

**Supplementary Information for:**

**Tyrosine kinase 2 modulates splenic B cells through type I IFN and TLR7 signaling**

Irene Bodega-Mayor<sup>1,\*†</sup>, Pablo Delgado-Wicke<sup>1,†</sup>, Alejandro Arrabal<sup>2</sup>, Estíbaliz Alegría-Carrasco<sup>1</sup>, Ana Nicolao-Gómez<sup>1</sup>, Marta Jaén-Castaño<sup>1</sup>, Enrique Vázquez de Luis<sup>3</sup>, Cristina Espadas<sup>3</sup>, Ana Dopazo<sup>3,4</sup>, Enrique Martín-Gayo<sup>5,6</sup>, María Luisa Gaspar<sup>2</sup>, Belén de Andrés<sup>2,††</sup>, Elena Fernández-Ruiz<sup>1,6,††</sup>

<sup>1</sup>Molecular Biology Unit, Hospital Universitario de La Princesa and Research Institute (IIS-Princesa), Madrid, Spain.

<sup>2</sup>Immunobiology Unit, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Majadahonda, Madrid, Spain.

<sup>3</sup>Genomics Unit, Centro Nacional de Investigaciones Cardiovasculares, Madrid, Spain.

<sup>4</sup>CIBER de Enfermedades Cardiovasculares (CIBERCV), Madrid, Spain.

<sup>5</sup>Immunology Department, Hospital Universitario de La Princesa and IIS-Princesa, Madrid, Spain.

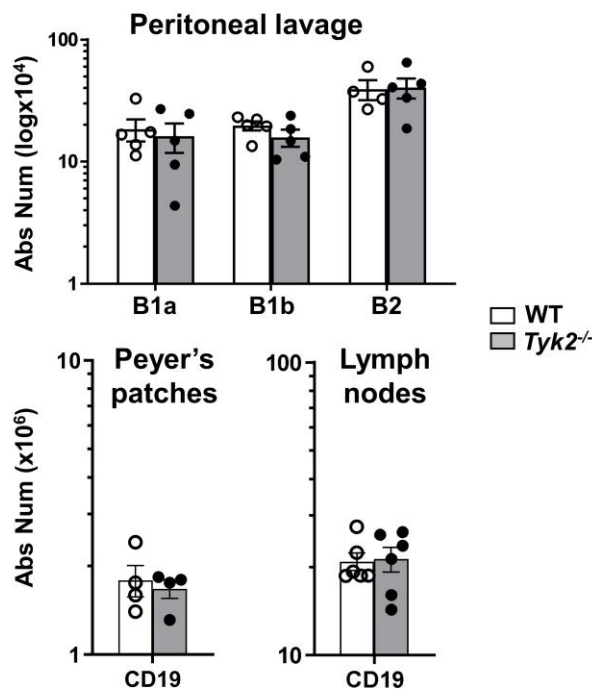
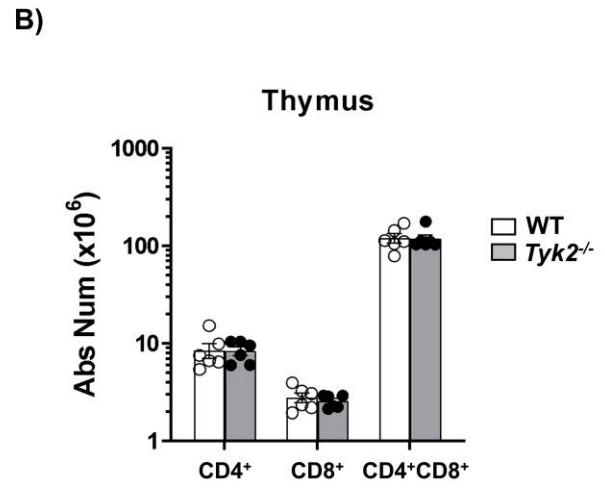
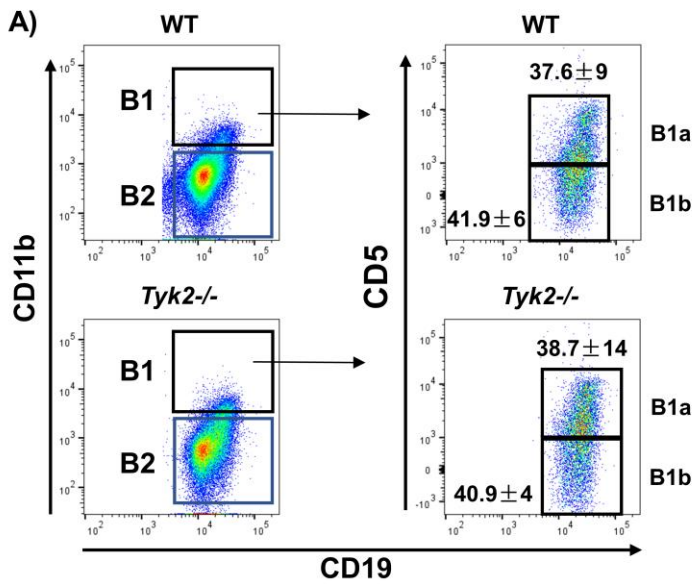
<sup>6</sup>Faculty of Medicine, Universidad Autónoma de Madrid, Madrid, Spain.

\*Current address: Immunobiology Unit, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Majadahonda, Madrid, Spain.

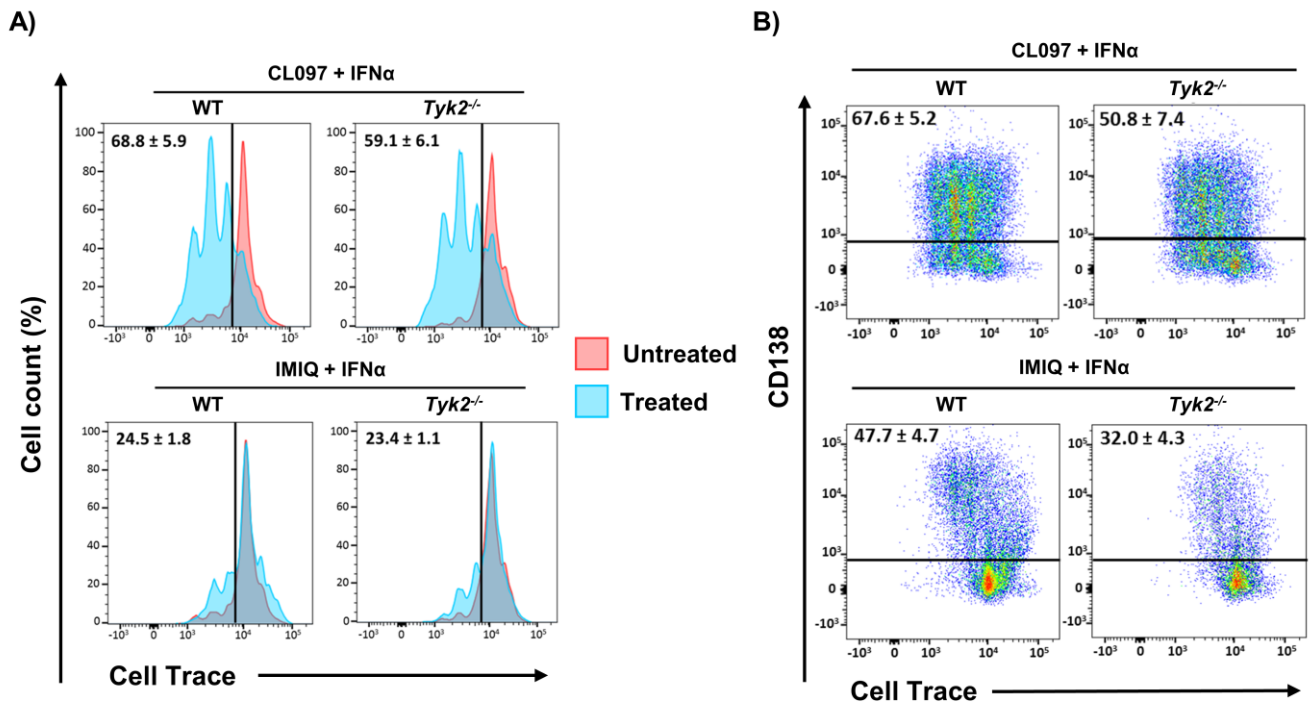
†These authors contributed equally to this work and share first authorship.

††These authors contributed equally to this work and share senior authorship.

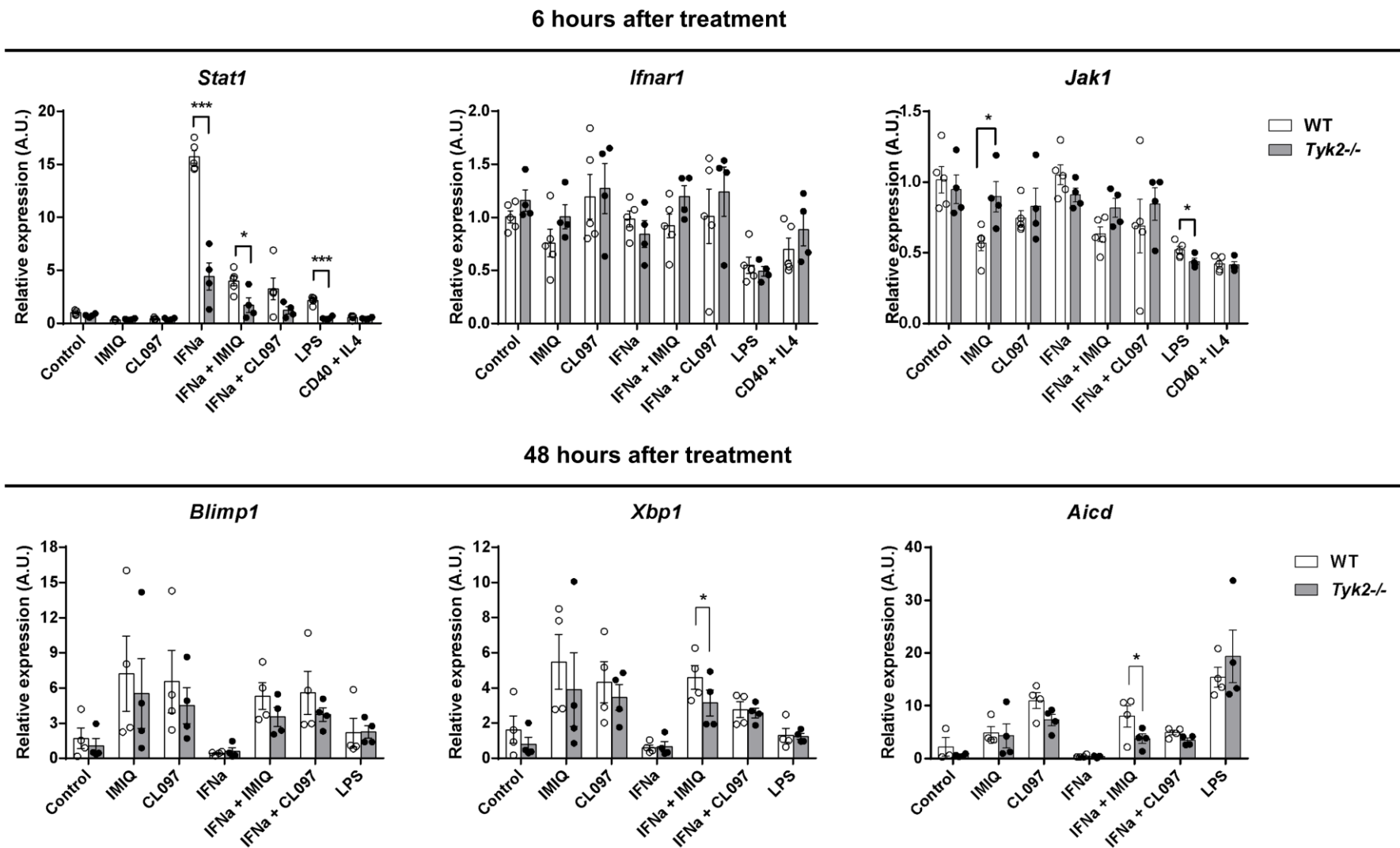
Corresponding author: Elena Fernández-Ruiz, [efruiz@salud.madrid.org](mailto:efruiz@salud.madrid.org) (ORCID: 0000-0001-5380-1686).



**Fig. S1. Quantitation of B and T lymphocytes in different hematopoietic locations of WT and *Tyk2*<sup>-/-</sup> adult mice.** **A)** B lymphocytes were analyzed in peritoneal lavages, Peyer's patches and lymph nodes. Upper left dot plots show a representative example of B2 cells (CD19<sup>+</sup>CD11b<sup>-</sup>) and B1 cells (CD19<sup>+</sup>CD11b<sup>+</sup>) and the discrimination between B1a and B1b on the basis of CD5 expression. Numbers denote percentage of each population expressed as means ± SEM (n = 4-6). Lower left histograms show the quantitation of B cells on the peritoneal lavages, Peyer's patches and lymph nodes expressed as absolute numbers/sample. **B)** T lymphocytes in the thymus were quantitated using CD3, CD4 and CD8. Data represent means ± SEM (n = 6).



**Fig. S2. Proliferation and differentiation of B cell cultures in the presence of IFN $\alpha$ .** Splenic B cells were obtained as described in Materials and Methods and stained with Cell Trace at the beginning of the culture. **A)** Proliferation was analyzed in cultured cells treated with CL097 + IFN $\alpha$  or IMIQ + IFN $\alpha$  for 72 h. Overlaid histograms show a representative result for control cells (red) and treated cells (blue) in WT and *Tyk2*<sup>-/-</sup> mice. Percentage of proliferating cells (shown as numbers inside) was referred to control cells (black line). **B)** Differentiation of cultured B cells treated with CL097 + IFN $\alpha$  or IMIQ + IFN $\alpha$  for 72 h by the expression of CD138 and Cell Trace. Numbers denote percentage of CD138<sup>+</sup> cells referred to isotype (black line).



**Fig. S3. Expression of early and late response genes in splenic B cell cultures by qPCR.** Upper panels: *Stat1*, *Ifnar1* and *Jak1* were determined at 6 h. Cultures were set up as described in Materials and Methods. Lower panels: The B cell-differentiation related transcription factors *Blimp1*, *Xbp1* and *Aicd* were studied at 48 h of cell culture. RNA extraction procedures and qPCR reactions were performed as described in Fig. 4. Data are presented as relative expression arbitrary units (A.U.) using the  $2^{-\Delta\Delta Ct}$  method (samples normalized to their *Gapdh* content). (n = 3-4 performed in triplicates). \*  $P < 0.05$ ; \*\*\*  $P < 0.0001$ .

**Table S1.** Antibodies employed in flow cytometry analysis.

| <b>MoAbs</b>     | <b>Clone</b> | <b>Label</b>                                    | <b>Company</b>               |
|------------------|--------------|---|------------------------------|
| B220             | RA3-6B2      | APC   | BioLegend                    |
| CD3              | 17A2         | PE-Cy7  | BioLegend                    |
| CD4              | GK1.5        | APC   | BioLegend                    |
| CD5              | 53-7.3       | APC   | BioLegend                    |
| CD8              | 53-5.8       | PE  | BioLegend                    |
| CD11b            | M1/70        | PE-Cy7, APC-Cy7                                 | BioLegend                    |
| CD11c            | N418         | FITC  | BioLegend                    |
| CD19             | 1D3          | PE, BV421                                       | eBioscience,<br>BioLegend    |
| CD21             | 7E9, 7G6     | FITC, APC                                       | BioLegend,<br>BD Biosciences |
| CD23             | B3B4         | PE-Cy7  | BioLegend                    |
| CD43             | S11          | PE  | BioLegend                    |
| CD90.2           | 30-H12       | Biotin  | BioLegend                    |
| CD93             | AA4.1        | APC   | BioLegend                    |
| CD138            | 281-2        | APC   | BioLegend                    |
| DX5              | DX5          | Biotin, APC                                     | BioLegend                    |
| Gr-1             | RB6-8C5      | PE  | BioLegend                    |
| IFNAR-1          | MAR1-5A3     | PE  | BioLegend                    |
| IgM              | RMM-1        | PE  | BioLegend                    |
| NK-1.1           | S17016D      | PE  | BioLegend                    |
| T-bet            | 4B10         | PE  | BioLegend                    |
| TLR7             | A94B10       | PE  | BioLegend                    |
| Isotype controls |              | FITC, PE, APC, PE-Cy7,<br>APC-Cy7, BV421, BV510 | BioLegend                    |
| LIVE/DEAD™       |              | Fixable Aqua 405                                | Invitrogen                   |
| Propidium iodide |              | PI  | Sigma Aldrich                |
| Streptavidin     |              | PE  | BioLegend                    |

**Table S2.** Phenotypes of the cell populations analyzed in this study.

| <b>Tissue</b>                       | <b>Population</b>   | <b>Phenotype</b>   |
|-------------------------------------|---|--|
| <b>Spleen</b>                       | Natural killer T (NKT)  | CD3 <sup>+</sup> DX5 <sup>+</sup> NK-1.1 <sup>+</sup>  |
|                                     | Granulocytes  | CD11b <sup>+</sup> GR1 <sup>+</sup>  |
|                                     | Monocytes   | CD11b <sup>+</sup> Gr-1 <sup>-</sup>   |
|                                     | Dendritic cells (DC)  | Lin <sup>-</sup> (Ly6G <sup>-</sup> CD19 <sup>-</sup> DX5 <sup>-</sup> Thy-1.2 <sup>-</sup> ) CD11c <sup>+</sup> |
|                                     | CD4 <sup>+</sup> T cells  | CD3 <sup>+</sup> CD4 <sup>+</sup> CD8 <sup>-</sup>   |
|                                     | CD8 <sup>+</sup> T cells  | CD3 <sup>+</sup> CD4 <sup>-</sup> CD8 <sup>+</sup>   |
|                                     | B cells   | CD19 <sup>+</sup>  |
|                                     | Marginal zone B cells (MZ)  | CD19 <sup>+</sup> CD21 <sup>++</sup> CD23 <sup>lo</sup>  |
|                                     | Follicular B cells (FO)   | CD19 <sup>+</sup> CD21 <sup>+</sup> CD23 <sup>++</sup>   |
|                                     | Aged B cells (ABC)  | CD19 <sup>+</sup> CD21 <sup>lo</sup> CD23 <sup>lo</sup> T-bet <sup>+</sup>                                       |
|                                     | Hardy's fractions A-C   | B220 <sup>+</sup> CD43 <sup>+</sup>  |
|                                     | Hardy's fractions D-F   | B220 <sup>+</sup> CD43 <sup>-</sup>  |
|                                     | Transitionals T1  | B220 <sup>+</sup> CD93 <sup>+</sup> IgM <sup>+</sup> CD23 <sup>-</sup>   |
|                                     | Transitionals T2  | B220 <sup>+</sup> CD93 <sup>+</sup> IgM <sup>+</sup> CD23 <sup>+</sup>   |
| Transitionals T3                    | B220 <sup>+</sup> CD93 <sup>+</sup> IgM <sup>lo</sup> CD23 <sup>+</sup> |  |
| <b>Peritoneal lavage</b>            | B1a   | CD19 <sup>+</sup> CD11b <sup>+</sup> CD5 <sup>+</sup>  |
|                                     | B1b   | CD19 <sup>+</sup> CD11b <sup>+</sup> CD5 <sup>-</sup>  |
| <b>Peyer's patches, lymph nodes</b> | B cells   | CD19 <sup>+</sup>  |
|                                     | CD4 <sup>+</sup> T cells  | CD3 <sup>+</sup> CD4 <sup>+</sup> CD8 <sup>-</sup>   |
|                                     | CD8 <sup>+</sup> T cells  | CD3 <sup>+</sup> CD4 <sup>-</sup> CD8 <sup>+</sup>   |
|                                     | CD4 <sup>+</sup> CD8 <sup>+</sup> T cells                               | CD3 <sup>+</sup> CD4 <sup>+</sup> CD8 <sup>+</sup>   |

**Table S3.** Differentially expressed genes (DEGs) of follicular (FO) cells between WT and *Tyk2*<sup>-/-</sup> mice and their respective fold-changes (FC), *P*-values and false discovery rate (FDR).

| Transcript ID      | Gene name     | log <sub>2</sub> (WT_FO) | log <sub>2</sub> (KO_FO) | log <sub>2</sub> (FC) | <i>P</i> -value | FDR < 0.05  |
|--------------------|---------------|--------------------------|--------------------------|-----------------------|-----------------|-------------|
| ENSMUSG00000020279 | Ii9r          | 2.856165659              | 1.451681938              | -1.404483721          | 3.10286E-08     | 0.00026167  |
| ENSMUSG00000041827 | Oas1          | 1.218996298              | 0.102168095              | -1.116828203          | 4.56E-08        | 0.00026167  |
| ENSMUSG00000032175 | Tyk2          | 2.623989179              | 1.179992767              | -1.443996413          | 1.05E-07        | 0.000453443 |
| ENSMUSG00000033538 | Casp4         | 1.220044568              | 0.431459816              | -0.788584752          | 1.32307E-07     | 0.000455559 |
| ENSMUSG00000025498 | Irf7          | 1.689214747              | 0.706201115              | -0.983013632          | 4.9925E-07      | 0.001432516 |
| ENSMUSG00000073491 | Ifi213        | 2.804907512              | 0.917339091              | -1.887568421          | 3.79065E-06     | 0.005321084 |
| ENSMUSG00000064215 | Ifi27         | 1.605589822              | 0.46764948               | -1.137940342          | 4.02E-06        | 0.005321084 |
| ENSMUSG00000017830 | Dhx58         | 1.123316612              | 0.392857324              | -0.730459288          | 4.33E-06        | 0.005321084 |
| ENSMUSG00000096255 | Dynl1b        | 0.376155062              | 1.288137549              | 0.911982487           | 7.14E-06        | 0.007683403 |
| ENSMUSG00000070327 | Rnf213        | 4.569050624              | 3.395006163              | -1.174044461          | 7.69E-06        | 0.007783618 |
| ENSMUSG00000054404 | Slfn5         | 2.464472562              | 0.406666293              | -2.057806269          | 8.36E-06        | 0.007998596 |
| ENSMUSG00000032661 | Oas3          | 0.831296603              | 0.029338081              | -0.801958521          | 1.02789E-05     | 0.00888429  |
| ENSMUSG00000037921 | Ddx60         | 0.739247108              | 0.034030153              | -0.705216956          | 1.0321E-05      | 0.00888429  |
| ENSMUSG00000044583 | Tlr7          | 1.462124564              | 0.508475146              | -0.953649418          | 1.47899E-05     | 0.010123034 |
| ENSMUSG00000079017 | Ifi2712a      | 1.633679872              | 0.135904454              | -1.497775418          | 1.53E-05        | 0.010123034 |
| ENSMUSG00000110537 | Gm4316        | 3.078176783              | 4.130420518              | 1.052243734           | 1.86E-05        | 0.011356231 |
| ENSMUSG00000025743 | Sdc3          | 0.649098334              | 0.011609386              | -0.637488948          | 2.10E-05        | 0.011356231 |
| ENSMUSG00000057596 | Trim30d       | 1.683545313              | 1.014707115              | -0.668838198          | 2.29E-05        | 0.011919874 |
| ENSMUSG00000035208 | Slfn8         | 2.455872719              | 1.319837156              | -1.136035563          | 4.85E-05        | 0.019531135 |
| ENSMUSG00000073409 | H2-Q6         | 5.537036705              | 4.595062665              | -0.94197404           | 5.07433E-05     | 0.019806071 |
| ENSMUSG00000034422 | Parp14        | 3.213749187              | 2.473788968              | -0.739960219          | 5.17701E-05     | 0.019806071 |
| ENSMUSG00000033880 | Lgals3bp      | 0.901196264              | 0.181128308              | -0.720067956          | 5.68361E-05     | 0.020385203 |
| ENSMUSG00000032690 | Oas2          | 1.135938145              | 0.008130826              | -1.127807319          | 5.86E-05        | 0.020598633 |
| ENSMUSG00000029322 | Plac8         | 2.519536613              | 1.785234894              | -0.734301719          | 6.85E-05        | 0.021944988 |
| ENSMUSG00000029561 | Oas12         | 0.825419678              | 0.095363992              | -0.730055686          | 6.8833E-05      | 0.021944988 |
| ENSMUSG00000097893 | 1700034P13Rik | 1.430837831              | 2.4393409                | 1.008503069           | 9.40E-05        | 0.02742817  |
| ENSMUSG00000075602 | Ly6a          | 2.635366901              | 0.756047518              | -1.879319384          | 0.000100242     | 0.027834991 |
| ENSMUSG00000105263 | Gm42427       | 4.560179669              | 6.12685471               | 1.56667504            | 0.000103684     | 0.02791418  |
| ENSMUSG00000061232 | H2-K1         | 6.676278625              | 6.012636057              | -0.663642568          | 0.00010377      | 0.02791418  |
| ENSMUSG00000096780 | Tmem181b-ps   | 0.121501003              | 0.721974762              | 0.600473759           | 0.000108961     | 0.028859475 |
| ENSMUSG00000020282 | Rhbdf1        | 1.274734689              | 0.570829498              | -0.703905191          | 0.000113132     | 0.029510302 |
| ENSMUSG00000078606 | Gm4070        | 3.810026408              | 2.086522061              | -1.723504347          | 0.000127761     | 0.031843911 |
| ENSMUSG00000105703 | Gm43305       | 6.868643871              | 8.039183996              | 1.170540125           | 0.00014852      | 0.03502634  |
| ENSMUSG00000110386 | Gm42031       | 4.577435121              | 6.046192628              | 1.468757507           | 0.000218941     | 0.040970564 |
| ENSMUSG00000000386 | Mx1           | 0.76659608               | 0.004686865              | -0.761909215          | 0.000229679     | 0.042517756 |
| ENSMUSG00000052776 | Oas1a         | 0.700977229              | 0.00730421               | -0.693673019          | 0.000236333     | 0.042828599 |
| ENSMUSG00000074896 | Ifit3         | 0.659887783              | 0.02149299               | -0.638394793          | 0.000264124     | 0.045021421 |

| Transcript ID      | Gene name  | log <sub>2</sub> (WT_FO) | log <sub>2</sub> (KO_FO) | log <sub>2</sub> (FC) | P-value     | FDR < 0.05  |
|--------------------|------------|--------------------------|--------------------------|-----------------------|-------------|-------------|
| ENSMUSG00000046841 | Ckap4      | 1.539013091              | 2.319639171              | 0.78062608            | 0.000317226 | 0.049648734 |
| ENSMUSG00000095041 | AC149090.1 | 4.36033084               | 5.374407266              | 1.014076426           | 0.000377501 | 0.055076702 |
| ENSMUSG00000037849 | Ifi206     | 2.364958347              | 1.413761481              | -0.951196866          | 0.000424255 | 0.058876016 |
| ENSMUSG00000103865 | Gm37416    | 0.780847554              | 1.514876868              | 0.734029315           | 0.0004309   | 0.058876016 |
| ENSMUSG00000002325 | Irf9       | 2.712355952              | 1.996378357              | -0.715977595          | 4.44E-04    | 0.059320019 |
| ENSMUSG00000082286 | Pisd-ps1   | 2.414403999              | 3.143845633              | 0.729441634           | 0.000499973 | 0.064235347 |
| ENSMUSG00000053835 | H2-T24     | 1.732565624              | 1.151041391              | -0.581524233          | 0.000543416 | 0.066350747 |
| ENSMUSG00000097971 | Gm26917    | 4.387933869              | 3.438252295              | -0.949681574          | 6.81E-04    | 0.075438876 |
| ENSMUSG00000030921 | Trim30a    | 3.066419399              | 2.18736237               | -0.87905703           | 0.000711356 | 0.076449826 |
| ENSMUSG00000105373 | Gm42429    | 1.830246612              | 2.819201014              | 0.988954402           | 0.000749143 | 0.078552077 |
| ENSMUSG00000027514 | Zbp1       | 1.387453979              | 0.705883847              | -0.681570132          | 0.000778516 | 0.080055316 |
| ENSMUSG00000060550 | H2-Q7      | 5.699833288              | 4.738023322              | -0.961809966          | 7.81E-04    | 0.080055316 |
| ENSMUSG00000045932 | Ifit2      | 0.844754795              | 0.247377378              | -0.597377417          | 0.000842863 | 0.084264219 |
| ENSMUSG00000105987 | AI506816   | 3.053500797              | 3.643693602              | 0.590192805           | 0.000988124 | 0.09138085  |
| ENSMUSG00000055413 | H2-Q5      | 3.992485497              | 3.319222432              | -0.673263065          | 0.00116141  | 0.098964304 |
| ENSMUSG00000104713 | Gbp6       | 0.826094321              | 0.089116145              | -0.736978176          | 1.48E-03    | 0.113094002 |
| ENSMUSG00000035929 | H2-Q4      | 4.780985374              | 4.197649806              | -0.583335568          | 0.001517543 | 0.11428119  |
| ENSMUSG00000072620 | Slfn2      | 2.978663766              | 2.177903301              | -0.800760465          | 1.52E-03    | 0.11428119  |
| ENSMUSG00000025888 | Casp1      | 1.562455432              | 0.947565774              | -0.614889658          | 0.001644965 | 0.119492462 |
| ENSMUSG00000066677 | Ifi208     | 1.927322726              | 1.121185715              | -0.806137011          | 1.80E-03    | 0.12660178  |
| ENSMUSG00000046879 | Irgm1      | 1.761383298              | 1.163271712              | -0.598111585          | 0.00233851  | 0.143784929 |
| ENSMUSG00000096768 | Erdr1      | 3.057707749              | 4.655351121              | 1.597643372           | 0.003022915 | 0.166269988 |
| ENSMUSG00000074151 | Nlrc5      | 3.06153918               | 2.397022386              | -0.664516794          | 0.003304603 | 0.172731945 |
| ENSMUSG00000054364 | Rhob       | 4.717439843              | 4.123527247              | -0.593912596          | 0.004009438 | 0.193622962 |
| ENSMUSG00000062783 | Csprs      | 1.294398136              | 0.573038718              | -0.721359419          | 4.60E-03    | 0.205796018 |
| ENSMUSG00000111202 | AC153954.3 | 2.079266159              | 2.974443441              | 0.895177283           | 0.004957461 | 0.208925782 |
| ENSMUSG00000026104 | Stat1      | 3.663134664              | 2.902057526              | -0.761077138          | 4.97E-03    | 0.208925782 |
| ENSMUSG00000095134 | Mid1-ps1   | 1.358845826              | 0.089041825              | -1.269804001          | 0.005337119 | 0.215542357 |
| ENSMUSG00000078921 | Tgtp2      | 0.980352131              | 0.354522206              | -0.625829925          | 0.005716327 | 0.219815738 |
| ENSMUSG00000036181 | Hist1h1c   | 2.816098867              | 2.124182411              | -0.691916456          | 0.006769416 | 0.233433153 |
| ENSMUSG00000035202 | Lars2      | 4.775945175              | 3.552642544              | -1.223302631          | 6.95E-03    | 0.233433153 |
| ENSMUSG00000056116 | H2-T22     | 2.786547685              | 2.197905158              | -0.588642527          | 0.00741022  | 0.240253008 |
| ENSMUSG00000095562 | Gm21887    | 0.426005803              | 1.427488758              | 1.001482955           | 0.008575855 | 0.24802043  |
| ENSMUSG00000070501 | Ifi214     | 1.695220537              | 1.10531976               | -0.589900777          | 0.00893012  | 0.248828807 |
| ENSMUSG00000024900 | Cpt1a      | 2.996840061              | 2.366169501              | -0.630670559          | 0.00910955  | 0.24889219  |
| ENSMUSG00000102049 | Zbed6      | 0.675768237              | 0.095498645              | -0.580269592          | 0.01220133  | 0.274798325 |
| ENSMUSG00000098178 | Gm42418    | 6.933858241              | 6.098351065              | -0.835507176          | 0.013251235 | 0.286599569 |
| ENSMUSG00000039001 | Rps21      | 3.875291719              | 3.2721443                | -0.603147419          | 0.021548705 | 0.349324397 |
| ENSMUSG00000041481 | Serpina3g  | 2.190829457              | 1.515371799              | -0.675457658          | 0.028949762 | 0.3881613   |
| ENSMUSG00000064341 | mt-Nd1     | 5.867906358              | 6.489006194              | 0.621099836           | 0.031003789 | 0.399317843 |
| ENSMUSG00000035299 | Mid1       | 3.432479898              | 1.781164912              | -1.651314986          | 3.43E-02    | 0.415980392 |



**Table S4.** Differentially expressed genes (DEGs) of the marginal zone (MZ) cells between WT and *Tyk2*<sup>-/-</sup> mice and their respective fold-changes (FC), *P*-values and false discovery rate (FDR).

| Transcript ID      | Gene name  | log <sub>2</sub> (WT_MZ) | log <sub>2</sub> (KO_MZ) | log <sub>2</sub> (FC) | <i>P</i> -value | FDR < 0.05  |
|--------------------|------------|--------------------------|--------------------------|-----------------------|-----------------|-------------|
| ENSMUSG00000033355 | Rtp4       | 1.630481261              | 0.057975402              | -1.572505859          | 8.68365E-11     | 1.68923E-06 |
| ENSMUSG00000111083 | AC153954.2 | 0.105805044              | 0.80362482               | 0.697819776           | 1.29438E-07     | 0.000629487 |
| ENSMUSG00000037849 | Ifi206     | 2.406872534              | 1.274112202              | -1.132760332          | 1.1903E-07      | 0.000629487 |
| ENSMUSG00000062488 | Ifit3b     | 0.963477983              | 0.024513624              | -0.938964359          | 3.95103E-07     | 0.001537186 |
| ENSMUSG00000046841 | Ckap4      | 0.537823666              | 1.762607004              | 1.224783338           | 1.7783E-06      | 0.003139609 |
| ENSMUSG00000025888 | Casp1      | 2.555576381              | 1.864033645              | -0.691542736          | 4.2921E-06      | 0.003258673 |
| ENSMUSG00000029561 | Oasl2      | 0.663315716              | 0.046089353              | -0.617226363          | 7.25168E-06     | 0.003258673 |
| ENSMUSG00000057143 | Trim12c    | 2.166684475              | 1.35807467               | -0.808609805          | 3.086E-06       | 0.003258673 |
| ENSMUSG00000030107 | Usp18      | 1.241045757              | 0.037130757              | -1.203915             | 3.6586E-06      | 0.003258673 |
| ENSMUSG00000064215 | Ifi27      | 2.405677672              | 0.640173452              | -1.76550422           | 7.85543E-06     | 0.003321993 |
| ENSMUSG00000033880 | Lgals3bp   | 1.746671821              | 0.23545555               | -1.511216271          | 9.75737E-06     | 0.003668558 |
| ENSMUSG00000032175 | Tyk2       | 2.440512309              | 1.434091712              | -1.006420597          | 1.04391E-05     | 0.003692217 |
| ENSMUSG00000114203 | AC154849.1 | 0.62694192               | 1.537416615              | 0.910474695           | 1.06972E-05     | 0.003715925 |
| ENSMUSG00000044583 | Tlr7       | 1.90432215               | 1.052807904              | -0.851514246          | 1.35558E-05     | 0.00405693  |
| ENSMUSG00000079017 | Ifi2712a   | 1.675448364              | 0.07133685               | -1.604111515          | 1.55608E-05     | 0.004287355 |
| ENSMUSG00000074896 | Ifit3      | 2.102777502              | 0.214094816              | -1.888682686          | 1.63044E-05     | 0.004287355 |
| ENSMUSG00000040511 | Pvr        | 1.713577924              | 2.45299069               | 0.739412767           | 1.65297E-05     | 0.004287355 |
| ENSMUSG00000017707 | Serinc3    | 3.500345272              | 4.594567339              | 1.094222067           | 2.07139E-05     | 0.005165991 |
| ENSMUSG00000026104 | Stat1      | 4.564655015              | 3.575045401              | -0.989609614          | 2.45104E-05     | 0.005744581 |
| ENSMUSG00000073491 | Ifi213     | 2.637114546              | 1.158739447              | -1.478375099          | 2.51118E-05     | 0.005815483 |
| ENSMUSG00000070327 | Rnf213     | 2.303868482              | 1.457381954              | -0.846486528          | 2.85123E-05     | 0.006232011 |
| ENSMUSG00000000386 | Mx1        | 0.661806002              | 0.006184005              | -0.655621997          | 2.91612E-05     | 0.006303025 |
| ENSMUSG00000105263 | Gm42427    | 3.478218919              | 5.588073269              | 2.10985435            | 3.26227E-05     | 0.006823767 |
| ENSMUSG00000066677 | Ifi208     | 2.071442107              | 1.319755407              | -0.751686699          | 3.72036E-05     | 0.006985043 |
| ENSMUSG00000050668 | Gpatch11   | 2.076375895              | 1.352197875              | -0.724178021          | 3.89325E-05     | 0.007078074 |
| ENSMUSG00000105353 | Gm42428    | 2.575347862              | 3.766253957              | 1.190906094           | 3.95506E-05     | 0.007123867 |
| ENSMUSG00000027514 | Zbp1       | 1.744228682              | 0.851499949              | -0.892728733          | 4.11598E-05     | 0.007196458 |
| ENSMUSG00000047412 | Zbtb44     | 1.381707411              | 2.076474592              | 0.694767181           | 4.43526E-05     | 0.007464264 |
| ENSMUSG00000010358 | Ifi35      | 2.973170609              | 2.140757228              | -0.832413381          | 5.09553E-05     | 0.007804985 |
| ENSMUSG00000032690 | Oas2       | 1.318771084              | 0.012373713              | -1.306397371          | 5.16811E-05     | 0.007854318 |
| ENSMUSG00000104713 | Gbp6       | 1.447705169              | 0.051515608              | -1.396189561          | 5.32402E-05     | 0.008028538 |
| ENSMUSG00000026222 | Sp100      | 4.762046649              | 4.123647894              | -0.638398754          | 7.06771E-05     | 0.009112424 |
| ENSMUSG00000041827 | Oasl1      | 1.217259477              | 0.206392731              | -1.010866747          | 7.69449E-05     | 0.009719541 |
| ENSMUSG00000002325 | Irf9       | 2.964104729              | 1.865459097              | -1.098645632          | 0.000100786     | 0.011201149 |
| ENSMUSG00000110537 | Gm4316     | 2.720277562              | 4.127152437              | 1.406874874           | 0.000105083     | 0.011231797 |
| ENSMUSG00000072772 | Grcc10     | 2.76944734               | 2.14173279               | -0.62771455           | 0.000104454     | 0.011231797 |
| ENSMUSG00000035208 | Sfn8       | 1.67331396               | 0.682023454              | -0.991290505          | 0.000118497     | 0.011939995 |

| Transcript ID       | Gene name   | log <sub>2</sub> (WT_MZ) | log <sub>2</sub> (KO_MZ) | log <sub>2</sub> (FC) | P-value     | FDR < 0.05  |
|---------------------|-------------|--------------------------|--------------------------|-----------------------|-------------|-------------|
| ENSMUSG00000006360  | Crip1       | 3.100077422              | 2.500300598              | -0.599776824          | 0.000125983 | 0.0122537   |
| ENSMUSG000000037921 | Ddx60       | 2.293439636              | 0.466953432              | -1.826486204          | 0.000139103 | 0.012858981 |
| ENSMUSG00000110386  | Gm42031     | 4.817351733              | 5.885325009              | 1.067973276           | 0.00014914  | 0.013068559 |
| ENSMUSG00000033538  | Casp4       | 1.130580445              | 0.511101359              | -0.619479086          | 0.000151363 | 0.013100362 |
| ENSMUSG000000024675 | Ms4a4c      | 2.446030489              | 1.708359668              | -0.737670822          | 0.0001546   | 0.013100362 |
| ENSMUSG000000027397 | Slc20a1     | 3.771017466              | 4.535625733              | 0.764608268           | 0.000155869 | 0.013100362 |
| ENSMUSG00000046805  | Mpeg1       | 1.717482098              | 1.124279756              | -0.593202342          | 0.000161297 | 0.013307867 |
| ENSMUSG000000078921 | Tgtp2       | 2.365675386              | 0.883838522              | -1.481836863          | 0.000169356 | 0.013653818 |
| ENSMUSG000000027189 | Trim44      | 1.60578658               | 2.234119368              | 0.628332788           | 0.000180091 | 0.013919107 |
| ENSMUSG00000105703  | Gm43305     | 6.763365858              | 7.632453293              | 0.869087435           | 0.000197509 | 0.014553599 |
| ENSMUSG000000078193 | Gm2000      | 5.009914961              | 3.958300928              | -1.051614032          | 0.000215219 | 0.015448946 |
| ENSMUSG000000062997 | Rpl35       | 5.24624856               | 4.249631479              | -0.996617081          | 0.000220319 | 0.015566224 |
| ENSMUSG000000037443 | Cep85       | 4.796574731              | 5.411362296              | 0.614787564           | 0.000231585 | 0.016032137 |
| ENSMUSG000000069049 | Eif2s3y     | 0.426810484              | 1.918403081              | 1.491592597           | 0.000262687 | 0.016888597 |
| ENSMUSG000000037321 | Tap1        | 3.731616699              | 3.089669284              | -0.641947414          | 0.000277466 | 0.017524501 |
| ENSMUSG000000044703 | Phf11a      | 0.889014831              | 0.195082392              | -0.693932439          | 0.000299917 | 0.018062818 |
| ENSMUSG000000079435 | Rpl36a      | 3.306960095              | 2.491072106              | -0.815887988          | 0.000314639 | 0.018741806 |
| ENSMUSG000000040483 | Xaf1        | 1.574419697              | 0.46046826               | -1.113951438          | 0.000320571 | 0.018954626 |
| ENSMUSG00000105987  | AI506816    | 3.146411453              | 3.758610816              | 0.612199363           | 0.000340673 | 0.019798166 |
| ENSMUSG000000052776 | Oas1a       | 1.007547929              | 0                        | -1.007547929          | 0.000340944 | 0.019798166 |
| ENSMUSG000000030921 | Trim30a     | 2.490007122              | 1.46680258               | -1.023204542          | 0.000348277 | 0.019951031 |
| ENSMUSG000000047735 | Samd9l      | 2.942383598              | 2.246468109              | -0.69591549           | 0.000364791 | 0.0202173   |
| ENSMUSG000000090137 | Uba52       | 3.929959173              | 2.970581249              | -0.959377924          | 0.000394665 | 0.021034012 |
| ENSMUSG000000020279 | Il9r        | 4.117796009              | 3.080695911              | -1.037100099          | 0.000397338 | 0.021118626 |
| ENSMUSG000000075602 | Ly6a        | 4.376523317              | 2.729092067              | -1.64743125           | 0.000413771 | 0.021325413 |
| ENSMUSG000000096768 | Erdr1       | 2.317501598              | 4.304865433              | 1.987363834           | 0.000423738 | 0.02150966  |
| ENSMUSG000000044712 | Slc38a6     | 2.297578077              | 2.90115966               | 0.603581584           | 0.000440101 | 0.021840036 |
| ENSMUSG000000094796 | BC147527    | 1.821279939              | 0.952568941              | -0.868710998          | 0.000513405 | 0.023597982 |
| ENSMUSG00000000275  | Trim25      | 2.167000238              | 1.562593373              | -0.604406865          | 0.000510717 | 0.023597982 |
| ENSMUSG000000045932 | Ifit2       | 1.014744725              | 0.287700662              | -0.727044063          | 0.000579373 | 0.025266185 |
| ENSMUSG000000096979 | Gm26880     | 2.851980552              | 3.931170606              | 1.079190054           | 0.000590802 | 0.025370583 |
| ENSMUSG000000046879 | Irgm1       | 2.649265858              | 1.767611633              | -0.881654226          | 0.000598467 | 0.025474788 |
| ENSMUSG000000022906 | Parp9       | 1.745053738              | 1.031426639              | -0.713627099          | 0.000604295 | 0.025499677 |
| ENSMUSG000000096255 | Dynl1b      | 0.994242321              | 1.794841036              | 0.800598715           | 0.000651127 | 0.026610022 |
| ENSMUSG000000060802 | B2m         | 6.571564669              | 5.610052449              | -0.96151222           | 0.000702118 | 0.027592528 |
| ENSMUSG000000007892 | Rplp1       | 4.221519356              | 3.460837768              | -0.760681589          | 0.00072806  | 0.027784653 |
| ENSMUSG000000072621 | Slfn10-ps   | 0.750707172              | 1.391466091              | 0.640758919           | 0.000730391 | 0.027784653 |
| ENSMUSG000000096780 | Tmem181b-ps | 0.319148762              | 1.116496124              | 0.797347362           | 0.000732716 | 0.027784653 |
| ENSMUSG000000038274 | Fau         | 3.866383664              | 3.01052532               | -0.855858345          | 0.000780517 | 0.029031362 |
| ENSMUSG000000078920 | Ifi47       | 2.039926655              | 1.345697442              | -0.694229213          | 0.000826509 | 0.030172337 |
| ENSMUSG000000022708 | Zbtb20      | 3.182858401              | 3.801568016              | 0.618709615           | 0.000842714 | 0.03041431  |
| ENSMUSG000000024079 | Eif2ak2     | 1.8249556                | 1.135568912              | -0.689386688          | 0.000849451 | 0.030600668 |

| Transcript ID       | Gene name | log <sub>2</sub> (WT_MZ) | log <sub>2</sub> (KO_MZ) | log <sub>2</sub> (FC) | P-value     | FDR < 0.05  |
|---------------------|-----------|--------------------------|--------------------------|-----------------------|-------------|-------------|
| ENSMUSG00000016252  | Atp5e     | 2.308564646              | 1.620100469              | -0.688464177          | 0.000857227 | 0.030823726 |
| ENSMUSG000000091649 | Phf11b    | 1.840043898              | 1.157276129              | -0.682767769          | 0.000874415 | 0.030983605 |
| ENSMUSG000000063457 | Rps15     | 3.615331113              | 2.773486426              | -0.841844687          | 0.000950055 | 0.031974778 |
| ENSMUSG000000029823 | Luc7l2    | 3.825269502              | 4.616190343              | 0.790920841           | 0.000964521 | 0.032238521 |
| ENSMUSG000000062783 | Csprs     | 2.362800273              | 1.543430287              | -0.819369986          | 0.000978769 | 0.032380956 |
| ENSMUSG000000046718 | Bst2      | 1.218878526              | 0.616199561              | -0.602678965          | 0.000991394 | 0.032508304 |
| ENSMUSG000000056501 | Cebpb     | 2.335996326              | 3.405486195              | 1.069489868           | 0.001030911 | 0.032822114 |
| ENSMUSG000000082286 | Pisd-ps1  | 1.662002721              | 2.679444564              | 1.017441842           | 0.001087236 | 0.034057989 |
| ENSMUSG000000020638 | Cmpk2     | 1.377087302              | 0.433432103              | -0.943655199          | 0.001114687 | 0.034473781 |
| ENSMUSG000000037563 | Rps16     | 4.293891866              | 3.414408004              | -0.879483862          | 0.001113046 | 0.034473781 |
| ENSMUSG000000043263 | Ifi209    | 3.922225006              | 3.323884994              | -0.598340012          | 0.00117209  | 0.034757115 |
| ENSMUSG000000038642 | Ctss      | 5.388315092              | 4.802796498              | -0.585518594          | 0.001177193 | 0.034782671 |
| ENSMUSG000000062006 | Rpl34     | 4.214358439              | 3.529868524              | -0.684489914          | 0.001194284 | 0.034883486 |
| ENSMUSG000000041841 | Rpl37     | 2.419201987              | 1.592329174              | -0.826872813          | 0.001213884 | 0.035037258 |
| ENSMUSG000000030256 | Bhlhe41   | 1.870052621              | 2.808476223              | 0.938423602           | 0.001220987 | 0.035135883 |
| ENSMUSG000000001123 | Lgals9    | 2.999547803              | 2.19723476               | -0.802313043          | 0.001244132 | 0.035591326 |
| ENSMUSG000000022014 | Epsti1    | 2.017626602              | 1.336683252              | -0.68094335           | 0.001369268 | 0.037128085 |
| ENSMUSG000000041481 | Serpina3g | 3.105483969              | 2.218863936              | -0.886620033          | 0.001395884 | 0.037380879 |
| ENSMUSG000000057322 | Rpl38     | 2.915574033              | 2.095912512              | -0.819661521          | 0.001414343 | 0.037486998 |
| ENSMUSG000000079523 | Tmsb10    | 5.600974118              | 4.925433975              | -0.675540143          | 0.001417594 | 0.037486998 |
| ENSMUSG000000046330 | Rpl37a    | 4.013385288              | 2.976072734              | -1.037312554          | 0.001464691 | 0.037939598 |
| ENSMUSG000000012848 | Rps5      | 4.765835593              | 4.027429766              | -0.738405827          | 0.001490677 | 0.038132922 |
| ENSMUSG000000012405 | Rpl15     | 5.123454132              | 4.362699126              | -0.760755006          | 0.001508445 | 0.038170012 |
| ENSMUSG000000098274 | Rpl24     | 3.487272984              | 2.603238575              | -0.88403441           | 0.001513397 | 0.0382339   |
| ENSMUSG000000106734 | Gm20559   | 2.420113893              | 1.811563158              | -0.608550735          | 0.001533397 | 0.038439646 |
| ENSMUSG000000058546 | Rpl23a    | 4.463785475              | 3.68142799               | -0.782357485          | 0.001610434 | 0.039031936 |
| ENSMUSG000000003429 | Rps11     | 4.863355235              | 4.115185306              | -0.748169929          | 0.001617522 | 0.039031936 |
| ENSMUSG000000063882 | Uqcrh     | 2.708989636              | 1.994082081              | -0.714907555          | 0.001612683 | 0.039031936 |
| ENSMUSG000000021200 | Asb2      | 3.099724283              | 2.318737985              | -0.780986297          | 0.00166871  | 0.039663802 |
| ENSMUSG000000017830 | Dhx58     | 1.221836272              | 0.605769721              | -0.616066551          | 0.00170564  | 0.040021191 |
| ENSMUSG000000027091 | Zc3h15    | 2.44601907               | 3.04575502               | 0.599735949           | 0.001743704 | 0.040574479 |
| ENSMUSG000000057841 | Rpl32     | 6.35821918               | 5.296410296              | -1.061808884          | 0.001751286 | 0.040655803 |
| ENSMUSG000000079641 | Rpl39     | 2.390022911              | 1.437423737              | -0.952599173          | 0.001781127 | 0.040955386 |
| ENSMUSG000000061477 | Rps7      | 4.926760926              | 4.0410226                | -0.885738326          | 0.001829586 | 0.041529675 |
| ENSMUSG000000022216 | Psme1     | 3.040238995              | 2.261299618              | -0.778939377          | 0.001871084 | 0.041837005 |
| ENSMUSG000000025794 | Rpl14     | 4.708321593              | 3.967339113              | -0.74098248           | 0.00187675  | 0.04188829  |
| ENSMUSG000000019984 | Med23     | 1.620658586              | 2.239758508              | 0.619099922           | 0.00203134  | 0.043567428 |
| ENSMUSG000000024677 | Ms4a6b    | 2.337917787              | 1.744552466              | -0.593365321          | 0.002037109 | 0.043587571 |
| ENSMUSG000000000682 | Cd52      | 4.932468392              | 4.07012698               | -0.862341411          | 0.002053577 | 0.043659263 |
| ENSMUSG000000025743 | Sdc3      | 0.608691522              | 0.019095496              | -0.589596025          | 0.002108801 | 0.044015564 |
| ENSMUSG000000043716 | Rpl7      | 4.32613367               | 3.640346496              | -0.685787174          | 0.002141733 | 0.044299491 |
| ENSMUSG000000090523 | Gypc      | 2.15069257               | 1.563144231              | -0.587548339          | 0.002169958 | 0.044495295 |

| Transcript ID      | Gene name     | log <sub>2</sub> (WT_MZ) | log <sub>2</sub> (KO_MZ) | log <sub>2</sub> (FC) | P-value     | FDR < 0.05  |
|--------------------|---------------|--------------------------|--------------------------|-----------------------|-------------|-------------|
| ENSMUSG00000045128 | Rpl18a        | 6.355997155              | 5.307471137              | -1.048526019          | 0.00217067  | 0.044495295 |
| ENSMUSG00000087528 | 9830144P21Rik | 1.735078315              | 2.456798889              | 0.721720574           | 0.002187604 | 0.044795216 |
| ENSMUSG00000090733 | Rps27         | 6.125036132              | 5.238079743              | -0.88695639           | 0.002203754 | 0.045010913 |
| ENSMUSG00000029322 | Plac8         | 4.727725415              | 3.910756856              | -0.816968559          | 0.002294366 | 0.045755086 |
| ENSMUSG00000040952 | Rps19         | 6.084573489              | 5.132526494              | -0.952046995          | 0.002350121 | 0.046168081 |
| ENSMUSG00000074129 | Rpl13a        | 5.533212797              | 4.719832668              | -0.81338013           | 0.002363879 | 0.046308703 |
| ENSMUSG00000041453 | Rpl21         | 4.638895239              | 3.961927368              | -0.676967871          | 0.00240456  | 0.046312784 |
| ENSMUSG00000060036 | Rpl3          | 5.499710228              | 4.876644925              | -0.623065303          | 0.002370803 | 0.046312784 |
| ENSMUSG00000070501 | Ifi214        | 1.894013647              | 1.245990199              | -0.648023448          | 0.002471101 | 0.04723441  |
| ENSMUSG00000063316 | Rpl27         | 2.665616619              | 2.013681585              | -0.651935034          | 0.002505312 | 0.047408397 |
| ENSMUSG00000025362 | Rps26         | 3.445709172              | 2.552606304              | -0.893102869          | 0.00255081  | 0.047942898 |
| ENSMUSG00000078606 | Gm4070        | 2.048399956              | 0.316073438              | -1.732326518          | 0.002553822 | 0.04795318  |
| ENSMUSG00000037754 | Ppp1r16b      | 5.091278847              | 5.744743318              | 0.653464471           | 0.002726106 | 0.049794313 |
| ENSMUSG00000039997 | Ifi203        | 3.446894961              | 2.828433844              | -0.618461117          | 0.002750731 | 0.05002865  |
| ENSMUSG00000046364 | Rpl27a        | 3.41358776               | 2.713813228              | -0.699774531          | 0.002843457 | 0.050746574 |
| ENSMUSG00000024423 | Impact        | 4.970621703              | 5.648112412              | 0.677490709           | 0.002850169 | 0.050752578 |
| ENSMUSG00000017404 | Rpl19         | 4.541935309              | 3.785777332              | -0.756157978          | 0.003047556 | 0.052844842 |
| ENSMUSG00000071644 | Eef1g         | 4.707566956              | 4.050374684              | -0.657192272          | 0.003090987 | 0.053149147 |
| ENSMUSG00000053565 | Eif3k         | 3.479880404              | 2.875756484              | -0.60412392           | 0.003131072 | 0.053616852 |
| ENSMUSG00000073702 | Rpl31         | 3.349536452              | 2.74168115               | -0.607855302          | 0.003156851 | 0.053843635 |
| ENSMUSG00000020460 | Rps27a        | 4.513612625              | 3.693534364              | -0.820078262          | 0.003336917 | 0.055245145 |
| ENSMUSG00000046962 | Zbtb21        | 2.536893794              | 3.282723113              | 0.74582932            | 0.003345306 | 0.055336944 |
| ENSMUSG00000059291 | Rpl11         | 3.944783125              | 3.108002976              | -0.836780148          | 0.003465201 | 0.056220653 |
| ENSMUSG00000090862 | Rps13         | 3.631651832              | 2.894965975              | -0.736685856          | 0.003688505 | 0.058189006 |
| ENSMUSG00000030744 | Rps3          | 5.005382512              | 4.32683488               | -0.678547632          | 0.003690289 | 0.058189006 |
| ENSMUSG00000008683 | Rps15a        | 3.737826742              | 2.850797923              | -0.887028819          | 0.003735061 | 0.058453857 |
| ENSMUSG00000047215 | Rpl9          | 4.976139315              | 4.147879694              | -0.828259622          | 0.003818185 | 0.059153744 |
| ENSMUSG00000068457 | Uty           | 0.550618299              | 1.5057079                | 0.955089601           | 0.003810577 | 0.059153744 |
| ENSMUSG00000028495 | Rps6          | 5.663888644              | 4.867000991              | -0.796887653          | 0.003854933 | 0.059303847 |
| ENSMUSG00000034892 | Rps29         | 3.45067027               | 2.669976043              | -0.780694227          | 0.003864304 | 0.05935009  |
| ENSMUSG00000026034 | Clk1          | 5.541539918              | 6.192220396              | 0.650680477           | 0.003963827 | 0.060053213 |
| ENSMUSG00000076501 | Igkv2-137     | 2.160104343              | 1.449294877              | -0.710809466          | 0.004056754 | 0.060647186 |
| ENSMUSG00000049775 | Tmsb4x        | 6.631510746              | 5.851062592              | -0.780448154          | 0.004085514 | 0.060668322 |
| ENSMUSG00000060636 | Rpl35a        | 3.27475817               | 2.640477062              | -0.634281108          | 0.004175055 | 0.061301299 |
| ENSMUSG00000006333 | Rps9          | 5.118134397              | 4.328427653              | -0.789706745          | 0.004178337 | 0.061301299 |
| ENSMUSG00000026643 | Nmt2          | 3.16746947               | 3.770816322              | 0.603346852           | 0.004229544 | 0.061677152 |
| ENSMUSG00000025498 | Irf7          | 1.760500893              | 0.86705255               | -0.893448343          | 0.00426378  | 0.061944215 |
| ENSMUSG00000036751 | Cox6b1        | 2.243101738              | 1.653457555              | -0.589644183          | 0.00432624  | 0.062363937 |
| ENSMUSG00000015165 | Hnrnp1        | 3.990826288              | 4.584363427              | 0.593537139           | 0.004351838 | 0.062569333 |
| ENSMUSG00000049517 | Rps23         | 4.510376589              | 3.648458727              | -0.861917862          | 0.004389109 | 0.062869149 |
| ENSMUSG00000000740 | Rpl13         | 6.48594878               | 5.566679091              | -0.919269689          | 0.004410339 | 0.062945206 |
| ENSMUSG00000008668 | Rps18         | 6.022972976              | 5.183809752              | -0.839163224          | 0.004461779 | 0.063384037 |

| Transcript ID       | Gene name  | log <sub>2</sub> (WT_MZ) | log <sub>2</sub> (KO_MZ) | log <sub>2</sub> (FC) | P-value     | FDR < 0.05  |
|---------------------|------------|--------------------------|--------------------------|-----------------------|-------------|-------------|
| ENSMUSG00000024608  | Rps14      | 5.53418584               | 4.821872147              | -0.712313693          | 0.004518971 | 0.063654993 |
| ENSMUSG00000024353  | Mzb1       | 4.634064255              | 4.052925698              | -0.581138557          | 0.004683822 | 0.064620137 |
| ENSMUSG000000093674 | Rpl41      | 4.453387214              | 3.492457904              | -0.96092931           | 0.004794983 | 0.065553967 |
| ENSMUSG000000062328 | Rpl17      | 3.571664731              | 2.89071145               | -0.680953281          | 0.004862352 | 0.066191273 |
| ENSMUSG000000003970 | Rpl8       | 4.196997847              | 3.499119985              | -0.697877863          | 0.005042538 | 0.067094733 |
| ENSMUSG000000031818 | Cox4i1     | 4.192819739              | 3.493813489              | -0.699006249          | 0.005084968 | 0.067474677 |
| ENSMUSG000000028234 | Rps20      | 3.705669175              | 2.981676462              | -0.723992713          | 0.005092199 | 0.06748257  |
| ENSMUSG000000072692 | Rpl37rt    | 2.97342273               | 2.176430534              | -0.796992196          | 0.005114494 | 0.067602013 |
| ENSMUSG000000067274 | Rplp0      | 6.026251366              | 5.284681671              | -0.741569695          | 0.005155099 | 0.067987898 |
| ENSMUSG000000048758 | Rpl29      | 3.264766161              | 2.614453968              | -0.650312193          | 0.005230275 | 0.068534226 |
| ENSMUSG000000029614 | Rpl6       | 4.730913032              | 4.006351882              | -0.72456115           | 0.005300209 | 0.068955421 |
| ENSMUSG000000045826 | Ptprcap    | 3.693035493              | 3.110992134              | -0.582043359          | 0.005324389 | 0.069034724 |
| ENSMUSG000000031723 | Txn14b     | 1.253847366              | 1.840138914              | 0.586291548           | 0.005403087 | 0.069791669 |
| ENSMUSG000000025290 | Rps24      | 3.969488709              | 3.310850185              | -0.658638524          | 0.005707391 | 0.071056279 |
| ENSMUSG000000032449 | Slc25a36   | 3.678093018              | 4.269876008              | 0.59178299            | 0.005752071 | 0.071094904 |
| ENSMUSG000000073640 | Rpl27-ps3  | 3.154193561              | 2.085209834              | -1.068983727          | 0.006240979 | 0.07416636  |
| ENSMUSG000000072620 | Slfn2      | 2.109685303              | 1.317336156              | -0.792349148          | 0.006320882 | 0.074680664 |
| ENSMUSG000000027487 | Cdk5rap1   | 0.913876655              | 1.599406034              | 0.685529379           | 0.006422377 | 0.075171179 |
| ENSMUSG000000061787 | Rps17      | 2.609872597              | 1.954020078              | -0.655852519          | 0.006460584 | 0.075482125 |
| ENSMUSG000000068240 | Gm11808    | 3.872524283              | 2.904110968              | -0.968413314          | 0.006662824 | 0.076738846 |
| ENSMUSG000000018476 | Kdm6b      | 4.860984622              | 5.557684852              | 0.69670023            | 0.006933948 | 0.078465695 |
| ENSMUSG000000056429 | Tgoln1     | 5.023702104              | 5.75869268               | 0.734990576           | 0.007235494 | 0.080109317 |
| ENSMUSG000000103696 | Gm37531    | 4.331913877              | 5.310711286              | 0.978797409           | 0.00727049  | 0.080243375 |
| ENSMUSG000000085148 | Mir22hg    | 1.748428972              | 2.365043791              | 0.616614819           | 0.007576778 | 0.081878702 |
| ENSMUSG000000057863 | Rpl36      | 3.827247701              | 2.856012525              | -0.971235176          | 0.007605444 | 0.081966038 |
| ENSMUSG000000095041 | AC149090.1 | 4.923096266              | 6.067784055              | 1.144687789           | 0.007709645 | 0.082358988 |
| ENSMUSG000000025279 | Dnase113   | 4.510643796              | 5.266678409              | 0.756034613           | 0.008005154 | 0.084206447 |
| ENSMUSG000000028081 | Rps3a1     | 4.772588429              | 4.185597166              | -0.586991263          | 0.00801343  | 0.084206447 |
| ENSMUSG000000067288 | Rps28      | 3.21737431               | 2.477210984              | -0.740163326          | 0.008688909 | 0.087036743 |
| ENSMUSG000000059070 | Rpl18      | 3.994487064              | 3.2966468                | -0.697840263          | 0.009077231 | 0.08940728  |
| ENSMUSG000000044533 | Rps2       | 5.146549206              | 4.427187384              | -0.719361822          | 0.009741575 | 0.092911306 |
| ENSMUSG000000037805 | Rpl10a     | 3.976311258              | 3.389625324              | -0.586685934          | 0.01003786  | 0.094108072 |
| ENSMUSG000000086583 | Gm15500    | 5.363375252              | 4.751075703              | -0.61229955           | 0.010172195 | 0.094588767 |
| ENSMUSG000000032803 | Cdv3       | 5.020930963              | 5.762796043              | 0.74186508            | 0.010627984 | 0.096361161 |
| ENSMUSG000000052040 | Klf13      | 4.707717731              | 5.331976234              | 0.624258503           | 0.010660749 | 0.096457461 |
| ENSMUSG000000034634 | Ly6d       | 6.54672361               | 5.89168931               | -0.6550343            | 0.010942492 | 0.097778732 |
| ENSMUSG000000061589 | Dot11      | 2.183489919              | 2.789471529              | 0.60598161            | 0.011458124 | 0.100222522 |
| ENSMUSG000000106044 | Gm42860    | 2.523908701              | 3.162656616              | 0.638747915           | 0.011676028 | 0.101218258 |
| ENSMUSG000000032035 | Ets1       | 6.384747525              | 5.777422506              | -0.607325019          | 0.011710712 | 0.101293229 |
| ENSMUSG000000040270 | Bach2      | 1.717554717              | 2.527577687              | 0.810022969           | 0.011904792 | 0.102154351 |
| ENSMUSG000000096954 | Gdap10     | 5.16677996               | 6.357334037              | 1.190554077           | 0.012254603 | 0.103814978 |
| ENSMUSG000000044734 | Serp1b1a   | 3.074404347              | 2.427448234              | -0.646956113          | 0.012551209 | 0.104924224 |

| Transcript ID      | Gene name     | log <sub>2</sub> (WT_MZ) | log <sub>2</sub> (KO_MZ) | log <sub>2</sub> (FC) | P-value     | FDR < 0.05  |
|--------------------|---------------|--------------------------|--------------------------|-----------------------|-------------|-------------|
| ENSMUSG00000061315 | Naca          | 3.827559254              | 3.24721759               | -0.580341665          | 0.012782619 | 0.105948144 |
| ENSMUSG00000029178 | Klf3          | 2.186364918              | 2.766527362              | 0.580162444           | 0.013228911 | 0.107809806 |
| ENSMUSG00000034120 | Srsf2         | 4.941011714              | 5.683904188              | 0.742892474           | 0.013286611 | 0.107927129 |
| ENSMUSG00000024334 | H2-Oa         | 3.852377381              | 3.214247846              | -0.638129535          | 0.013354847 | 0.108204483 |
| ENSMUSG00000052423 | B4galt3       | 2.766432582              | 3.374467542              | 0.60803496            | 0.014381809 | 0.113083807 |
| ENSMUSG00000022048 | Dpysl2        | 2.957366775              | 3.749665781              | 0.792299006           | 0.014860936 | 0.115405106 |
| ENSMUSG00000008682 | Rpl10         | 4.323818851              | 3.671841738              | -0.651977113          | 0.01758293  | 0.125289648 |
| ENSMUSG00000113476 | AC154517.3    | 2.906334067              | 3.486533313              | 0.580199246           | 0.017778237 | 0.125577359 |
| ENSMUSG00000062647 | Rpl7a         | 3.902663934              | 3.269895562              | -0.632768372          | 0.017857154 | 0.125906205 |
| ENSMUSG00000031258 | Xkrx          | 1.007367113              | 1.747309783              | 0.739942669           | 0.017941405 | 0.126180095 |
| ENSMUSG00000021701 | Plk2          | 4.217400945              | 4.908674403              | 0.691273459           | 0.01812177  | 0.12694375  |
| ENSMUSG00000033685 | Ucp2          | 3.965011263              | 3.329496427              | -0.635514836          | 0.018250993 | 0.127234563 |
| ENSMUSG00000033364 | Usp37         | 2.574214887              | 3.270282819              | 0.696067932           | 0.018880576 | 0.129819856 |
| ENSMUSG00000024063 | Lbh           | 3.382011305              | 3.977547217              | 0.595535911           | 0.019920311 | 0.133303652 |
| ENSMUSG00000032602 | Slc25a20      | 2.166761777              | 1.439081874              | -0.727679903          | 0.020906658 | 0.136234371 |
| ENSMUSG00000094006 | Igkv4-59      | 2.135906769              | 1.441488159              | -0.69441861           | 0.021191675 | 0.137459706 |
| ENSMUSG00000112822 | AC126943.1    | 1.343210156              | 2.265198121              | 0.921987965           | 0.022463921 | 0.141764359 |
| ENSMUSG00000076940 | Iglv2         | 3.581947183              | 2.822099186              | -0.759847997          | 0.022853893 | 0.142705718 |
| ENSMUSG00000021754 | Map3k1        | 5.07903905               | 5.71373048               | 0.634691429           | 0.023631041 | 0.145102079 |
| ENSMUSG00000103867 | 9630010A21Rik | 1.684992889              | 2.403594309              | 0.71860142            | 0.026574669 | 0.153947897 |
| ENSMUSG00000103996 | 4833421G17Rik | 1.480484851              | 2.166516071              | 0.68603122            | 0.027146468 | 0.155424411 |
| ENSMUSG00000094472 | Gm21897       | 1.427687267              | 2.177165921              | 0.749478654           | 0.027511051 | 0.156574742 |
| ENSMUSG00000089726 | Mir17hg       | 1.125188867              | 1.744663827              | 0.61947496            | 0.02901729  | 0.16118599  |
| ENSMUSG00000038375 | Trp53inp2     | 4.008997378              | 4.990982141              | 0.981984763           | 0.029844354 | 0.163995892 |
| ENSMUSG00000030213 | Atf7ip        | 4.358315644              | 4.952128338              | 0.593812694           | 0.031266277 | 0.16726321  |
| ENSMUSG00000036432 | Siah2         | 1.886062396              | 2.489502999              | 0.603440603           | 0.032023425 | 0.169096549 |
| ENSMUSG00000107041 | Gm42735       | 1.528429464              | 2.18021442               | 0.651784956           | 0.03239381  | 0.170226111 |
| ENSMUSG00000103591 | Gm38365       | 2.873442697              | 3.819573569              | 0.946130871           | 0.033650273 | 0.173524175 |
| ENSMUSG00000056579 | Tug1          | 4.575290054              | 5.226153856              | 0.650863802           | 0.034161702 | 0.174376171 |
| ENSMUSG00000015597 | Zfp318        | 2.234059805              | 2.873836804              | 0.639776998           | 0.034133641 | 0.174376171 |
| ENSMUSG00000020275 | Rel           | 6.334359772              | 7.028371128              | 0.694011356           | 0.03439274  | 0.175105419 |
| ENSMUSG00000107362 | Gm40309       | 2.767310808              | 3.516488757              | 0.749177949           | 0.034939118 | 0.176629092 |
| ENSMUSG00000098814 | Igkv19-93     | 2.199621053              | 1.066415488              | -1.133205566          | 0.035361148 | 0.177700961 |
| ENSMUSG00000026915 | Strbp         | 3.454316748              | 4.108123348              | 0.6538066             | 0.035344501 | 0.177700961 |
| ENSMUSG00000025451 | Paip1         | 1.571030263              | 2.297791962              | 0.726761699           | 0.03582969  | 0.178952994 |
| ENSMUSG00000108803 | 4930533N22Rik | 1.224582675              | 1.832567419              | 0.607984744           | 0.037123588 | 0.182136937 |
| ENSMUSG00000050299 | Gm9843        | 2.544776154              | 1.743795643              | -0.800980511          | 0.038393083 | 0.185878705 |
| ENSMUSG00000074698 | Csnk2a1       | 4.784805565              | 5.38508739               | 0.600281825           | 0.039167361 | 0.187158604 |
| ENSMUSG00000025283 | Sat1          | 5.23612275               | 5.922655832              | 0.686533081           | 0.039294495 | 0.187408493 |
| ENSMUSG00000104339 | C130089K02Rik | 0.838692594              | 1.52446205               | 0.685769455           | 0.041356558 | 0.193066744 |
| ENSMUSG00000030059 | Tmf1          | 3.647781161              | 4.25954591               | 0.611764749           | 0.043164423 | 0.19808387  |

**Table S5.** Differentially expressed genes characteristic of TYK2 deficiency shared in both FO and MZ cells and their respective fold-changes and *P*-values.

| Transcript ID      | Gene name  | Follicular            |                 | Marginal zone         |                 |
|--------------------|------------|-----------------------|-----------------|-----------------------|-----------------|
|                    |            | log <sub>2</sub> (FC) | <i>P</i> -value | log <sub>2</sub> (FC) | <i>P</i> -value |
| ENSMUSG00000095041 | AC149090.1 | 1.014076426           | 0.000377501     | 1.144687789           | 0.007709645     |
| ENSMUSG00000105987 | AI506816   | 0.590192805           | 0.000988124     | 0.612199363           | 0.000340673     |
| ENSMUSG00000025888 | Casp1      | -0.614889658          | 0.001644965     | -0.691542736          | 4.2921E-06      |
| ENSMUSG00000033538 | Casp4      | -0.788584752          | 1.32307E-07     | -0.619479086          | 0.000151363     |
| ENSMUSG00000046841 | Ckap4      | 0.78062608            | 0.000317226     | 1.224783338           | 1.7783E-06      |
| ENSMUSG00000062783 | Csprs      | -0.721359418          | 0.0046022       | -0.819369986          | 0.000978769     |
| ENSMUSG00000037921 | Ddx60      | -0.705216956          | 1.0321E-05      | -1.826486204          | 0.000139103     |
| ENSMUSG00000017830 | Dhx58      | -0.730459288          | 4.32709E-06     | -0.616066551          | 0.00170564      |
| ENSMUSG00000096255 | Dynlt1b    | 0.911982487           | 7.14071E-06     | 0.800598715           | 0.000651127     |
| ENSMUSG00000096768 | Erdr1      | 1.597643372           | 0.003022915     | 1.987363834           | 0.000423738     |
| ENSMUSG00000104713 | Gbp6       | -0.736978175          | 0.001484622     | -1.396189561          | 5.32402E-05     |
| ENSMUSG00000078606 | Gm4070     | -1.723504347          | 0.000127761     | -1.732326518          | 0.002553822     |
| ENSMUSG00000110386 | Gm42031    | 1.468757507           | 0.000218941     | 1.067973276           | 0.00014914      |
| ENSMUSG00000105263 | Gm42427    | 1.56667504            | 0.000103684     | 2.10985435            | 3.26227E-05     |
| ENSMUSG00000110537 | Gm4316     | 1.052243734           | 1.86191E-05     | 1.406874874           | 0.000105083     |
| ENSMUSG00000105703 | Gm43305    | 1.170540125           | 0.00014852      | 0.869087435           | 0.000197509     |
| ENSMUSG00000037849 | Ifi206     | -0.951196866          | 0.000424255     | -1.132760332          | 1.1903E-07      |
| ENSMUSG00000066677 | Ifi208     | -0.806137011          | 0.001801663     | -0.751686699          | 3.72036E-05     |
| ENSMUSG00000073491 | Ifi213     | -1.887568421          | 3.79065E-06     | -1.478375099          | 2.51118E-05     |
| ENSMUSG00000070501 | Ifi214     | -0.589900777          | 0.00893012      | -0.648023448          | 0.002471101     |
| ENSMUSG00000064215 | Ifi27      | -1.137940342          | 4.02264E-06     | -1.76550422           | 7.85543E-06     |
| ENSMUSG00000079017 | Ifi27l2a   | -1.497775418          | 1.5288E-05      | -1.604111515          | 1.55608E-05     |
| ENSMUSG00000045932 | Ifit2      | -0.597377417          | 0.000842863     | -0.727044063          | 0.000579373     |
| ENSMUSG00000074896 | Ifit3      | -0.638394793          | 0.000264124     | -1.888682686          | 1.63044E-05     |
| ENSMUSG00000020279 | Il9r       | -1.404483721          | 3.10286E-08     | -1.037100099          | 0.000397338     |
| ENSMUSG00000025498 | Irf7       | -0.983013632          | 4.9925E-07      | -0.893448343          | 0.00426378      |
| ENSMUSG00000002325 | Irf9       | -0.715977595          | 0.000444487     | -1.098645632          | 0.000100786     |
| ENSMUSG00000046879 | Irgm1      | -0.598111585          | 0.00233851      | -0.881654226          | 0.000598467     |
| ENSMUSG00000033880 | Lgals3bp   | -0.720067956          | 5.68361E-05     | -1.511216271          | 9.75737E-06     |
| ENSMUSG00000075602 | Ly6a       | -1.879319384          | 0.000100242     | -1.64743125           | 0.000413771     |
| ENSMUSG00000000386 | Mx1        | -0.761909215          | 0.000229679     | -0.655621997          | 2.91612E-05     |
| ENSMUSG00000052776 | Oas1a      | -0.693673019          | 0.000236333     | -1.007547929          | 0.000340944     |
| ENSMUSG00000032690 | Oas2       | -1.127807319          | 5.86276E-05     | -1.306397371          | 5.16811E-05     |
| ENSMUSG00000041827 | Oasl1      | -1.116828203          | 4.55977E-08     | -1.010866747          | 7.69449E-05     |
| ENSMUSG00000029561 | Oasl2      | -0.730055686          | 6.8833E-05      | -0.617226363          | 7.25168E-06     |
| ENSMUSG00000082286 | Pisd-ps1   | 0.729441634           | 0.000499973     | 1.017441842           | 0.001087236     |
| ENSMUSG00000029322 | Plac8      | -0.734301719          | 6.84626E-05     | -0.816968559          | 0.002294366     |
| ENSMUSG00000070327 | Rnf213     | -1.174044461          | 7.68596E-06     | -0.846486528          | 2.85123E-05     |

| Transcript ID      | Gene name   | Follicular            |                 | Marginal zone         |                 |
|--------------------|-------------|-----------------------|-----------------|-----------------------|-----------------|
|                    |             | log <sub>2</sub> (FC) | <i>P</i> -value | log <sub>2</sub> (FC) | <i>P</i> -value |
| ENSMUSG00000025743 | Sdc3        | -0.637488948          | 2.09748E-05     | -0.589596025          | 0.002108801     |
| ENSMUSG00000041481 | Serpina3g   | -0.675457658          | 0.028949762     | -0.886620033          | 0.001395884     |
| ENSMUSG00000072620 | Slfn2       | -0.800760465          | 0.00152012      | -0.792349148          | 0.006320882     |
| ENSMUSG00000035208 | Slfn8       | -1.136035563          | 4.84913E-05     | -0.991290505          | 0.000118497     |
| ENSMUSG00000026104 | Stat1       | -0.761077138          | 0.004970557     | -0.989609614          | 2.45104E-05     |
| ENSMUSG00000078921 | Tgtp2       | -0.625829925          | 0.005716327     | -1.481836863          | 0.000169356     |
| ENSMUSG00000044583 | Tlr7        | -0.953649418          | 1.47899E-05     | -0.851514246          | 1.35558E-05     |
| ENSMUSG00000096780 | Tmem181b-ps | 0.600473759           | 0.000108961     | 0.797347362           | 0.000732716     |
| ENSMUSG00000030921 | Trim30a     | -0.87905703           | 0.000711356     | -1.023204542          | 0.000348277     |
| ENSMUSG00000032175 | Tyk2        | -1.443996413          | 1.05354E-07     | -1.006420597          | 1.04391E-05     |



**Table S6.** Significance levels for proliferation and differentiation in the *in vitro* B cell cultures. IMIQ group was compared to the IFN $\alpha$  + IMIQ and CL097 group with IFN $\alpha$  + CL097, in WT and *Tyk2*<sup>-/-</sup>, respectively with a two-tailed Student t-test (data shown in Fig. 5). Each comparison shows their respective significance level and *P*-value in brackets. ns = not statistically significant; \* *P* < 0.05; \*\* *P* < 0.01; \*\*\* *P* < 0.001.

|  | WT                             |                                  |                   |
|--|--------------------------------|----------------------------------|-------------------|
|  | IMIQ vs<br>IFN $\alpha$ + IMIQ | CL097 vs<br>IFN $\alpha$ + CL097 | C vs IFN $\alpha$ |
| <b>Proliferation</b>                             | *<br>(0.037)                   | **<br>(0.0021)                   | ***<br>(0.0001)   |
| <b>Differentiation<br/>(% CD138<sup>+</sup>)</b> | **<br>(0.0069)                 | ***<br>(0.00069)                 | *<br>(0.02)       |

|  | <i>Tyk2</i> <sup>-/-</sup>     |                                  |                   |
|--|--------------------------------|----------------------------------|-------------------|
|  | IMIQ vs<br>IFN $\alpha$ + IMIQ | CL097 vs<br>IFN $\alpha$ + CL097 | C vs IFN $\alpha$ |
| <b>Proliferation</b>                             | ***<br>(0.0001)                | ***<br>(0.0003)                  | *<br>(0.02)       |
| <b>Differentiation<br/>(% CD138<sup>+</sup>)</b> | ***<br>(0.0010)                | ***<br>(0.0001)                  | ns<br>(0.20)      |

**Table S7.** Significance levels achieved by *Tlr7* gene expression at 6 h. The control group was compared to the different treatments in WT and *Tyk2*<sup>-/-</sup> with a two-tailed Student t-test (data shown in Fig. 6). Each comparison shows their respective significance level and *P*-value in brackets. ns = not statistically significant; \* *P* < 0.05; \*\* *P* < 0.01; \*\*\* *P* < 0.001

|                            | C vs<br>IMIQ   | C vs<br>CL097   | C vs<br>IFN $\alpha$ | C vs<br>IFN $\alpha$ + IMIQ | C vs<br>IFN $\alpha$ + CL097 | C vs<br>LPS    | C vs<br>antiCD40 +<br>IL4 |
|----------------------------|----------------|-----------------|----------------------|-----------------------------|------------------------------|----------------|---------------------------|
| WT                         | ns<br>(0.0519) | ***<br>(0.0005) | ***<br>(< 0.0001)    | ***<br>(0.0003)             | ***<br>(0.0004)              | **<br>(0.0018) | *<br>(0.025)              |
| <i>Tyk2</i> <sup>-/-</sup> | *<br>(0.0211)  | ***<br>(0.0002) | **<br>(0.001)        | ***<br>(0.0001)             | ***<br>(< 0.0001)            | ns<br>(0.5775) | ***<br>(0.0001)           |

**Table S8.** Significance levels for the production of IL6 and IgG in the *in vitro* B cell cultures. IMIQ group was compared to IFN $\alpha$  + IMIQ and CL097 group with IFN $\alpha$  + CL097, in WT and *Tyk2*<sup>-/-</sup>, respectively with a two-tailed Student t-test (data shown in Fig. 6). Each comparison shows their respective significance level and *P*-value in brackets. ns = not statistically significant; \* *P* < 0.05; \*\* *P* < 0.01; \*\*\* *P* < 0.001.

|     |  | WT                             |                                  |                   |
|-----|--|--------------------------------|----------------------------------|-------------------|
|     |  | IMIQ vs<br>IFN $\alpha$ + IMIQ | CL097 vs<br>IFN $\alpha$ + CL097 | C vs IFN $\alpha$ |
| IL6 |  | ns<br>(0.99)                   | *<br>(0.049)                     | ns<br>(0.41)      |
| IgG |  | **<br>(0.025)                  | **<br>(0.022)                    | ns<br>(0.72)      |

|     |  | <i>Tyk2</i> <sup>-/-</sup>     |                                  |                   |
|-----|--|--------------------------------|----------------------------------|-------------------|
|     |  | IMIQ vs<br>IFN $\alpha$ + IMIQ | CL097 vs<br>IFN $\alpha$ + CL097 | C vs IFN $\alpha$ |
| IL6 |  | ns<br>(0.48)                   | ns<br>(0.24)                     | ns<br>(0.45)      |
| IgG |  | **<br>(0.0058)                 | **<br>(0.0014)                   | ns<br>(0.38)      |