MHC-restricted Ig V region-driven T-B lymphocyte collaboration: B cell Receptor ligation facilitates switch to IgG production

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In Table I, in Expt. B’ 4, the B cell donor should be NIP-KLH Id\(^+\) (i.e., Id negative), not NIP-KLH Id\(^-\). The corrected table is shown below.

Table I. Nonlinked Id-driven T-B collaboration, hapten and transfer experiments

<table>
<thead>
<tr>
<th>Expt (^a)</th>
<th>Group</th>
<th>B Cell Donor</th>
<th>T Cells</th>
<th>Recipient Mice</th>
<th>Boost</th>
<th>Id(^+) Ig Anti-NIP (µg/ml) (^a)</th>
<th>IgG1 Anti-NIP (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (^b)</td>
<td>1</td>
<td>NIP-KLH Id(^+)</td>
<td>Id-spec Th2</td>
<td>RAG2(^{-/-})</td>
<td>NIP-BSA</td>
<td>11 (2)</td>
<td>2.5 (0.5)</td>
</tr>
<tr>
<td>2</td>
<td>NIP-KLH Id(^+)</td>
<td>Id-spec Th2</td>
<td>RAG2(^{-/-})</td>
<td>None</td>
<td>3.0 (2)</td>
<td>0.08 (0.05)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Id(^+)</td>
<td>Id-spec Th2</td>
<td>RAG2(^{-/-})</td>
<td>NIP-BSA</td>
<td>0.9 (0.5)</td>
<td>0.04 (0.01)</td>
<td></td>
</tr>
<tr>
<td>B (^c)</td>
<td>1</td>
<td>NIP-KLH Id(^+)</td>
<td>Id-spec Th2</td>
<td>C.B-17</td>
<td>NIP-BSA</td>
<td>20 (5)</td>
<td>19 (16)</td>
</tr>
<tr>
<td>2</td>
<td>NIP-KLH Id(^+)</td>
<td>Id-spec Th2</td>
<td>C.B-17</td>
<td>None</td>
<td>12 (2)</td>
<td>1.3 (1)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Id(^+)</td>
<td>Id-spec Th2</td>
<td>C.B-17</td>
<td>NIP-BSA</td>
<td>&lt;0.06</td>
<td>&lt;0.1</td>
<td></td>
</tr>
<tr>
<td>C (^d)</td>
<td>1</td>
<td>NIP-KLH Id(^+)</td>
<td>Id-spec Th2</td>
<td>RAG2(^{-/-})</td>
<td>NIP-OVA</td>
<td>18 (3)</td>
<td>1.5 (0.5)</td>
</tr>
<tr>
<td>2</td>
<td>NIP-KLH Id(^+)</td>
<td>Id-spec Th2</td>
<td>C.B-17</td>
<td>NIP-BSA</td>
<td>&lt;0.06</td>
<td>&lt;0.1</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>NIP-KLH Id(^+)</td>
<td>Id-spec Th2</td>
<td>DO.11.10 Th2</td>
<td>RAG2(^{-/-})</td>
<td>NIP-OVA</td>
<td>23 (3)</td>
<td>6.3 (1)</td>
</tr>
<tr>
<td>4</td>
<td>NIP-KLH Id(^+)</td>
<td>DO.11.10 Th2</td>
<td>C.B-17</td>
<td>NIP-BSA</td>
<td>None</td>
<td>2.0 (0.7)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

\(^a\) Total anti-NIP Ab with VA1/2 L chain, irrespective of H chain isotype or allotype.

\(^b\) Expt. A: Splenocytes from immunized ((NIP\(_6\)-KLH)) or nonimmunized Id\(^+\) mice were depleted of T cells and injected (1\(^0\)) into RAG2\(^/-/-\) BALB/c mice on day 0 (five mice per group). Id-specific (spec) Th2 cells (6 \(\times\) 10\(^5\)) and boost (150 µg (NIP\(_5\)-BSA in PBS i.p.) were given on day 1 as indicated. Mean (SD) of anti-NIP Ab in day 15 sera is given, \(p\) values were calculated by Mann-Whitney Test and are given in main text.

\(^c\) Expt. B: Splenic B cells from immunized or nonimmunized Id\(^+\) or Id\(^-\) mice were injected (3 \(\times\) 10\(^6\)) into IgH\(_b\) C.B-17 mice (5), followed by Th2 cells (5 \(\times\) 10\(^6\)) and boost as indicated. Ab H chains from transferred B cells were detected by IgG1-specific ELISA. Data are from day 6, before immune responses in the unirradiated immune-competent C.B-17 hosts could contribute to an increased background of A2\(^+\) anti-NIP.

\(^d\) Expt. C: As Exp. A, but with Id-specific Th2 or DO.11.10 Th2 and (NIP\(_9\)-OVA boost.


The fifth author’s name is listed incorrectly. The correct name is Salvatore Pasquale Prete.

There is an error in the grant information. The correct footnote is shown below.

\(^1\)This work was supported in part by a grant from “Istituto Superiore di Sanità” no. 1A2/F7 (Research Unit, to E.B.) and in part by a grant of MIUR “Programma di Ricerca Scientifica di rilevante interesse Nazionale” 2004 (coordinator E.B.).


In Table I, in the Reactant B column, Bax should be tBid:Bax\(_2\) for both Cyto.c and Smac in the Reactant A” column. The nongeneric reaction shown in the Comment column for Cyto.c (tBid:Bax\(_2\)) applies to both this and the Smac (tBid:Bax\(_2\)) reactions. The corrected table is shown below.

In Table II, the unit for k10 should be s\(^{-1}\) nM\(^{-1}\), instead of s\(^{-1}\). The corrected table is shown below.

In Table III, the unit for ATP should be 10,000 nM. The corrected table is shown below.
<table>
<thead>
<tr>
<th>Reactant A</th>
<th>Reactant B</th>
<th>Reactant C</th>
<th>Forward Reaction Rate</th>
<th>Reverse Reaction Rate</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>FasL</td>
<td>Fas</td>
<td>FasC</td>
<td>( k_{1_f} )</td>
<td>( k_{1_r} )</td>
<td>Assume noncooperative binding between FADD and Fas, which means that regardless of other molecules in the complex, the FADD-Fas interaction always has the same rate constant.</td>
</tr>
<tr>
<td>FasC:FADD</td>
<td>FADD</td>
<td>FasC:FADD</td>
<td>( k_{2_f} )</td>
<td>( k_{2_r} )</td>
<td></td>
</tr>
<tr>
<td>FasC:FADD_2</td>
<td>FADD</td>
<td>FasC:FADD_2</td>
<td>( k_{2_f} )</td>
<td>( k_{2_r} )</td>
<td></td>
</tr>
<tr>
<td>FasC:FADD_3</td>
<td>Casp8</td>
<td>FasC:FADD_3:Casp8</td>
<td>( k_{2_f} )</td>
<td>( k_{2_r} )</td>
<td></td>
</tr>
<tr>
<td>FasC:FADD_3</td>
<td>FLIP</td>
<td>FasC:FADD_3:FLIP</td>
<td>( k_{3_f} )</td>
<td>( k_{3_r} )</td>
<td></td>
</tr>
<tr>
<td>Casp3</td>
<td>FasC:FADD</td>
<td>FasC:FADD:Casp8</td>
<td>( k_{3_f} )</td>
<td>( k_{3_r} )</td>
<td></td>
</tr>
<tr>
<td>Casp3</td>
<td>FasC:FADD_2</td>
<td>FasC:FADD_2:Casp8</td>
<td>( k_{3_f} )</td>
<td>( k_{3_r} )</td>
<td></td>
</tr>
<tr>
<td>Casp3</td>
<td>FasC:FADD_3</td>
<td>FasC:FADD_3:Casp8</td>
<td>( k_{3_f} )</td>
<td>( k_{3_r} )</td>
<td></td>
</tr>
<tr>
<td>Casp3</td>
<td>FasC:FADD_3</td>
<td>FasC:FADD_3:FLIP</td>
<td>( k_{3_f} )</td>
<td>( k_{3_r} )</td>
<td></td>
</tr>
<tr>
<td>Casp3</td>
<td>FasC:FADD_3</td>
<td>FasC:FADD_3:FLIP</td>
<td>( k_{3_f} )</td>
<td>( k_{3_r} )</td>
<td></td>
</tr>
</tbody>
</table>

Continued on the next page...
Table I.  
Continued

<table>
<thead>
<tr>
<th>Reactant A</th>
<th>Reactant B</th>
<th>Reactant C</th>
<th>Forward Reaction Rate</th>
<th>Reverse Reaction Rate</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Casp9*</td>
<td>Casp3*</td>
<td>Casp9*:Casp3</td>
<td></td>
<td></td>
<td>k17</td>
</tr>
<tr>
<td>Casp9</td>
<td>XIAP</td>
<td>Casp9:XIAP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Casp3*</td>
<td>XIAP</td>
<td>Casp3*:XIAP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bcl2</td>
<td>Bax</td>
<td>Bcl2:Bax</td>
<td>k20_f</td>
<td>k20_r</td>
<td></td>
</tr>
<tr>
<td>Bcl2</td>
<td>Bid</td>
<td>Bcl2:Bid</td>
<td>k20_f</td>
<td>k20_r</td>
<td></td>
</tr>
<tr>
<td>Bcl2</td>
<td>tBid</td>
<td>Bcl2:tBid</td>
<td>k20_f</td>
<td>k20_r</td>
<td></td>
</tr>
<tr>
<td>Bcl2</td>
<td>Bax</td>
<td>Bcl2:Bax</td>
<td>k20_f</td>
<td>k20_r</td>
<td></td>
</tr>
</tbody>
</table>

Equations used for different models:

- Bcl2 binding to Bax alone:
  \[ k_{1} \]

\[ Bcl2 \rightarrow Bax \rightarrow Bcl2:Bax \]

- Bcl2 binding to Bid alone:
  \[ k_{2} \]

\[ Bcl2 \rightarrow Bid \rightarrow Bcl2:Bid \]

- Bcl2 binding to tBid alone:
  \[ k_{3} \]

\[ Bcl2 \rightarrow tBid \rightarrow Bcl2:tBid \]

- Bcl2 binding to both tBid and Bax:
  \[ k_{4} \]

\[ Bcl2 \rightarrow tBid \rightarrow Bcl2:tBid \]

General reaction:

\[ A + B \rightarrow C \]

\[ k_{f} \quad k_{r} \]

Table II.  
Reaction rate constants

<table>
<thead>
<tr>
<th>Rate Constant</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>k1_f</td>
<td>9.09E-05 nM (^{-1})s(^{-1})</td>
<td>( K_{f} = k_{1,f} = 1.1 ) ( \text{nM} ) from (39)</td>
</tr>
<tr>
<td>k1_r</td>
<td>1.00E-04 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k2_f</td>
<td>5.00E-04 nM (^{-1})s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k2_r</td>
<td>0.2 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k3_f</td>
<td>3.50E-03 nM (^{-1})s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k3_r</td>
<td>0.018 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k4</td>
<td>0.3 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k5</td>
<td>0.1 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k6_f</td>
<td>1.00E-05 nM (^{-1})s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k6_r</td>
<td>0.06 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k7</td>
<td>0.1 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k8_f</td>
<td>5.00E-03 nM (^{-1})s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k8_r</td>
<td>0.005 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k9_f</td>
<td>2.00E-04 nM (^{-1})s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k9_r</td>
<td>0.02 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k10</td>
<td>1e-3 s (^{-1})nM(^{-1})</td>
<td>( k_{on} = k11.f = 7e6(M \text{s}) ) and ( k_{off} = k11.r = 2.2 \times 10^{-3}/s ) from (40)</td>
</tr>
<tr>
<td>k11_f</td>
<td>7.00E-03 nM (^{-1})s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k11_r</td>
<td>2.21E-03 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k12_f</td>
<td>2.78E-07 nM (^{-1})s(^{-1})nM(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k12_r</td>
<td>5.70E-03 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k13_f</td>
<td>2.84E-04 nM (^{-1})s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k13_r</td>
<td>0.07493 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k14_f</td>
<td>4.41E-04 nM (^{-1})s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k14_r</td>
<td>0.1 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k15</td>
<td>0.7 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k16_f</td>
<td>1.96E-05 nM (^{-1})s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k16_r</td>
<td>0.05707 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k17</td>
<td>4.8 s(^{-1})</td>
<td>( k_{cat} = k17 = 4.8/s ) from (41)</td>
</tr>
<tr>
<td>k18_f</td>
<td>1.06E-04 nM (^{-1})s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k18_r</td>
<td>9.4e-9 M (^{-1})</td>
<td>( K_{i} = k18.r/k18.f = 9.4e-9 ) from (42)</td>
</tr>
<tr>
<td>k19_f</td>
<td>1.00E-03 s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k19_r</td>
<td>2.47E-03 nM (^{-1})s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k20_f</td>
<td>2.00E-03 nM (^{-1})s(^{-1})</td>
<td></td>
</tr>
<tr>
<td>k20_r</td>
<td>0.02 s(^{-1})</td>
<td></td>
</tr>
</tbody>
</table>

\( k_{on} = k11.f = 7e6(M \text{s}) \) and \( k_{off} = k11.r = 2.2 \times 10^{-3}/s \) from (40)

Table III.  
Initial conditions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value (nM)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fas</td>
<td>10.00</td>
<td></td>
</tr>
<tr>
<td>FasL</td>
<td>2.00</td>
<td>Equivalent to 100 ng/ml FasL</td>
</tr>
<tr>
<td>FADD</td>
<td>16.67</td>
<td>Unpublished observations</td>
</tr>
<tr>
<td>Flip</td>
<td>81.00</td>
<td></td>
</tr>
<tr>
<td>Casp8</td>
<td>33.33</td>
<td>(45)</td>
</tr>
<tr>
<td>Casp3</td>
<td>200.00</td>
<td>(45)</td>
</tr>
<tr>
<td>Bid</td>
<td>25.00</td>
<td></td>
</tr>
<tr>
<td>Bcl2</td>
<td>75.00</td>
<td></td>
</tr>
<tr>
<td>Bax</td>
<td>83.33</td>
<td></td>
</tr>
<tr>
<td>Cytoc</td>
<td>100.00</td>
<td></td>
</tr>
<tr>
<td>Smac</td>
<td>100.00</td>
<td></td>
</tr>
<tr>
<td>XIAP</td>
<td>30.00</td>
<td>(45)</td>
</tr>
<tr>
<td>Casp9</td>
<td>20.00</td>
<td>(41)</td>
</tr>
<tr>
<td>ATP</td>
<td>10,000.00</td>
<td></td>
</tr>
<tr>
<td>Apaf</td>
<td>100.00</td>
<td></td>
</tr>
</tbody>
</table>

In the *Abstract*, in the third sentence, the word “rust” should have been published as “runt.” The correct sentence is shown below.

The transcription factor Runx3/AML-2 (Runx, runt dominant factor; AML, acute myeloid leukemia) is expressed specifically during the development of CD8 single-positive (SP) thymocytes, where it silences CD4 expression.

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In Table I, the HLA restrictions for two of the LMP2 epitopes are incorrect. The correct HLA restriction for TVCGGIMFL in the sixth row should be A*0201/06 and for LLWTLVVL in the seventh row should be A*0201. The corrected table is shown below.

<table>
<thead>
<tr>
<th>Minimum Epitope</th>
<th>Amino Acids</th>
<th>HLA Restriction</th>
<th>No. Responding/No. Tested</th>
<th>SFC/10^5 CTL (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLGGGLTLMV</td>
<td>416–434</td>
<td>A*0201/06/07/09</td>
<td>4/12</td>
<td>84 (19–236)</td>
</tr>
<tr>
<td>GLGTLGAAI</td>
<td>293–301</td>
<td>A2</td>
<td>1/12</td>
<td>459</td>
</tr>
<tr>
<td>LTAGFLIFL</td>
<td>453–461</td>
<td>A2</td>
<td>0/12</td>
<td></td>
</tr>
<tr>
<td>FLYALALLL</td>
<td>356–364</td>
<td>A*0201</td>
<td>7/12</td>
<td>381 (7–1990)</td>
</tr>
<tr>
<td>LIVDAVIQL</td>
<td>257–265</td>
<td>A<em>0204 or A</em>0217</td>
<td>1/12</td>
<td>651</td>
</tr>
<tr>
<td>TVCGGIMFL</td>
<td>243–251</td>
<td>A*0201/06</td>
<td>2/12</td>
<td>198 (175–222)</td>
</tr>
<tr>
<td>LLWTLVVL</td>
<td>329–337</td>
<td>A*0201</td>
<td>2/12</td>
<td>19 (14–24)</td>
</tr>
<tr>
<td>FTASVSTVV</td>
<td>144–152</td>
<td>A68</td>
<td>2/6</td>
<td>53 (23–53)</td>
</tr>
<tr>
<td>SSCSCPLISKI</td>
<td>340–350</td>
<td>A11</td>
<td>3/3</td>
<td>43 (8–90)</td>
</tr>
<tr>
<td>TYGPVFEMS</td>
<td>419–427</td>
<td>A24</td>
<td>2/5</td>
<td>58 (16–101)</td>
</tr>
<tr>
<td>PLYFWLAAD</td>
<td>131–139</td>
<td>A23/24</td>
<td>3/6</td>
<td>462 (12–1132)</td>
</tr>
<tr>
<td>ILLARLFLY</td>
<td>349–358</td>
<td>A29</td>
<td>1/2</td>
<td>6</td>
</tr>
<tr>
<td>RRWRRLTVC</td>
<td>237–245</td>
<td>B*1402</td>
<td>1/1</td>
<td>41</td>
</tr>
<tr>
<td>RRWRRLTVC</td>
<td>236–244</td>
<td>B*2704/05/09</td>
<td>1/2</td>
<td>16</td>
</tr>
<tr>
<td>RRILTVCGGIMF</td>
<td>240–250</td>
<td>B27</td>
<td>1/3</td>
<td>129</td>
</tr>
<tr>
<td>MGSLMMVPM</td>
<td>1–9</td>
<td>B*3501</td>
<td>1/5</td>
<td>880</td>
</tr>
<tr>
<td>LPVLIVAPY</td>
<td>125–133</td>
<td>B53</td>
<td>1/2</td>
<td>5</td>
</tr>
<tr>
<td>IEDPPFNSL</td>
<td>200–208</td>
<td>B60</td>
<td>1/2</td>
<td>918</td>
</tr>
<tr>
<td>DYQPLGTQDSLYLG</td>
<td>73–87</td>
<td>DR4 or DR16</td>
<td>1/1</td>
<td>57</td>
</tr>
</tbody>
</table>

*Listed are the amino acid sequence of newly identified (in bold) as well as previously described LMP2 epitopes (27, 29–33); their location in the LMP2 molecule; HLA restriction; the number of CTL lines from NPC, HL, and NHL patients in which responses to these epitopes were identified; and the strength of these responses. When responses to the indicated epitope were found in more than one patient, CTL line average response and range are shown.*