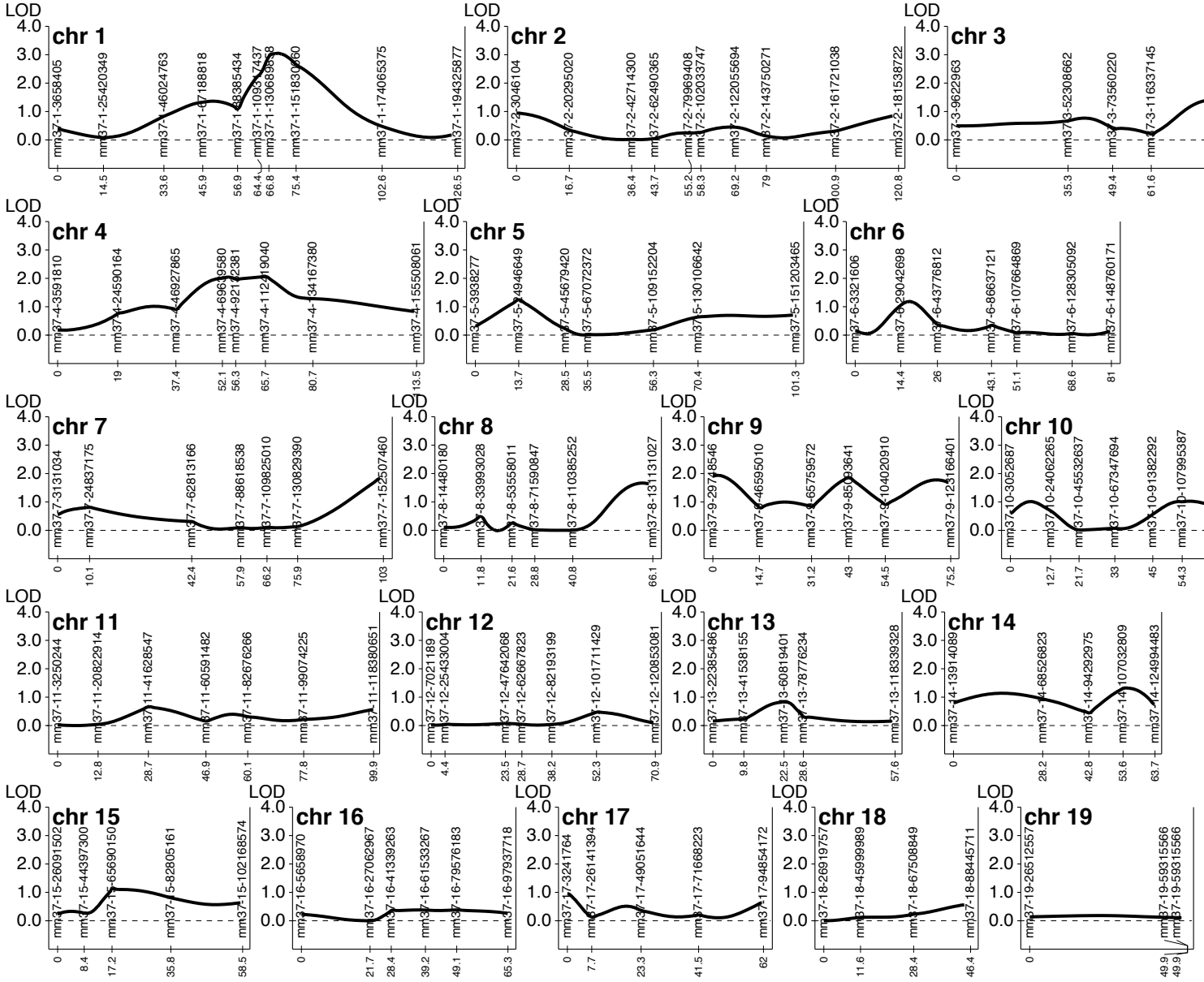
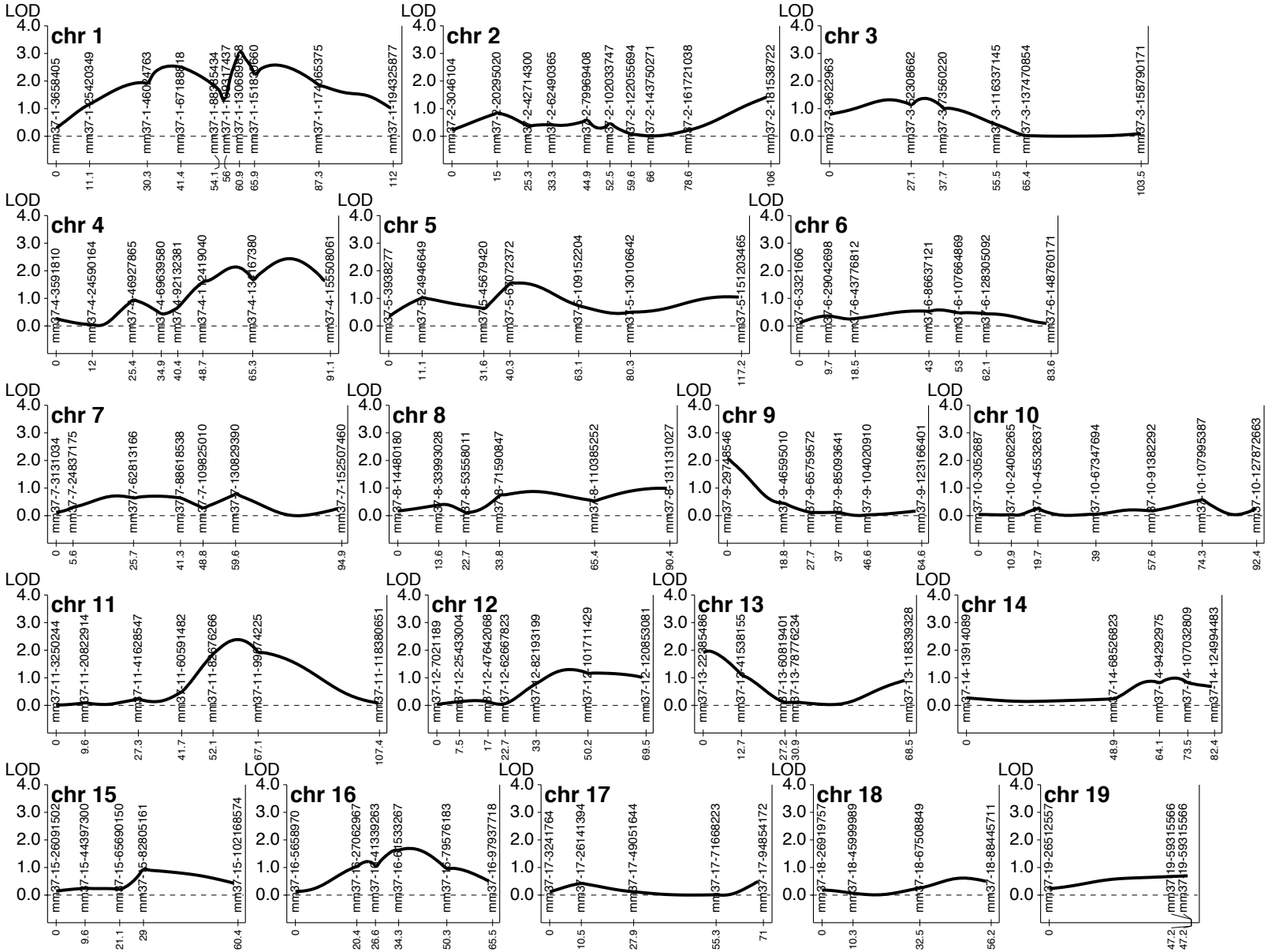
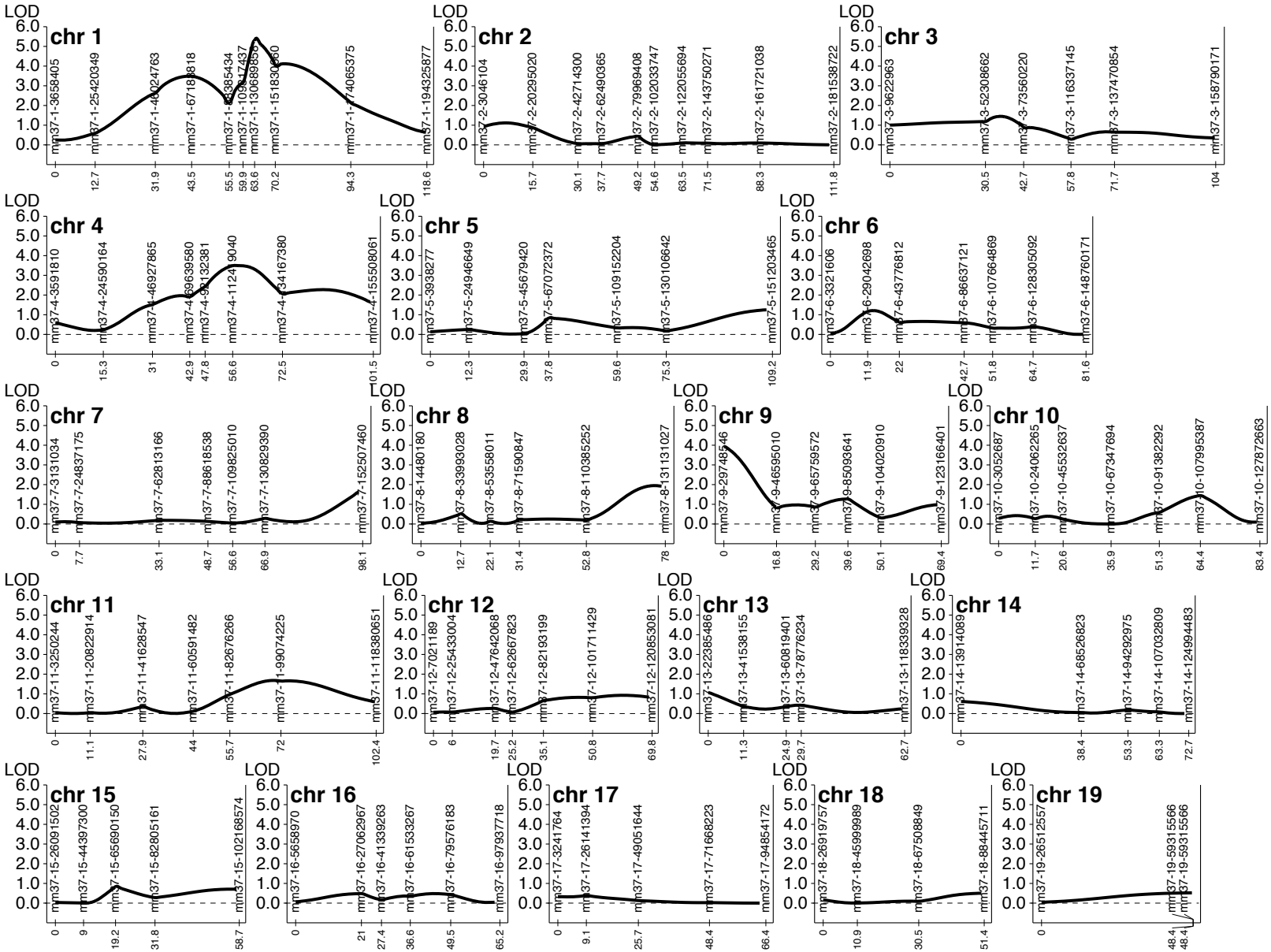


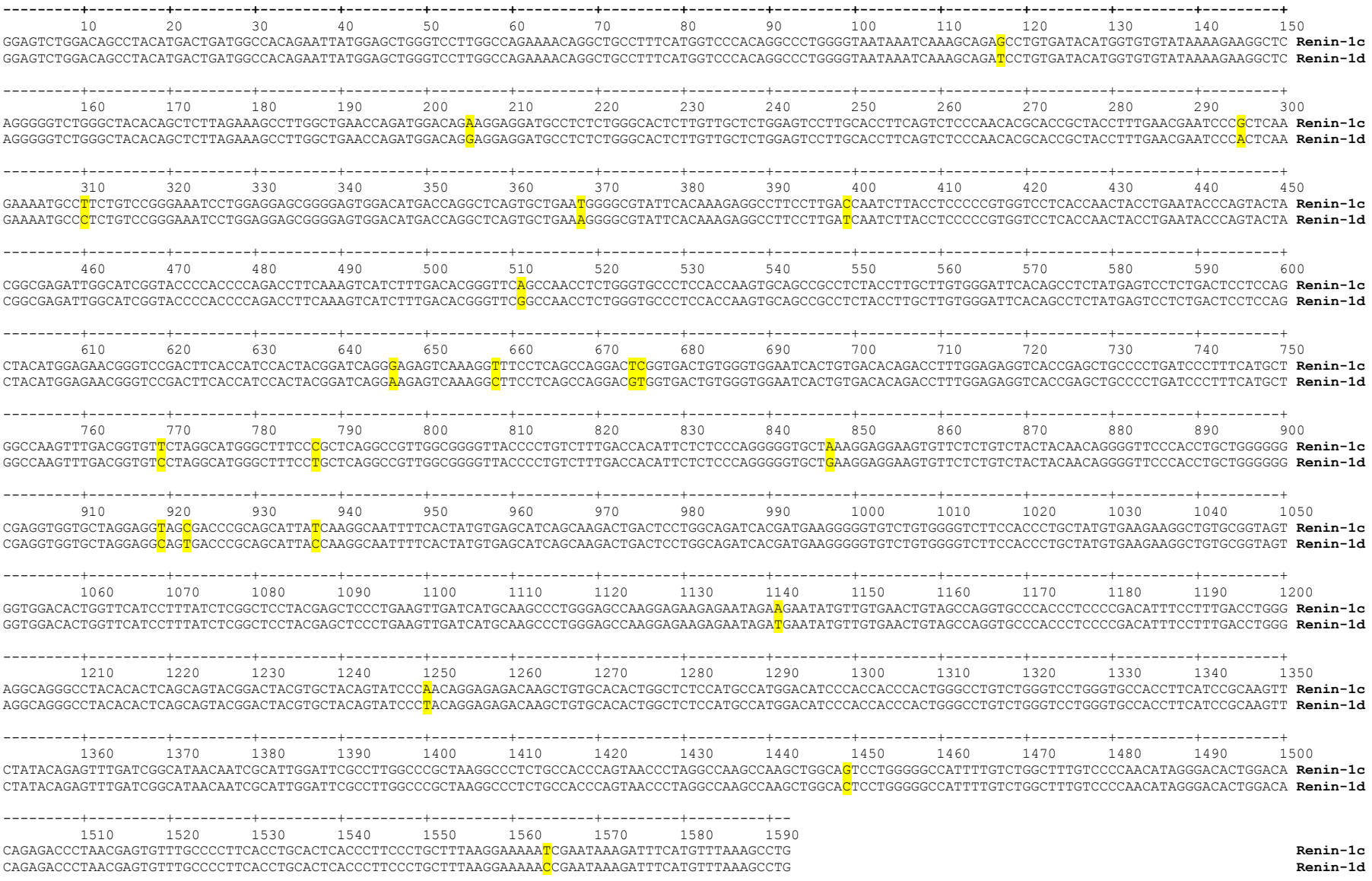
Supplemental Figure 1. Genome-wide linkage scan, using 120 single nucleotide polymorphism (SNP) markers, for blood pressure in 92 male sGC$\alpha_1^{-/-F2}$ (sGC$\alpha_1^{-/-S6}$ X sGC$\alpha_1^{-/-B6}$) progeny. Separate plots were generated for chromosome (chr) 1 through 19 with the SNP markers used to genotype the mice plotted on the X-axis. The Y-axis represents the LOD scores. One locus (on chromosome 1) showed suggestive linkage to blood pressure.



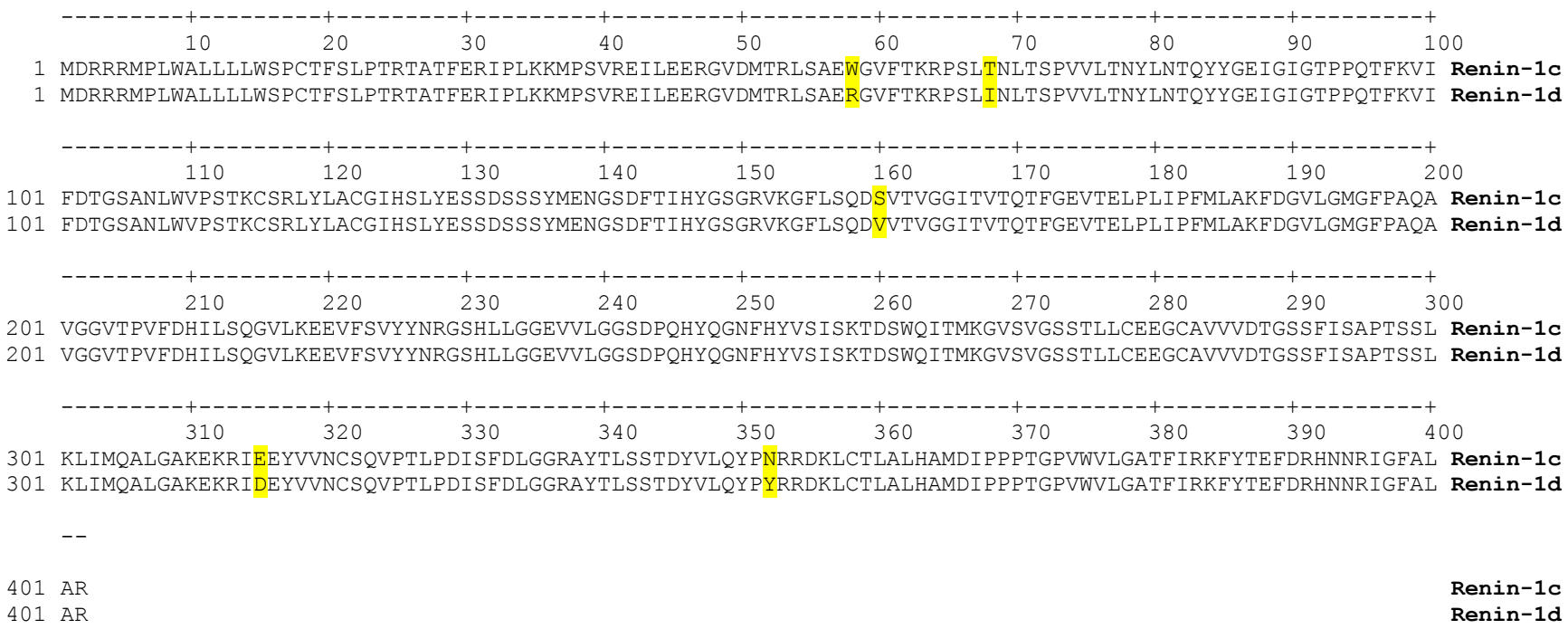
Supplemental Figure 2. Genome-wide linkage scan, using 120 single nucleotide polymorphism (SNP) markers, for blood pressure in a separate cohort of 96 male sGC$\alpha_1^{-/-F2}$ (sGC$\alpha_1^{-/-S6}$ X sGC$\alpha_1^{-/-B6}$) progeny. Separate plots were generated for chromosome (chr) 1 through 19 with the SNP markers used to genotype the mice plotted on the X-axis. The Y-axis represents the LOD scores. One locus (on chromosome 1) showed suggestive linkage to blood pressure.



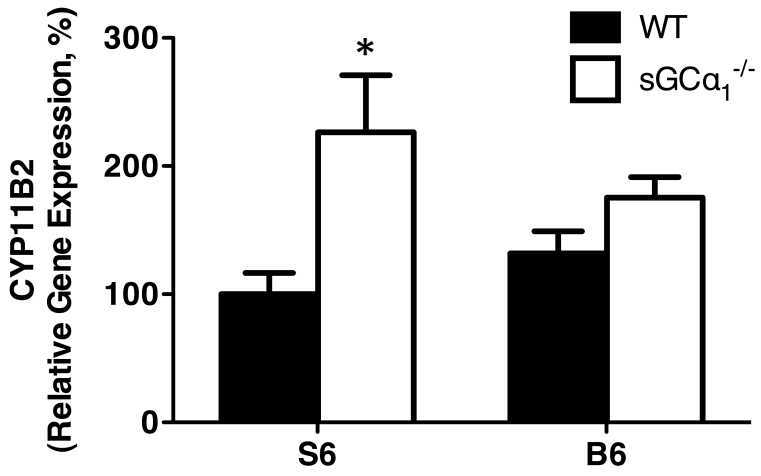
Supplemental Figure 3. Genome-wide linkage scan, using 120 single nucleotide polymorphism (SNP) markers, for blood pressure in 188 male $sGC\alpha_1^{-/-F2}$ ($sGC\alpha_1^{-/-S6}$ X $sGC\alpha_1^{-/-B6}$) progeny (the combined linkage analysis of all 92 and 96 $sGC\alpha_1^{-/-F2}$ mice in supplemental figures 1 and 2, respectively). Separate plots were generated for chromosome (chr) 1 through 19 with the SNP markers used to genotype the mice plotted on the X-axis. The Y-axis represents the LOD scores. One locus (on chromosome 1) showed significant linkage to blood pressure. Two loci (on chromosomes 4 and 9) showed suggestive linkage to blood pressure (LODs of 3.6 and 3.9, respectively).



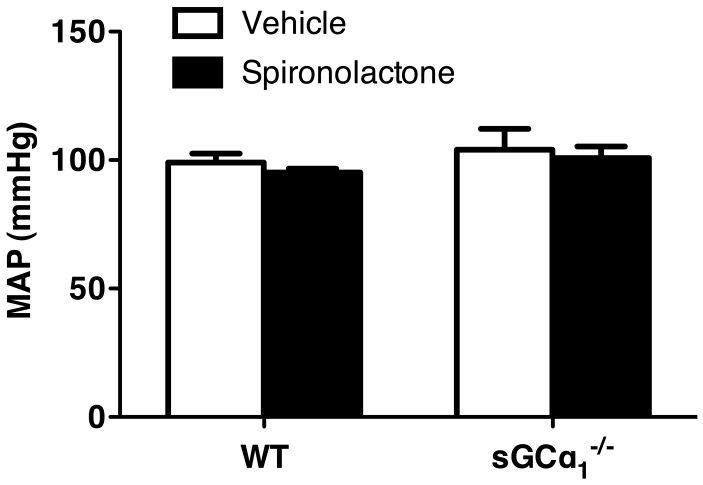
Supplemental Figure 4. Alignment of the cDNA sequences of renin1-d (the S6 allele, upper strand) and renin1-c (the B6 allele, lower strand). The 21 residues that differ between the 2 strains are highlighted in yellow.



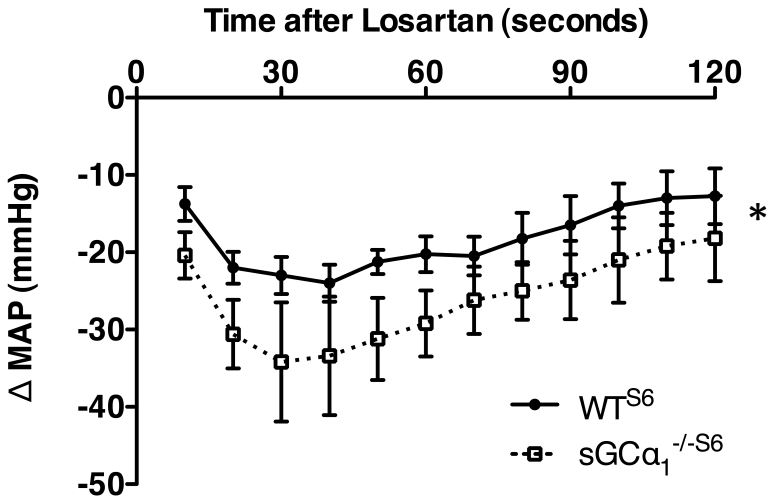
Supplemental Figure 5. Alignment of the amino acid sequences of renin1-d (the S6 allele, upper strand) and renin1-c (the B6 allele, lower strand). The 5 amino acids that differ between the 2 strains are highlighted in yellow.



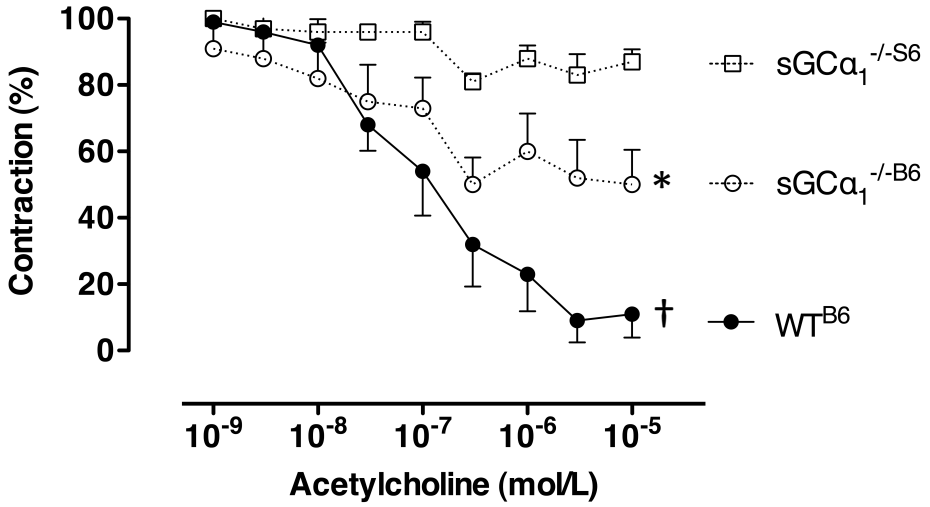
Supplemental Figure 6. **Adrenal CYP11B2 expression is higher in sGC$\alpha_1^{-/-S6}$ than in WT^{S6} mice .** mRNAs encoding the cytochrome P450, family 11, subfamily b, polypeptide 2 (CYP11B2 or aldosterone synthase) were measured via quantitative RT-PCR in adrenal glands of male WT and sGC$\alpha_1^{-/-}$ mice on the S6 or B6 genetic background. N=8-11/ group. Adrenal expression level of CYP11B2 was higher in sGC$\alpha_1^{-/-S6}$ than in WT^{S6} mice. *P<0.01 vs WT^{S6}.



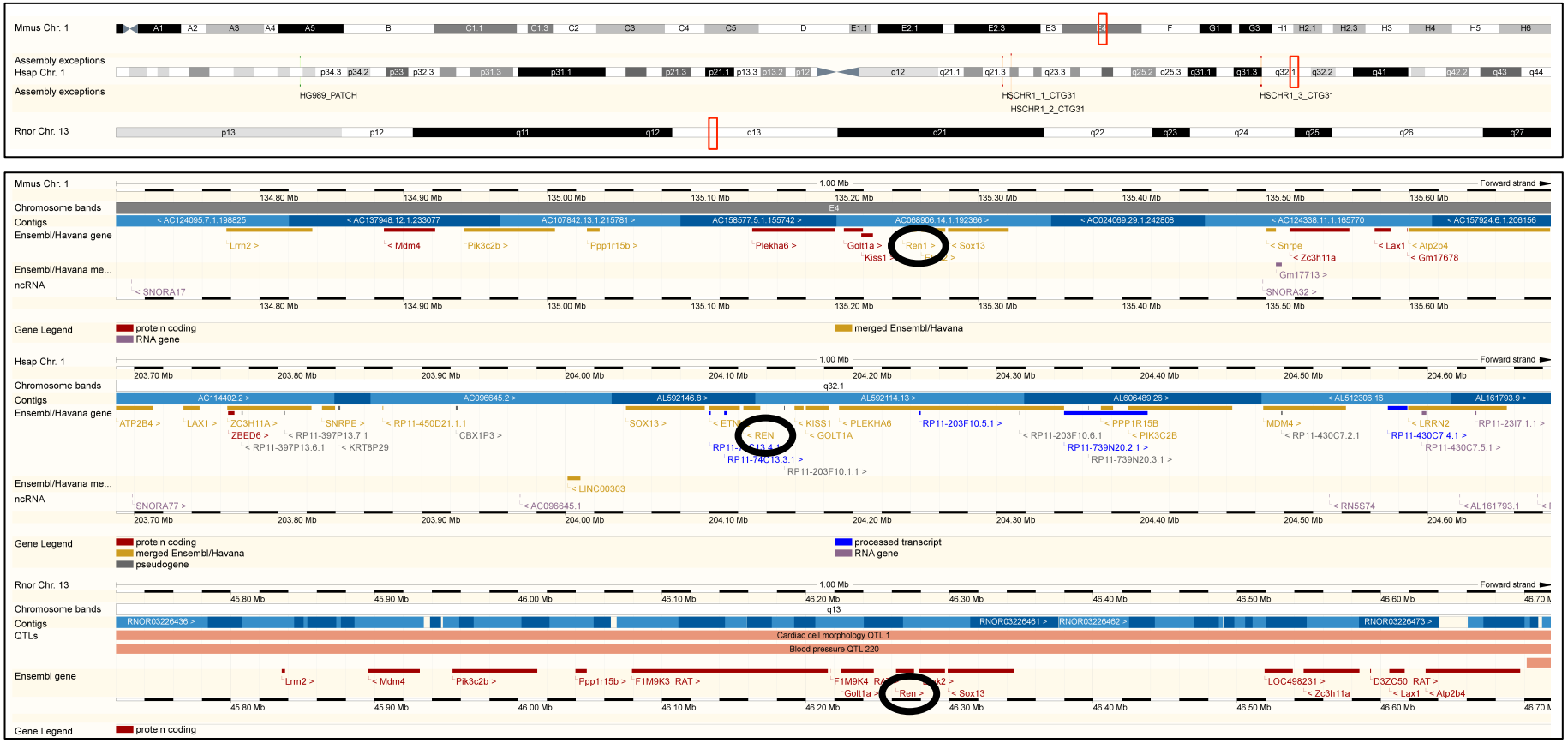
Supplemental Figure 7. **Spironolactone does not affect blood pressure in WT^{B6} or $sGC\alpha_1^{-/-B6}$ mice.** Mean arterial blood pressure (MAP) measured invasively in anesthetized male WT and $sGC\alpha_1^{-/-}$ mice on the B6 background, treated with vehicle (n=5 and 3, respectively) or spironolactone (n=5 and 6, respectively). P=NS for WT vehicle vs WT Spironolactone and for $sGC\alpha_1^{-/-}$ vehicle vs $sGC\alpha_1^{-/-}$ spironolactone (*t* test).



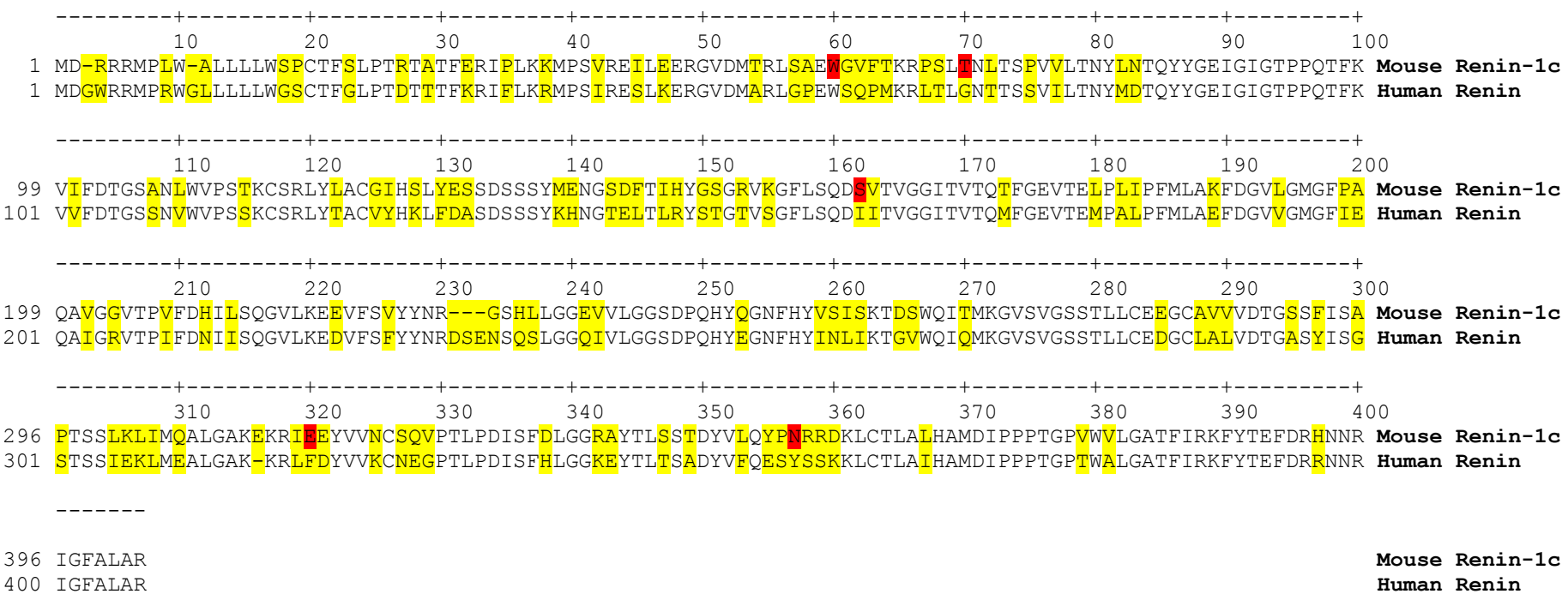
Supplemental Figure 8. **Losartan decreases blood pressure more in sGC$\alpha_1^{-/-S6}$ mice than in WT^{S6} mice.** Decrease in mean arterial blood pressure (MAP) measured invasively in anesthetized male WT and sGC$\alpha_1^{-/-}$ mice on the S6 background, treated intravenously with 0.1 mg/kg Losartan (n=4 and 5, respectively). Repeated measures Anova *P< 0.001.



***Supplemental Figure 9*. The strain-specific hypertension in sGC$\alpha_1^{-/-}$ mice is associated with greater impairment of vascular reactivity in sGC$\alpha_1^{-/-S6}$ mice than in sGC$\alpha_1^{-/-B6}$ mice.** Acetylcholine-induced relaxation was studied in phenylephrine-precontracted mesenteric arteries from male wild-type (WT, closed symbols, full line) and sGC$\alpha_1^{-/-}$ mice on the B6 (circles) or S6 (squares) genetic background. Acetylcholine-induced vascular relaxation was impaired to a greater extent in sGC$\alpha_1^{-/-S6}$ than in sGC$\alpha_1^{-/-B6}$ mice. N= 3, 5, and 6 for sGC$\alpha_1^{-/-S6}$, sGC$\alpha_1^{-/-B6}$, and WT^{B6}, respectively. *P<0.05 vs sGC$\alpha_1^{-/-S6}$, †P<0.05 vs sGC$\alpha_1^{-/-S6}$ and sGC$\alpha_1^{-/-B6}$.



Supplemental Figure 10. Schematic representation, generated via e!Ensembl of *Mus musculus* chromosome 1 (Mmus Chr.1), *Rattus norvegicus* chromosome 13 (Rnor Chr.13) , and *Homo sapiens* chromosome 1 (Hsap Chr.1). The red boxes in the top panel represent part of the syntenic region containing the renin locus and are magnified in the multi-species view in the bottom panel. Black ovals highlight the location of the renin gene in the murine, human, and rat genome.



Supplemental Figure 11. Alignment of the amino acid sequences of mouse renin1-c (the B6 allele, upper strand) and human renin-1 (lower strand). Amino acids that differ between murine renin1-c and human renin-1 are highlighted in yellow. The amino acids that differ between B6 and S6 (see ***Supplemental Figure 5***) are highlighted in red.