



Article

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

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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)

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

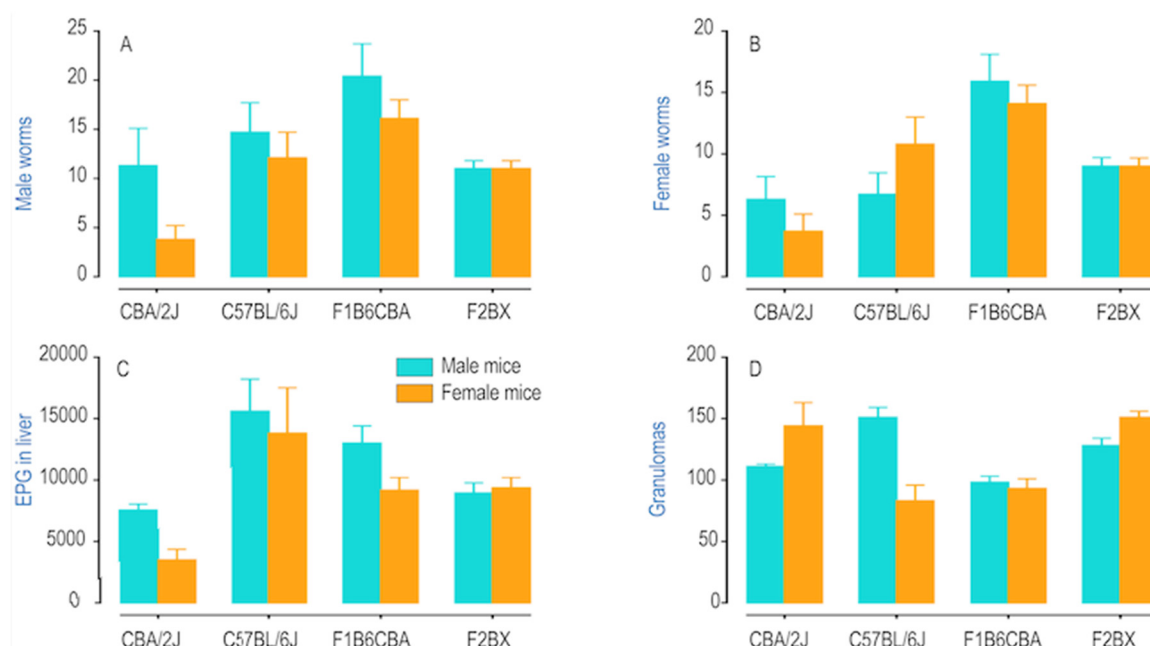


Figure S1. Representation of parasitological and pathological variables (A) number of recovered male worms, (B) number of recovered female worms, (C) eggs per gram of liver and (D) number of granulomas/cm² of liver surface between parental strains (CBA/2J, C57/2J) F1 progeny (F1B6CBA) and Backcross (F1BCX).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

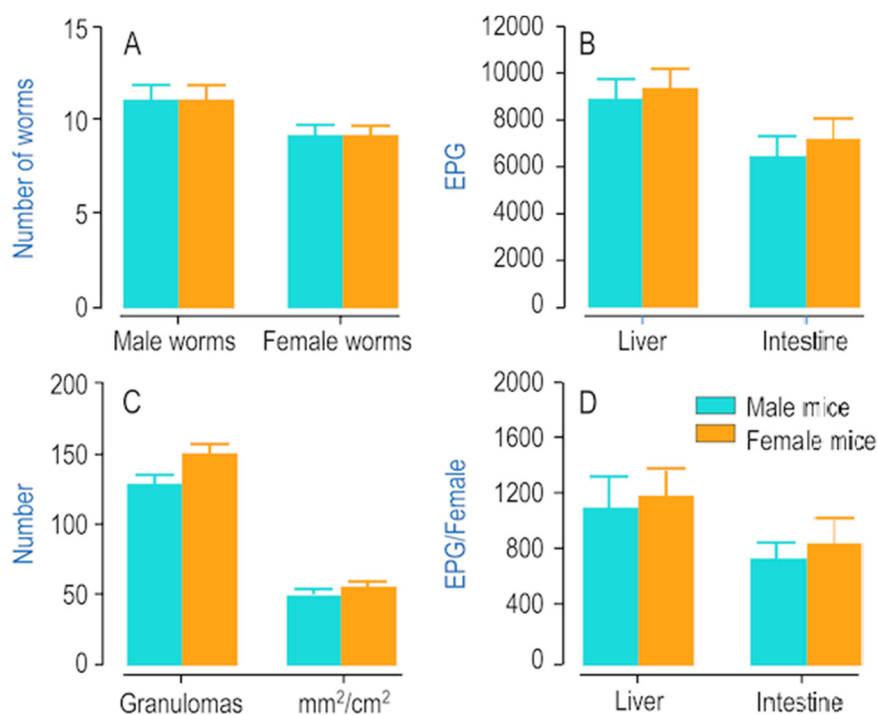


Figure S2. Comparison between BX male and female mice: (A) number of recovered male and female worms, (B) number of eggs per gram (EPG) of liver and small intestine, (C) number of granulomas and affected surface of the liver and (D) fecundity of female worms in liver and small intestine. The means and the standard error of the mean (SEM) were represented.

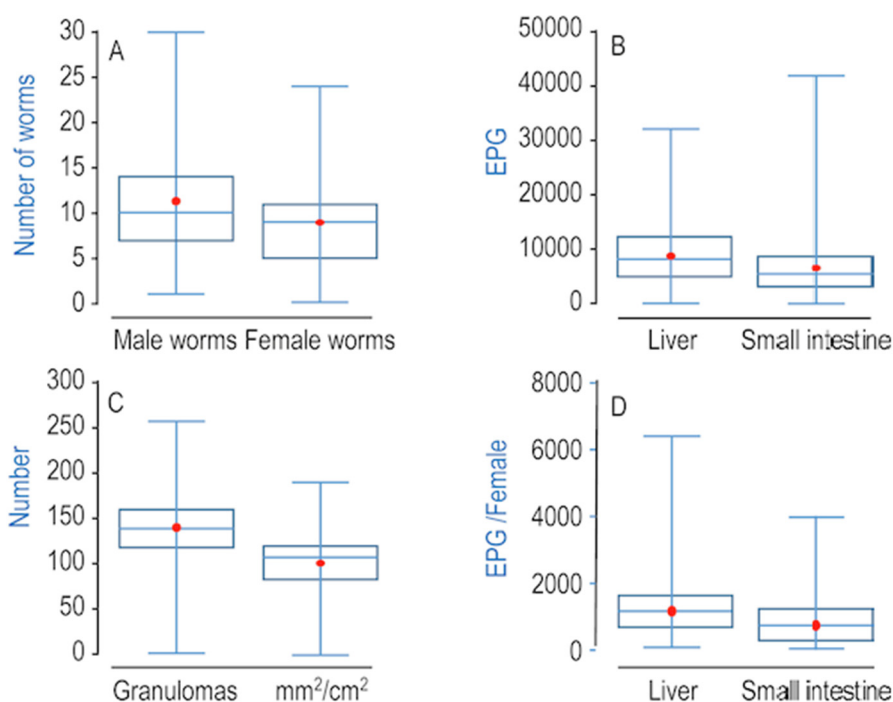


Figure S3. Box plot of BX male and female mice: (A) number of recovered male and female worms; (B) Number of eggs per gram (EPG) of liver and small intestine; (C) number of granulomas and (D) affected liver surface (mm²/cm²) of for the BX cohort. Box plot and the mean as a red circle.

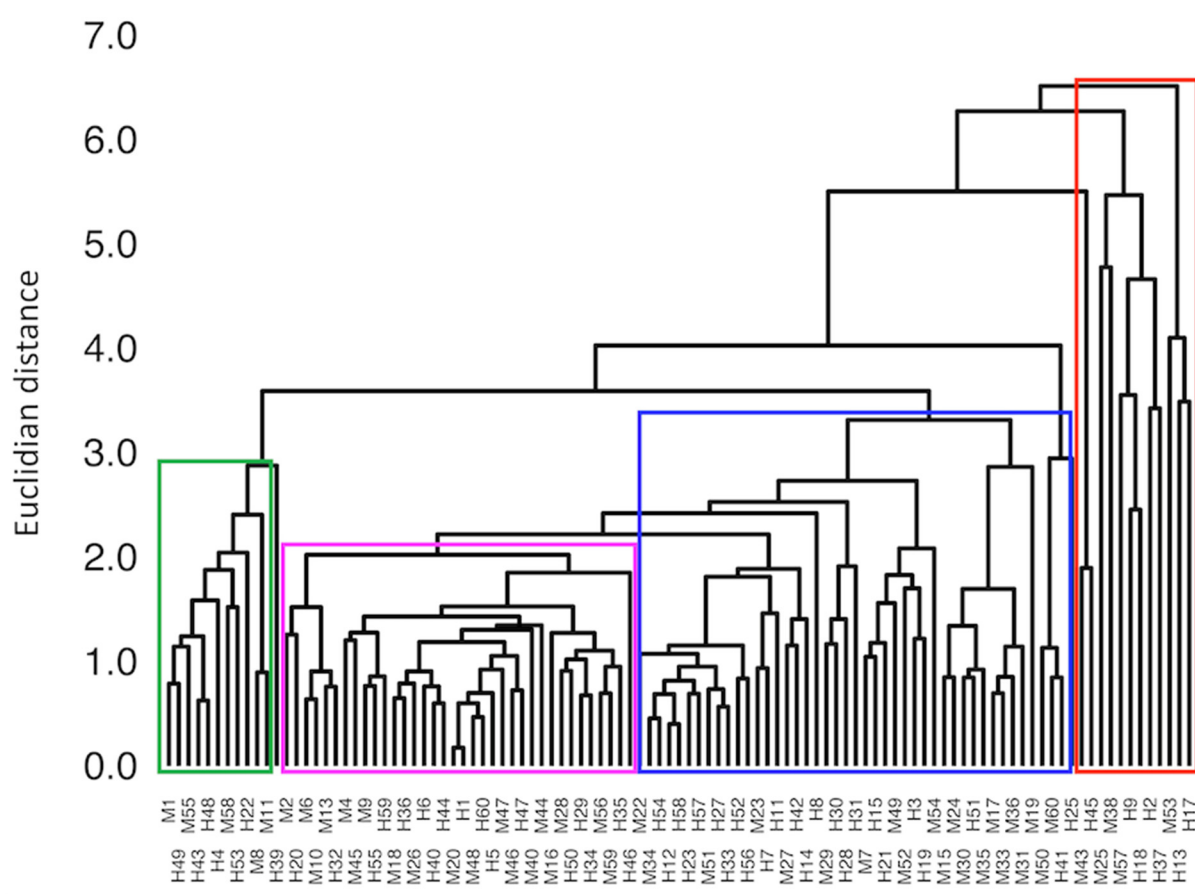
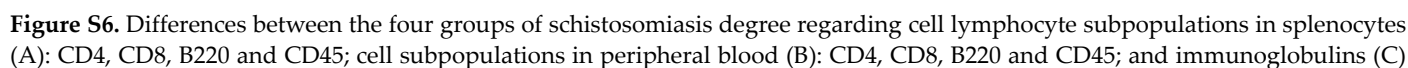
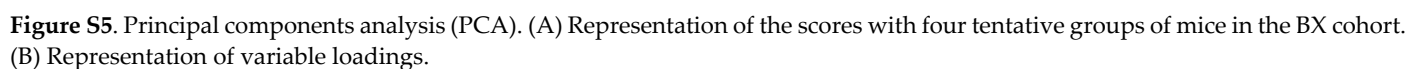


Figure S4. Dendrogram with all parasitological and pathological variables for schistosomiasis susceptibility: mild in green, mild-moderate in pink, moderate-severe in blue and severe in red.



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.

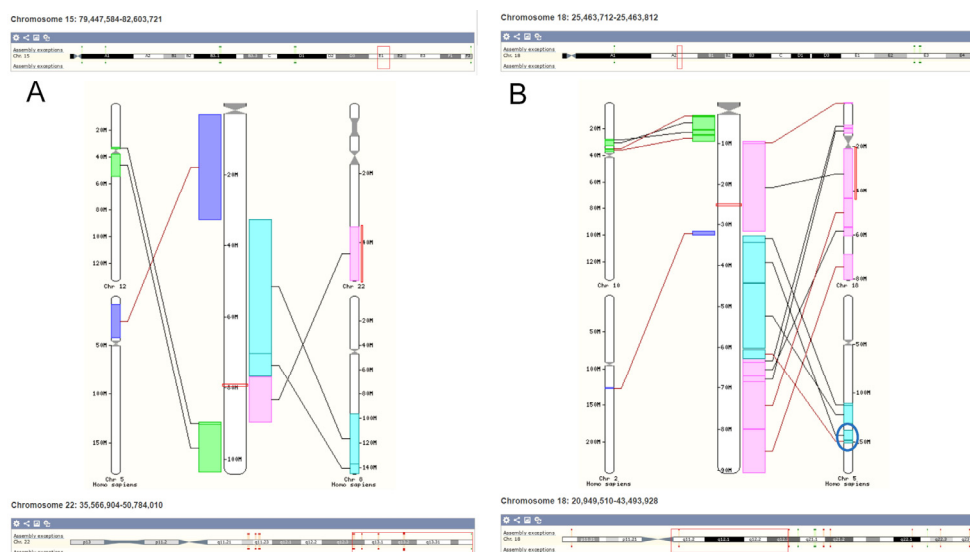


Figure S7. Syntenic regions in human beings from identified quantitative trait loci (QTL) in mice. A) The QTL1 on mouse chromosome 15 was mainly on human chromosome 8. B) The QTL2 on mouse chromosome 18 was mainly located on human chromosome 18.

Table S1. Quantitative trait loci (QTL), associated chromosome (Chr) and 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 parasitological and pathological phenotypes in the backcross cohort BX. (EPG- Eggs per gram).

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

EPG of gut/female	--	-	-	-	-					
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Table S2. Quantitative trait 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 0.029	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 trait 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 circulating 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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