrial carcinoma Suppression of ATAD2 inhibits hepato-cellular carcinoma progression through activation of p53 and p38-mediated apoptotic signalling High protein expression is significantly associated with established clinical-pathological variables for aggressive endometrial cancers, also in the subset of estrogen receptor α (ERα) positive tumours While in exponentially growing cells Atad2 appears dispensable for cell growth, in differentiating ES cells Atad2 becomes critical in sustaining specific gene expression programmes, controlling proliferation and differentiation</td>
<td>(15, 57-66) - -</td>
</tr>
<tr>
<td><strong>ATAD2</strong></td>
<td></td>
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<td>(1, 15, 28, 29) - -</td>
</tr>
<tr>
<td>V</td>
<td>TRIM24</td>
<td>Over-expression negatively correlates with survival of breast cancer patients</td>
<td>Fusion in PTC and myelo-proliferative syndrome</td>
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<tr>
<td></td>
<td>TRIM33</td>
<td>Abolishes tumorigenesis by destabilizing b-catenin</td>
<td>Fusion in PTC and breast cancer</td>
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<tr>
<td></td>
<td>TRIM66</td>
<td>Over-expression correlates with poor prognosis of osteosarcoma</td>
<td>Recurrently mutated in paediatric leukemias</td>
</tr>
</tbody>
</table>

### ATAD2B
- Highly expressed in gastrointestinal and breast carcinomas
- Recurrently mutated in paediatric leukemia

### BRD1
- Mono-allelic variant found in malignant mesothelioma cell lines
- Down-regulated genes in spinal ependymomas (SEPN)
- Fusion with PAX5 in leukaemia

### BRPF3
- Mutated in paediatric leukaemia

### BRD7
- Tumour suppressor required for efficient transcription of a subset of p53 target genes
- Down-regulated in the ovarian cancer tissues and colorectal tumour tissues
- Recurrently mutated in paediatric leukemia

### BRD9
- Mutated in human cancers

### SP140
- Identified as a susceptibility gene for CML
- Truncating or missense mutations in multiple myeloma

### SP140L
- No

### SP100
- Down-regulated in laryngeal cancer

### SP110
- Mutated in breast cancer
- Increased expression in glioblastoma cell lines

### TRIM24
- Over-expression negatively correlates with survival of breast cancer patients
- Fusion in PTC and myelo-proliferative syndrome
- Over-expressed in SPOP-mutant prostate cancer and head and neck squamous cell carcinoma and TRIM24 over-expression correlates with aggressive malignant phenotypes
- Promotes tumour growth and enhances resistance to chemotherapy via phosphatidylinositol 3-kinase (PI3K)/Akt signalling
- Elevated level are found in hepatocellular carcinoma tissues and correlate with shorter tumor-free survival time

### TRIM33
- Abolishes tumorigenesis by destabilizing b-catenin
- Fusion in PTC and breast cancer
- Recurrently mutated in paediatric leukemias

### TRIM66
- Over-expression correlates with poor prognosis of osteosarcoma
- Recurrently mutated in paediatric leukemias
<table>
<thead>
<tr>
<th>Gene</th>
<th>Function</th>
<th>Comments</th>
</tr>
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</table>
| **BAZ2A** | • Fusion with ETV6 in paediatric pre-B acute lymphoblastic leukaemia  
• Involved in maintaining prostate cancer cell growth, a correlation between BAZ2A expression and recurrence in prostate cancer  
• Recurrently mutated in paediatric leukemia | (1, 91, 92)  
(ETV6 not expected to produce any chimeric protein) |
| **BAZ2B** | - | - |
| **MLL** | • Recurrently mutated in paediatric leukemias  
• Multiple chromosomal translocations give rise to acute lymphoid leukemias and acute myeloid leukemias.  
• MLL complex acts as a co-activator of androgen-receptor (AR) signalling | (1, 93, 94)  
> 80  
Yes |
| **TRIM28** | • Tumour suppressor in liver  
• Elevated TRIM28 level in early-stage non-small cell lung cancer correlates with shorter tumor-free survival time  
• Increased expression in glioblastoma cell lines | (15, 96, 97)  
-  
- |
| **TAF1** | • Increased expression in castration-resistant prostate cancers with prolonged hormone treatment and glioblastoma cell lines  
• Recurrently mutated in paediatric leukemias | (1, 15, 98)  
-  
- |
| **TAF1L** | • Increased expression in glioblastoma cell lines  
• Recurrently mutated in paediatric leukemias | (1, 15)  
-  
- |
| **ZMYND8** | • Mutated in colorectal cancers  
• Recurrently mutated in paediatric leukemias  
• Promotes tumour angiogenesis  
• Complex with KDM5C controls enhancer activity and its malfunction contributes to tumorigenesis | (1, 99-101)  
RelA CEP250 BCAS4  
No |
| **ZMYND11** | • Copy number alteration in hematologic cancers  
• Low ZMYND11 expression levels in triple-negative breast cancer patients correlate with worse disease-free survivals | (105-107)  
MBTD1  
No |
| **ASH1L** | • Mutations, copy number changes and increased expression in various cancers  
• Frame-shift mutation in gastric cancer tissue  
• Mutations in oesophageal squamous cell carcinoma, in colorectal cancer cell lines  
• Recurrently mutated in paediatric leukemia  
• Increased expression in breast cancer  
• miR-142-3p down-regulates ASH1L protein expression contributing to thyroid follicular tumorigenesis | (41, 109, 110)  
(1, 41, 110-113)  
C1ORF61  
Yes |
| **PB1** | • Tumour suppressor and regulator of p21 expression. Truncations and mutants in PB1 are a cause of renal cell carcinoma (RCC) and other cancer types. | (115-118)  
-  
- |
### References


