Supplementary Figure 1. γδT-cells proportions are restored in induced Tg endoR2^−/− mice. Proportions of γδT cells in thymi of RAG2-deficient (R2^−/−), wild type (WT) and transgenic Rag2-incompetent (Tg endoR2^−/−) mice fed with normal (−) versus TAM food during 4 weeks (+) (2 animals each). γδT-cells are absent in Tg endoR2^−/− animals. The induction of the rag2-ER transgene by tamoxifen restores the levels of γδT-cells observed in WT. Data is representative of 3 independent experiments.
Supplementary Figure 2. **Lymphocyte development does not depend on TAM intake duration.** FACS profiles show similar profiles after 16 weeks of normal and TAM food alternations as after only 4 weeks of TAM administration (see figure 2).
Supplementary Figure 3. The leaky Tg\textsuperscript{hi} line exhibits defects of lymphoid development. (A) Circulating IgM levels of RAG2-deficient (R2\textsuperscript{−/−}), wild type (WT) and Tg\textsuperscript{hi} mice Rag2-incompetent (Tg\textsuperscript{hi} endoR2\textsuperscript{−/−}) or -competent (Tg\textsuperscript{hi} endoR2\textsuperscript{+/−}) fed with normal (-) versus TAM food (+) are shown. IgM levels in WT mice sera are significantly higher than in Tg\textsuperscript{hi} mice. (* p-val = 0.03 and ** p-val = 0.008 compared to untreated Tg\textsuperscript{hi} endoR2\textsuperscript{−/−} and TAM\textsuperscript{+} Tg\textsuperscript{hi} endoR2\textsuperscript{+/−} mice respectively). WT mice display significantly higher levels of IgM than Tg\textsuperscript{hi} mice (* p-val = 0.04 and p-val = 0.02 compared to untreated and TAM-induced Tg\textsuperscript{hi} endoR2\textsuperscript{+/−} mice respectively). (B) Percentages of DP cells in thymocytes show a defect of lymphoid differentiation in TAM\textsuperscript{+} Tg\textsuperscript{hi} endoR2\textsuperscript{+/−} mice. (C) The Tg line (low expressor, RAG competent) does not exhibit lower thymocytes numbers upon TAM induction. (D) EF fraction cells in B220\textsuperscript{+} bone marrow cells are also diminished upon TAM-induction of Tg\textsuperscript{hi} endoR2\textsuperscript{+/−} mice.
Supplementary Figure 4. TAM-induction of the rag2 transgene in MEF shows RAG activity in non-lymphoid organs. (A) Evolution of FACS profiles of Tg hi and WT MEF treated either by 2% ethanol (etOH) or 200nM of 2% ethanol 4-hydroxy-tamoxifen (TAM), assessed every week. Presence of GFP MEF transgenic MEF treated by TAM only accounts for induced RAG activity from transgenic origin. (B) FACS profiles of Tg MEF 4 weeks post induction shows a lower proportion of GFP-expressing cells.
Supplementary Table 1: Sequences of primers used for RT-PCR

<table>
<thead>
<tr>
<th>Primer name</th>
<th>Primer Sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-Tubuline FW</td>
<td>GGTGGATCTAGAACCTGGG</td>
</tr>
<tr>
<td>B-tubuline RV</td>
<td>CCCAGTGAGTGGGTCAGC</td>
</tr>
<tr>
<td>RAG1-endo/tg FW</td>
<td>GAG GTT CCG CTA CGA CTC TG</td>
</tr>
<tr>
<td>RAG1-endo/tg RV</td>
<td>TGG CAA TGT GCT AGG TGC TA</td>
</tr>
<tr>
<td>RAG1-tg FW</td>
<td>CAA CTC ACA GCG TTT CGC GG</td>
</tr>
<tr>
<td>RAG1-tg RV</td>
<td>GAA TTC TTT GCC AAA GTG ATG G</td>
</tr>
<tr>
<td>RAG2-endo/tg FW</td>
<td>CCT CTC TAA GAT AAA AGA CC</td>
</tr>
<tr>
<td>RAG2-endo/tg RV</td>
<td>TCC CTC GAC TAT ACA CCA CGT CAA</td>
</tr>
<tr>
<td>RAG2-tgER FW</td>
<td>TCAACG GAG CTC AAT AAA CC</td>
</tr>
<tr>
<td>RAG2-tgER RV</td>
<td>GCG GTT CAG CAT CCA ACA AG</td>
</tr>
</tbody>
</table>
## Supplementary Table 2: RT-PCR conditions

<table>
<thead>
<tr>
<th></th>
<th>Beta-Tubulin</th>
<th>rag1 endo/tg</th>
<th>rag1 tg</th>
<th>rag2 tg-ER</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First denaturation step</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>94°C/1min</td>
<td>94°C/5min</td>
<td>94°C/5min</td>
<td>94°C/5min</td>
<td></td>
</tr>
<tr>
<td><strong>Amplification step1: number of cycles</strong></td>
<td>35</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Denaturation</td>
<td>94°C/1min</td>
<td>94°C/5min</td>
<td>94°C/5min</td>
<td>94°C/5min</td>
</tr>
<tr>
<td>Annealing</td>
<td>58°C/30sec</td>
<td>58°C/30sec</td>
<td>60°C/30sec</td>
<td>54°C/30sec</td>
</tr>
<tr>
<td>Elongation</td>
<td>72°C/30sec</td>
<td>72°C/1.5min</td>
<td>72°C/30sec</td>
<td>72°C/30sec</td>
</tr>
<tr>
<td><strong>Amplification step2: number of cycles</strong></td>
<td>-</td>
<td>31</td>
<td>28</td>
<td>26</td>
</tr>
<tr>
<td>Denaturation</td>
<td>-</td>
<td>94°C/30sec</td>
<td>94°C/30sec</td>
<td>94°C/30sec</td>
</tr>
<tr>
<td>Annealing</td>
<td>-</td>
<td>58°C/30sec</td>
<td>60°C/30sec</td>
<td>54°C/30sec</td>
</tr>
<tr>
<td>Elongation</td>
<td>-</td>
<td>72°C/1.5min</td>
<td>72°C/30sec</td>
<td>72°C/30sec</td>
</tr>
<tr>
<td><strong>Last elongation step</strong></td>
<td>72°C/7min</td>
<td>72°C/7min</td>
<td>72°C/7min</td>
<td>72°C/7min</td>
</tr>
</tbody>
</table>
Supplementary Table 3: List of fluorochrome-coupled antibodies used in FACS experiments

<table>
<thead>
<tr>
<th>Epitope</th>
<th>Clone*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4</td>
<td>RM4-5</td>
</tr>
<tr>
<td>CD8</td>
<td>YTS169.4</td>
</tr>
<tr>
<td>CD44</td>
<td>IM7</td>
</tr>
<tr>
<td>CD25</td>
<td>PC61</td>
</tr>
<tr>
<td>CD43</td>
<td>S7</td>
</tr>
<tr>
<td>B220</td>
<td>RA3-6B2</td>
</tr>
<tr>
<td>IgM</td>
<td>R331.24.12</td>
</tr>
<tr>
<td>IgD</td>
<td>1.19</td>
</tr>
<tr>
<td>Ter</td>
<td>TER-119</td>
</tr>
<tr>
<td>TCRb</td>
<td>H57_597</td>
</tr>
<tr>
<td>Thy1.2</td>
<td>30H12</td>
</tr>
<tr>
<td>CD19</td>
<td>1D3</td>
</tr>
<tr>
<td>-CD16/CD32</td>
<td>2.4G2</td>
</tr>
</tbody>
</table>

* All antibodies used were purchased from BD Pharmingen™ or in house produced.