



Article

Identification of Genomic Regions Implicated in Susceptibility to *Schistosoma mansoni* Infection in a Murine Backcross Genetic Model

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Supplementary Materials: The following are available online at www.mdpi.com/xxx/s1.

Figure S1: Representation of parasitological and pathological variables (A) number of recovered male worms, (B) number of recovered female worms, (C) eggs per gram of liver and (D) number of granulomas/cm² of liver surface between parental strains (CBA/2J, C57/2J) F1 progeny (F1B6BCA) and Backcross (F1BCX). The means and the standard error of the mean (SEM) were represented. Figure S2: Comparison between BX male and female mice: (A) number of recovered male and female worms, (B) number of eggs per gram (EPG) of liver and small intestine, (C) number of granulomas and affected surface of the liver and (D) fecundity of female worms in the liver and small intestine. The means and the standard error of the mean (SEM) were represented. Figure S3: Box plot of BX male and female mice: (A) number of recovered male and female worms; (B) Number of eggs per gram (EPG) of liver and small intestine; (C) number of granulomas and (D) affected liver surface (mm²/cm²) of for the BX cohort. Box plot and the mean as a red circle. Figure S4: Dendrogram with all parasitological and pathological variables for schistosomiasis susceptibility: mild in green, mild-moderate in pink, moderate-severe in blue and severe in red. Figure S5: Principal components analysis (PCA). A) Representation of the scores with four tentative groups of mice in the BX cohort. B) Representation of variable loadings. Figure S6: Differences between the four groups of schistosomiasis degree regarding cell lymphocyte subpopulations in splenocytes(A): CD4, CD8, B220 and CD45; cell subpopulations in peripheral blood (B): CD4, CD8, B220; and CD45 and immunoglobulins (C): IgG, Ig1, IgG2a and IgM nine-week postinfection. The comparison among the four groups was made by ANOVA, and the Tukey test was made between every two groups. Figure S7: Syntenic regions located in humans from identified quantitative trace loci (QTL) in mice. A) The QTL1 on mouse chromosome 15 was mainly located on human chromosome 8. B) The QTL2 on mouse chromosome 18 was mainly located on human chromosome 18. Table S1: Quantitative trace loci (QTL), associated chromosome (Chr) and location (cM) with LDO scores, and the average of the variables in homozygous (AA), heterozygous (AB) and male X alleles (AY and BY) genotypes and the allele combination with higher effect in parasitological and pathological phenotypes in the backcross cohort BX. (EPG- Eggs per gram). Table S2: Quantitative trace loci (QTL), associated chromosome (Chr), location (cM) with LOD scores and the average of the variables in homozygous (AA), heterozygous (AB) and male X alleles (AY and BY) genotypes and the allele combination with higher effect in cell populations at nine-week (W9) post-infection in the backcross cohort BX. Table S3: Quantitative trace loci (QTL), associated chromosome (Chr), location (cM) with LOD scores and average of the variables in homozygous (AA), heterozygous (AB) and male X alleles (AY and BY)

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genotypes and the allele combination with higher effect in circulating antibodies at nine-weeks (W9) post-infection in the backcross cohort BX.

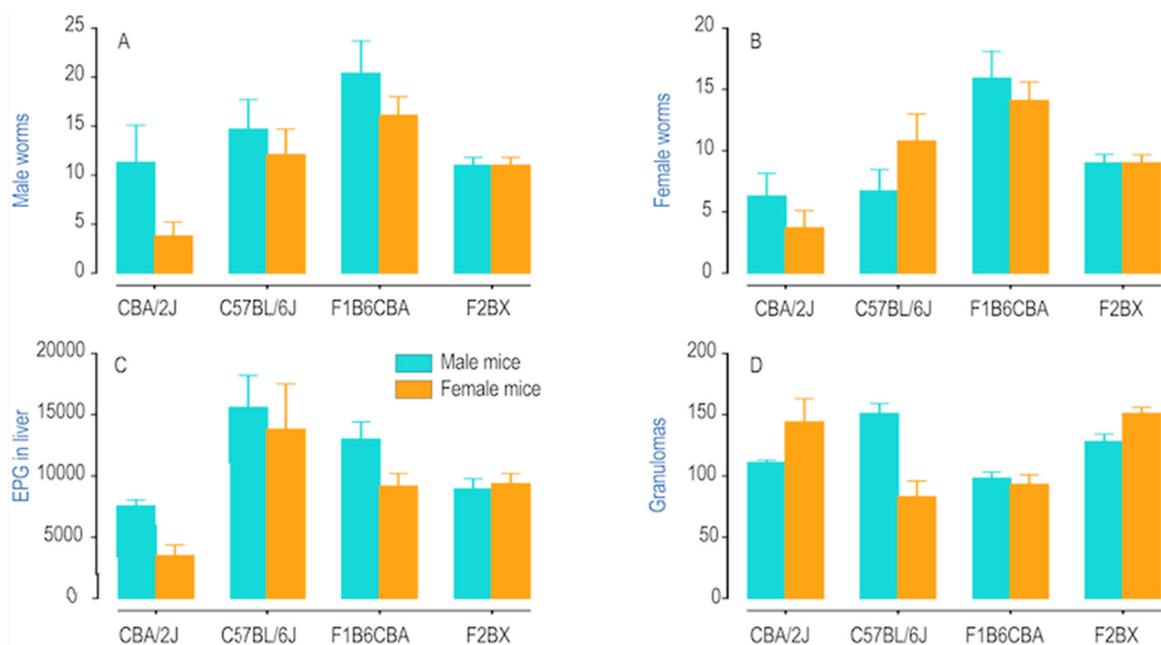


Figure S1. Representation of parasitological and pathological variables (A) number of recovered male worms, (B) number of recovered female worms, (C) eggs per gram of liver and (D) number of granulomas/cm² of liver surface between parental strains (CBA/2J, C57/2J) F1 progeny (F1B6CBA) and Backcross (F1BCX). The means and the standard error of the mean (SEM) were represented.

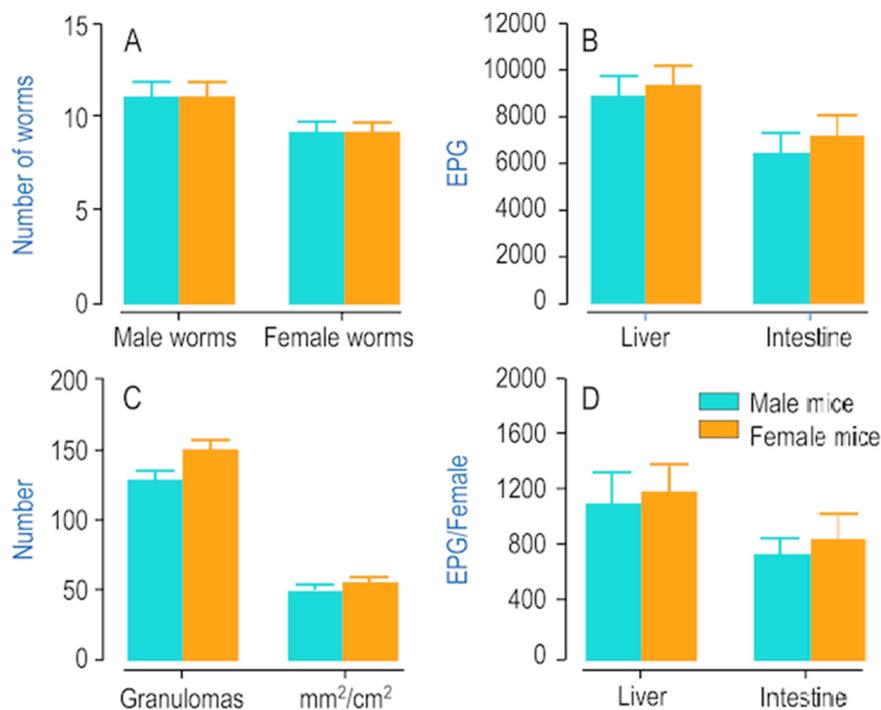


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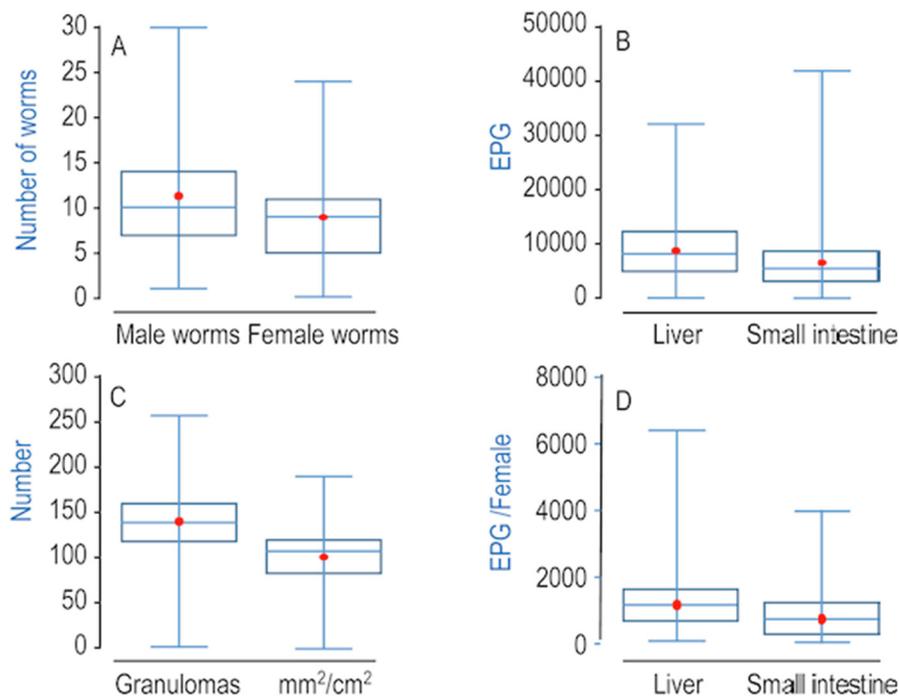


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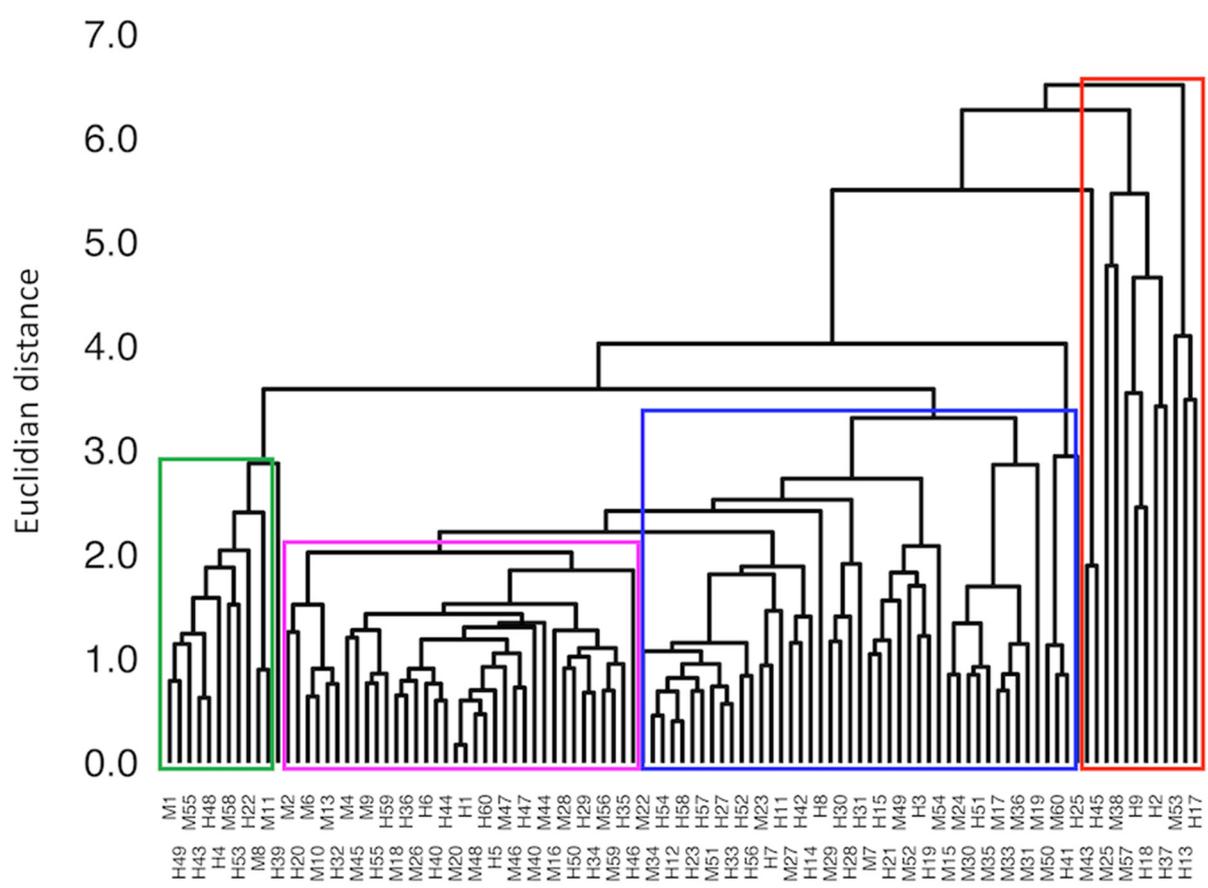


Figure S4. Dendrogram with all parasitological and pathological variables for schistosomiasis susceptibility: mild in green, mild-moderate in pink, moderate-severe in blue and severe in red.

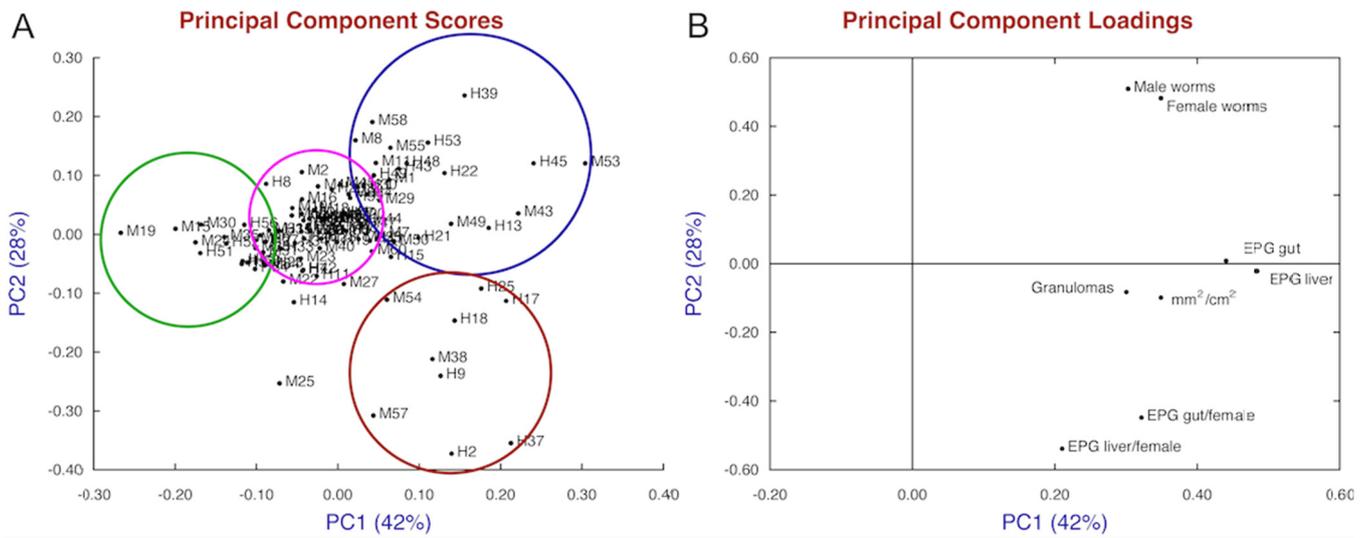


Figure S5. Principal components analysis (PCA). (A) Representation of the scores with four tentative groups of mice in the BX cohort. (B) Representation of variable loadings.

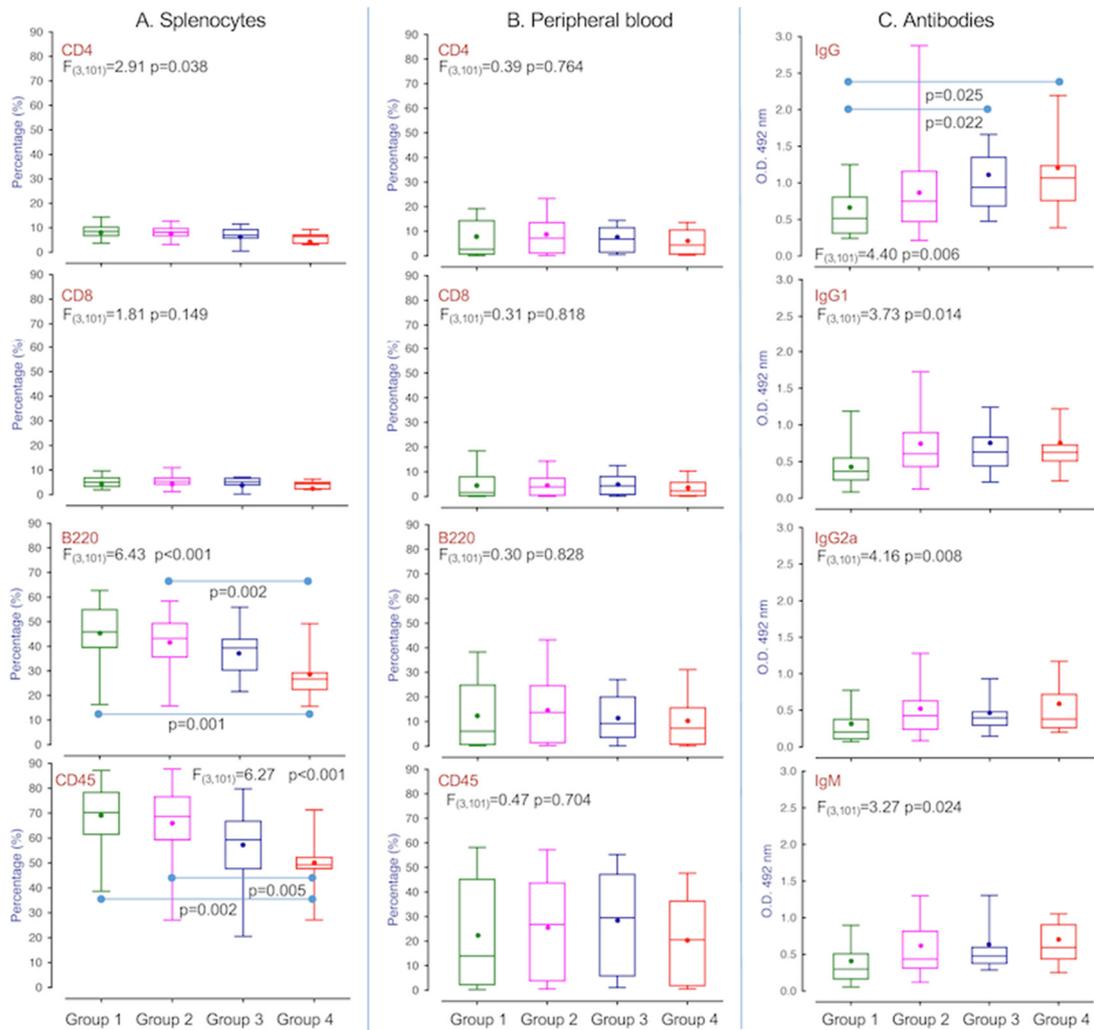


Figure S6. Differences between the four groups of schistosomiasis degree regarding cell lymphocyte subpopulations in splenocytes (A): CD4, CD8, B220 and CD45; cell subpopulations in peripheral blood (B): CD4, CD8, B220 and CD45; and immunoglobulins (C)

IgG, Ig1, IgG2a and IgM nine-week post-infection. The comparison among the four groups was made by ANOVA, and the Tukey test was made between every two groups.

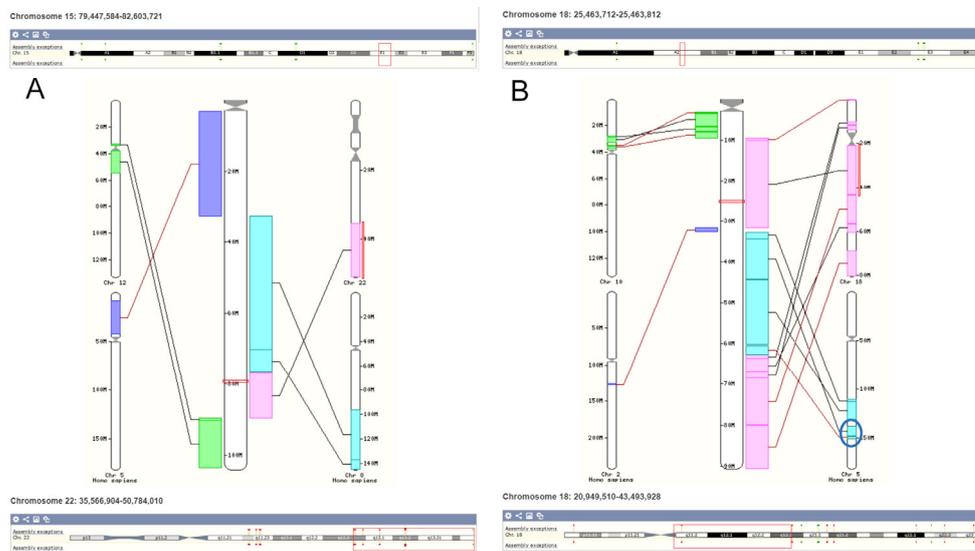


Figure S7. Syntenic regions in human beings from identified quantitative trace loci (QTL) in mice. A) The QTL1 on mouse chromosome 15 was mainly on human chromosome 8. B) The QTL2 on mouse chromosome 18 was mainly located on human chromosome 18.

Table S1. Quantitative trace loci (QTL), associated chromosome (Chr) and location (cM) with LDO scores, and the average of the variables in homozygous (AA), heterozygous (AB) and male X alleles (AY and BY) genotypes and the allele combination with higher effect in parasitological and pathological phenotypes in the backcross cohort BX. (EPG- Eggs per gram).

| Phenotype | eQTL | Chr. | Marker Peak | Location (cM) | LOD Score | Average ± SEM | | | | Higher Effect Allele |
|-------------------------|--------|------|-------------|---------------|-----------|----------------|-----------------|------------|-----------|----------------------|
| | | | | | | AA | AB | AY | BY | |
| Granulomas | eQTL1 | 15 | rs6169611 | 32.17 | 1.51 | 152.61±6.49 | 127.64±6.64 | | | AA |
| | eQTL2 | 18 | rs13483259 | 14.18 | 1.48 | 129.29±6.40 | 153.78±6.70 | | | AB |
| Injured hepatic surface | eQTL3 | 2 | rs13476772 | 63.25 | 1.47 | 56.63±2.76 | 46.70±2.52 | | | AA |
| | eQTL1 | 15 | rs13482664 | 37.72 | 2.03 | 56.84±2.56 | 45.31±2.62 | | | AA |
| | eQTL4 | 17 | rs13482845 | 2.52 | 1.54 | 45.59±2.80 | 55.65±2.49 | | | AB |
| | eQTL2 | 18 | rs13483259 | 14.18 | 1.54 | 46.59±2.55 | 56.78±2.80 | | | AB |
| Male worms | eQTL5 | 6 | rs13478799 | 30.04 | 2.01 | 13.11±0.92 | 9.31±0.80 | | | AA |
| | eQTL6 | 7 | rs13479382 | 51.74 | 1.64 | 9.31±0.84 | 12.73±0.88 | | | AB |
| | eQTL7 | X | rs13483769 | 30.62 | 2.28 | 12.81±1.20 | 10.46±1.08 | 13.07±1.29 | 7.74±1.22 | AY/AA/AB/BY |
| Female worms | eQTL5 | 6 | c6.loc57.5 | 59.38 | 2.11 | 10.51±0.73 | 7.28±0.70 | | | AA |
| | eQTL7 | X | rs13483769 | 30.62 | 1.45 | 9.67±1.03 | 8.15±0.93 | 10.73±1.10 | 7.07±1.05 | AY/AA/AB/BY |
| EPG liver | eQTL8 | 8 | rs13479680 | 19.01 | 2.82 | 6974.25±885.31 | 11560.76±844.22 | | | AB |
| | eQTL4 | 17 | rs13474581 | 4.55 | 1.41 | 7481.65±966.22 | 10806.63±839.62 | | | AB |
| EPG gut | eQTL9 | 3 | rs13477093 | 20.78 | 1.67 | 5162.24±809.89 | 8584.90±892.88 | | | AB |
| | eQTL5 | 6 | rs3023064 | 7.99 | 1.50 | 8424.47±893.53 | 5169.28±849.21 | | | AA |
| | eQTL8 | 8 | rs13479680 | 19.01 | 1.61 | 4967.71±869.99 | 8301.83±831.33 | | | AB |
| | eQTL10 | 1 | rs13475979 | 47.01 | 1.49 | 1685.07±199.20 | 1031.32±142.09 | | | AA |
| EPG of liver/fe-male | eQTL3 | 2 | rs6257221 | 102.73 | 1.56 | 1552.30±159.78 | 922.42±167.33 | | | AA |
| | eQTL11 | 5 | rs13478485 | 60.10 | 2.37 | 954.78±142.56 | 1752.94±185.19 | | | AB |
| | eQTL12 | 11 | rs13481156 | 55.29 | 1.41 | 967.27±159.11 | 1573.58±169.49 | | | AB |

| | | | | | | | | | | |
|-------------------|----|---|---|---|---|--|--|--|--|--|
| EPG of gut/female | -- | - | - | - | - | | | | | |
|-------------------|----|---|---|---|---|--|--|--|--|--|

Table S2. Quantitative trace loci (QTL), associated chromosome (Chr), location (cM) with LOD scores and the average of the variables in homozygous (AA), heterozygous (AB) and male X alleles (AY and BY) genotypes and the allele combination with higher effect in cell populations at nine-week (W9) post-infection in the backcross cohort BX.

| Phenotype | eQTL | Chr. | Marker Peak | Location (cM) | LOD Score | Average \pm SEM | | | | Higher Effect Allele |
|----------------|--------|------|-------------|---------------|-----------|-------------------|------------------|----|----|----------------------|
| | | | | | | AA | AB | AY | BY | |
| CD4 Blood W9 | eQTL13 | 13 | rs13481740 | 13.23 | 1.68 | 5.77 \pm 0.83 | 9.13 \pm 0.84 | | | AB |
| | eQTL14 | 19 | rs13483665 | 45.23 | 1.95 | 9.34 \pm 0.86 | 5.73 \pm 0.80 | | | AA |
| CD8 Blood W9 | eQTL15 | 14 | rs8251327 | 28.08 | 1.81 | 7.56 \pm 0.73 | 4.42 \pm 0.78 | | | AA |
| | eQTL4 | 17 | rs13482998 | 20.63 | 1.92 | 7.92 \pm 0.80 | 4.67 \pm 0.71 | | | AA |
| CD45 Blood W9 | eQTL13 | 13 | rs13481826 | 30.69 | 1.86 | 30.27 \pm 4.21 | 49.03 \pm 4.62 | | | AB |
| | eQTL15 | 14 | rs8251327 | 28.08 | 1.44 | 46.47 \pm 4.61 | 29.93 \pm 4.57 | | | AA |
| | eQTL14 | 19 | c19.loc40 | 44.08 | 1.85 | 48.68 \pm 4.57 | 30.17 \pm 4.26 | | | AA |
| B220_Blood_W9 | eQTL13 | 13 | rs13481826 | 30.69 | 1.69 | 11.65 \pm 1.80 | 19.30 \pm 1.98 | | | AB |
| | eQTL16 | 19 | rs13483665 | 45.23 | 1.83 | 19.42 \pm 1.96 | 11.41 \pm 1.81 | | | AA |
| CD4 Spleen W9 | eQTL10 | 1 | rs13475740 | 4.95 | 2.03 | 6.92 \pm 0.39 | 8.56 \pm 0.35 | | | AB |
| CD8 Spleen W9 | eQTL13 | 13 | rs4229866 | 35.76 | 1.68 | 4.69 \pm 0.29 | 5.97 \pm 0.33 | | | AB |
| | eQTL1 | 15 | rs13482696 | 43.56 | 1.49 | 5.81 \pm 0.30 | 4.65 \pm 0.31 | | | AA |
| CD45 Spleen W9 | eQTL10 | 1 | rs13475749 | 6.03 | 2.10 | 58.42 \pm 2.34 | 68.29 \pm 1.99 | | | AB |
| B220 Spleen W9 | eQTL4 | 17 | rs13483013 | 24.72 | 1.64 | 42.45 \pm 2.56 | 32.61 \pm 2.30 | | | AA |

Table S3. Quantitative trace loci (QTL), associated chromosome (Chr), location (cM) with LOD scores and the average of the variables in homozygous (AA), heterozygous (AB) and male X alleles (AY and BY) genotypes and the allele combination with higher effect in circulant antibodies at nine-weeks (W9) post-infection in the backcross cohort BX.

| Phenotype | eQTL | Chr. | Marker Peak | Location (cM) | LOD Score | Average \pm SEM | | | | Higher Effect Allele |
|-----------|--------|------|-------------|---------------|-----------|-------------------|------------------|------------------|------------------|----------------------|
| | | | | | | AA | AB | AY | BY | |
| IgG W9 | eQTL12 | 11 | rs13481062 | 38.91 | 2.03 | 0.7 \pm 0.07 | 1.02 \pm 0.07 | | | AB |
| | eQTL4 | 17 | rs13482845 | 2.52 | 3.42 | 0.15 \pm 0.01 | 0.17 \pm 0.009 | | | AB |
| IgG1 W9 | eQTL17 | 16 | rs4204623 | 42.53 | 2.85 | 0.48 \pm 0.04 | 0.70 \pm 0.04 | | | AB |
| | eQTL16 | 19 | rs13483612 | 32.11 | 1.74 | 0.49 \pm 0.04 | 0.67 \pm 0.04 | | | AB |
| IgG2a W9 | eQTL8 | 8 | rs13479846 | 37.83 | 2.13 | 0.31 \pm 0.036 | 0.48 \pm 0.037 | | | AB |
| | eQTL18 | 9 | rs4227609 | 24.58 | 2.31 | 0.31 \pm 0.035 | 0.48 \pm 0.036 | | | AB |
| | eQTL19 | 12 | c12.loc57.5 | 59.92 | 1.54 | 0.46 \pm 0.037 | 0.32 \pm 0.037 | | | AA |
| | eQTL7 | X | rs13483959 | 49.16 | 1.44 | 0.33 \pm 0.047 | 0.52 \pm 0.052 | 0.34 \pm 0.055 | 0.37 \pm 0.053 | AB/BY/AY/AA |
| IgGM W9 | eQTL3 | 2 | c2.loc20 | 23.68 | 1.57 | 0.61 \pm 0.045 | 0.44 \pm 0.044 | | | AA |
| | eQTL4 | 17 | rs13482845 | 2.52 | 4.96 | 0.37 \pm 0.030 | 0.67 \pm 0.047 | | | AB |

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