The class-specific BCR tonic signal modulates lymphomagenesis in a c-myc deregulation transgenic model

Supplementary Material

Supplemental Figure 1: Development and proliferation of B cell in α1KI c-myc3’RR

(A) Evaluation of B cells in spleen (n=5) and LNs (n=3) from 6 weeks old mice before any disease development. Percentage of B220+ cells from α1KI c-myc3’RR (white bars) compared to α1KI (black bars). (NS, not significant; *, p <0.05) (B) Splenocytes from the same α1KI c-myc3’RR (white circles) and α1KI/control mice (black circles) were stimulated in vitro with LPS or with anti-CD40 plus IL4 for 4 days. Absorbance in the MTS assay evaluates proliferation. Results from 5 independent experiments are shown. (NS, not significant; *, p <0.05, unpaired t-test).

Supplemental Figure 2: Clonality of lymphomas in α1KI c-myc3’RR mice

Southern blot analysis was used to check lymphoma clonality with a JH4 probe. Genomic DNA from hyperplasic spleens (S) and LNs were prepared and digested with EcoRI from different tumors (3 individual mice per group, each analyzed for spleen and LN).
Supplemental Figure 3: RNA profiling of type Ia and Ib double transgenic tumors vs “Burkitt-like” (BL) and anaplastic (ANA) tumors from single transgenic c-myc mice: The clustered genes shows the most significantly genes up-regulated (A) and down-regulated (B) in type Ia (n=4) and type Ib (n=4) from α1KI c-myc3’RR tumors vs c-myc3’RR. Red represents up-regulation of gene expression, and green represents down regulation of gene expression.

Supplemental Table 1: RNA profiling of type Ia and Ib α1KI c-myc3’RR tumors compared to c-myc3’RR lymphomas. Data for the 213 most different genes were reported. The up-regulated (A) and down-regulated (B) genes in type Ia and Ib vs c-myc3’RR were represented in two different sub-tables. Columns include gene names, gene descriptions, absolute fold-change (FC), signal ratio between double transgenic and single transgenic tumors and P-values.
<table>
<thead>
<tr>
<th>Gene symbol</th>
<th>Gene name</th>
<th>Abundance (FC)</th>
<th>log2(FC)</th>
<th>Adjust p-value</th>
</tr>
</thead>
</table>

**Abnormal results**

### Transformation factors and Jak2-binding proteins

- **Foxo**
  - Fli1 represses cancerogene B
  - HIF1A
  - HIF1A
  - HIF1A
  - HIF1A

### Highly expressed in immune system

- **Gzms**
  - predicted gene 8909
  - Kiss1
  - C10orf51
  - C10orf51
  - C10orf51

### Immortalized signal transduction modulators and effectors

- **Drugs**
  - dual specificity phosphatase 6
  - TRAF2
  - Drak8
  - Drak8

### Mitochondrial metabolism

- **Lgs**
  - unc-25:RY-46 containing 6 protein coupled receptor 5
  - similar to cyclin nucleotide gated channel beta 1
  - EN3AB:00000003612
  - Actb4
  - Actb4

### Carbohydrate-related protein

- **P60**
  - protein sphingomyelin 1, regulatory (Wildtype) subset 13A
  - growth arrest specific 6 (GAS6)
  - Bcg

### Mitochondrial-related protein

- **Dros**
  - aphaic VMP-1 synthase 2 (mitochondrial)
  - Salk20717
  - Salk20717
  - Micr1

### Others (Table 1, suite)

- **RELN-CA**
  - RELN-CA
  - RELN-CA
  - RELN-CA
  - RELN-CA
  - RELN-CA
  - RELN-CA
  - RELN-CA
  - RELN-CA
  - RELN-CA
  - RELN-CA

**FC = Fold Change. Adjust p-values were calculated using Benjamin-Hochberg method.**
### Supplemental Table 2

**Top regulated network in up-regulated genes**

1. **Cell Cycle, Cancer, Gastrointestinal disease**
   - Atad2, Btg1, Cort, Dnajb9, Eif2s1, Eif4a2, Gpd1, H3f3b, Hist1h3b, Hist1h2aa, Gm12260, hist1h3f, Hist1h1e, hist2h2bb, hist1h2bg, Pkb, RPL21, Slc25a37, Tirap

2. **Cellular development, Cellular growth and proliferation, Hepatic system, development and function**
   - Abcb4, Atad2, Ehd2, Eif2s1, Gas5, Gzmm, Hist1h2ac, hist2h2be, Hsd17b7, Lgr5, Mt-nd6, Rpl17, Satb2, Tram2

3. **Cell death and survival, Cell morphology, Cellular assembly and organization**
   - Ccl25, CD69, Dup6, Eif2s1, Fosb, Hla-b, Ppp1r15a, Ptk2, pvr2, Rbl1, Trnb1

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**Top regulated network in down-regulated genes**

1. **Cellular Movement, Immune cell trafficking, Hematological System development and function**
   - Abcb1b, ana2a, Anxa6, Bcl2a1, Col4a1, Csf2rb, Cybb, Fam132a, Hck, Igf1r, Itgb1, Lilrb3, ncf1, nid1, rap1gap, Sirpa, Snpa, Spn, Tgmb2, Zbtb20

2. **Cellular growth and proliferation, Lymphoid tissue structure and development, Organ morphology**
   - Adcy7, Bcl2a1c, Cbr2, Cdk20, Cybb, exoc1, Gpr18, hba1/hba2, Hck, Nrp2, Osbpl3, Plin3, ppt2, Sgpl1, Sympk, x

3. **Cancer, Cell death and survival, Gastrointestinal disease**
   - abcb1b, abc1g, aca1a, anpep, c1r, Cts5, Cybb, gaa, Manba, rassf4, Rbn47, rpl21, Sh2d3c, Sdc7a7, thbs3

4. **Development disorder, Hematological disease, Organ morphology**
   - Abcg1, Aias2, ApoE, CD300lf, Ctsd, dusp16, Hba1/Hba2, Hbb, HLA-DMB, Ncf1, Ptprj, Rarg, Rps6ka1, Sla

5. **Hematological disease, Infectious disease, RNA damage and repair**
   - Apobec3b, B4galt6, Cyp4v2, Gng12, Lrgm2, Mthfd2l, piekho2, rdx, Sema7a, tcn2, tgm2

6. **Cell death and survival, Cell morphology, Cellular function and maintenance**
   - ggh, Kctd17, mpeg1, nab2, slc39a4, Snca, St8sia6, Tbkbp1