

SUPPLEMENTARY INFORMATION

Common variants in the *NLRP3* region contribute to Crohn's disease susceptibility

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SUPPLEMENTARY METHODS

Subjects. Five sample sets from four different centres, totaling 710 Crohn's disease trios, 239 Crohn's disease cases, and 107 controls, were assembled for this project (**Table 1**). All patients were recruited through specialized hospitals, academic centres, and practitioners. Inflammatory bowel disease (IBD) specialists involved in this study confirmed the diagnosis of Crohn's disease and patients were excluded from the study in the case of doubtful diagnosis. In all the participating centres, the diagnosis of IBD was made by IBD specialists after fulfilling standard clinical, radiological, endoscopic, and pathological criteria¹ that required (1) one or more of the following symptoms: diarrhea, rectal bleeding, abdominal pain, weight loss, fever or complicated perianal disease; (2) occurrence of symptoms on two or more occasions in the past or ongoing symptoms of at least 4-6 weeks' duration; (3) evidence of inflammation, strictures or fistula from radiological, endoscopic, and histological evaluation (with some specific Crohn's disease characteristics); (4) exclusion of all other diagnoses besides Crohn's disease. Informed consent was obtained from all participants, and protocols were approved by the local Institutional Review Board of all participating Institutions. Only subjects of European ancestry were used in the final analysis.

SNP selection for the exploratory and follow-up genotyping phases. We first investigated a 67.8kb region spanning 1q44 (243890897-243958709) (NCBI Build 35, hg17), including *NLRP3* (32.9kb). 43 tagging SNPs were selected using data from HapMap Public Release #22 ($r^2 \geq 0.8$) (minor allele frequency (MAF) ≥ 0.05) and 14 additional SNPs were selected from dbSNP Build126 in regions with lower coverage. Following the 9kb resequencing experiment, 13 SNPs located within *OR2B11* coding, conserved or predicted regulatory regions were prioritized (**Supplementary Table 3**). For the 58 SNPs not previously genotyped, we used a pairwise tagging approach² ($r^2 \geq$

0.8) to select tagging SNPs that best captured the variation in the region (**Supplementary Table 3**). A total of 24 SNPs were genotyped in the Leuven exploratory Crohn's disease trios, and 15 of them were analysed after excluding 4 rare SNPs (MAF<0.05), 2 with a low success rate (<95%), and 3 not in Hardy-Weinberg equilibrium ($p<0.01$).

Tissue collection. Animal: Male BALB/c mice (6-8 weeks) from Charles River Laboratory (St-Constant, Quebec, Canada) were maintained under conventional housing conditions. Acute colitis was induced by rectal instillation of 2.5mg of trinitrobenzene sulfonate (TNBS) (Sigma Aldrich Canada Ltd., Ontario, Canada) and mice were sacrificed on day 2 or day 4 (ref. 3). Chronic colitis was induced by a secondary instillation of TNBS on day 7 and mice were sacrificed 4 days later. All mice were handled according to institutionally recommended animal care guidelines and all experiments were approved by the Animal Studies Ethics Committee of McGill University. Human: Colonic or ileal biopsy specimens were obtained from Crohn's disease patients and from patients undergoing colorectal cancer screening (i.e. healthy controls). All participants gave informed consent and the study was approved by the Institutional Review Board.

Monocyte isolation and culture. Peripheral blood cells (PBCs) were isolated by density gradient centrifugation from healthy volunteers' whole blood. Collected cells were further purified by cold aggregation and rosetting with sheep's red blood cells. Monocyte-enriched PBCs were plated at a concentration of 3×10^6 cells/ml in serum-free RPMI 1640 (Invitrogen, Ontario, Canada), and non-adherent cells were removed after 1 hour of incubation at 37°C. Adherent cells were cultured for 3 hours in the presence or absence of lipopolysaccharide (LPS) (E.Coli, Sigma-Aldrich, 1µg/ml) in RPMI 1640 +10% fetal bovin serum (FBS) (Invitrogen). Upon harvest, culture supernatants were

collected for cytokine assessment, and monocytes were lysed in RLT buffer (Qiagen RNeasy Mini Kit).

REFERENCES

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2. de Bakker, P.I. *et al.* Efficiency and power in genetic association studies. *Nat. Genet.* **37**, 1217-1223 (2005).
3. Neurath, M.F., Fuss, I., Kelsall, B.L., Stüber, E. & Strober, W. Antibodies to interleukin 12 abrogate established experimental colitis in mice. *J. Exp. Med.* **182**, 1281-1290 (1995).

Supplementary Table 1: Primers and probes of the 3 genotyping panels used in the study

ID	Sequence	Panel ID
rs4925671-F	AGAGGGAGAGTAACTGCACCA	SNPstream exploratory panel
rs4925671-R	ATTTTAATTCATGAGCTACAATTCATG	SNPstream exploratory panel
rs4925671-GA-U1	CAGCACTATTACCATCACGTGGTGCTGCTATTCACAGTGGTTCCC	SNPstream exploratory panel
rs10157379-F	AGAGTCCTTGGCAATGGC	SNPstream exploratory panel
rs10157379-R	TTAATTGGGAAGATAGAAACCAGT	SNPstream exploratory panel
rs10157379-GA-U2	CTCAGACTACGAATCCACGTGTTTTTTAAGCTCTTTGGTGTCTAC	SNPstream exploratory panel
rs12133212-F	TTAAACATTTTGTCTTTGCTCT	SNPstream exploratory panel
rs12133212-GA-R	ATCACAATAAAAGCAGCACAAA	SNPstream exploratory panel
rs12133212-GA-U3	CAGCCATCCATTCATCTATGTTCTCCACCACACTGAATGACG	SNPstream exploratory panel
rs9988572-F	AACTGGTGGGTGCTCATTC	SNPstream exploratory panel
rs9988572-R	TACAAAGGGGTTTGAGGACA	SNPstream exploratory panel
rs9988572-GA-U4	ATCTAACGCACCTACGACCTTACTTCCCTTCTCCTCTCAATGCTA	SNPstream exploratory panel
rs10925019-F	CCAACTTCAAGCAAATGGAC	SNPstream exploratory panel
rs10925019-R	TAGTGCCATGGAGACTGGTT	SNPstream exploratory panel
rs10925019-GA-U5	CAACAAGTAATCCGCAGACTTTTGGGCATGAAGTTGGAGAAATAA	SNPstream exploratory panel
rs10925027-F	CTCCACGATTTTCAATCTCC	SNPstream exploratory panel
rs10925027-R	TGGCAAATGATTCCATTGTA	SNPstream exploratory panel
rs10925027-GA-U6	ACAACTCACGCAAGTACCATTTTTCAATCTCCTATCCTATCAAAG	SNPstream exploratory panel
rs10733113-F	CAGAACAATGAGTGGCACAG	SNPstream exploratory panel
rs10733113-R	ACTACTTCTTGCGGCCTGTC	SNPstream exploratory panel
rs10733113-GA-U7	TACAAGCACGCACTAGACATGCTTTTTGTTGTTGTTGTTGTTGAT	SNPstream exploratory panel
rs6698597-F	CAAACACTCTGACGGTGATG	SNPstream exploratory panel
rs6698597-R	TGTGTCTTTGCTCTCCTTCC	SNPstream exploratory panel
rs6698597-GA-U8	AGACTTCTACGCAAGCACTGTTCTCACATACTTAATGTCTCTATC	SNPstream exploratory panel
rs10733112-F	TCTCCACAAATTTTACACGACTT	SNPstream exploratory panel
rs10733112-R	AGGATCCACAATGTTTTCCA	SNPstream exploratory panel
rs10733112-GA-U9	CCGCCAGTAAGACCTAGACGCCACAAATTTTACACGACTTTTTCA	SNPstream exploratory panel

rs2027432_F	ATGGAGACTCAGGTCTGCTG	SNPstream exploratory panel
rs2027432_R	CGTGAGGCCTTTAAAACAGA	SNPstream exploratory panel
rs2027432_GA-U10	TCCAGAATAGACAACAGACGCTCTGCAGTTCTGTAGAAAGGTGGT	SNPstream exploratory panel
rs10737805-F	TTTCTTTTTATCTGAGTTTGTCGC	SNPstream exploratory panel
rs10737805-R	TTCTCTGTGAGATGAAAGAATTTACA	SNPstream exploratory panel
rs10737805-GA-U11	AGCAAGACCACCTAGACCAGCATCATTTCATCTCCTTTGCATCAG	SNPstream exploratory panel
rs10802510-F	TGATATTACCCATTTCTTTGCAT	SNPstream exploratory panel
rs10802510-R	TGCTAATTGAATCATTCCACA	SNPstream exploratory panel
rs10802510-GA-U12	CCAGATCCTCACCATGTAAGACTACATATTTATGAATTACAATGC	SNPstream exploratory panel
rs10754561-F	ATTTAATCACATGAATTGTAGCTCAT	SNPstream exploratory panel
rs10754561-R	TTCTCAGTTGTTTGGCTTAA	SNPstream exploratory panel
rs10754561-GA-U13	CAACAATACGAGCCAGCAAGCTACAAGAATTCTATTTGGCCATAA	SNPstream exploratory panel
rs4925650_F	GGAGAATTGCTTGAACATGG	SNPstream exploratory panel
rs4925650_R	TTTGCCTCCACCTTCTCATA	SNPstream exploratory panel
rs4925650-GA-U14	AACATACAGACGCACTCCTCGGTTTTTYCTCTTTTCCCCTCTCAC	SNPstream exploratory panel
rs947181-F	GGTGGGGTTAGGTTTTAGGT	SNPstream exploratory panel
rs947181-R	CAGCCATAAAAGACCTCTG	SNPstream exploratory panel
rs947181-GA-U15	ACAATCAACATACGAACAGCTTACTCAGGTGGCTGAAGTGGGTGC	SNPstream exploratory panel
rs3806265-F	GGAGCATTTCTGCACTCCTA	SNPstream exploratory panel
rs3806265-R	TGTTTGCTGATTGATTTCCA	SNPstream exploratory panel
rs3806265-GA-U16	ATACCTACCACGCTACAGCCTTTCTGCACTCCTAGTTTCAAACA	SNPstream exploratory panel
rs12089794-F	TCCAGCTTGGGTTTCATC	SNPstream exploratory panel
rs12089794-R	CAAGATCATGCCACAGCA	SNPstream exploratory panel
rs12089794-GA-U17	GCAGACAACGAACAACACTACCAAAAATTCATCTAGTTCCACCTCA	SNPstream exploratory panel
rs10925039-F	GGATGCAGAGGATGGAGTAA	SNPstream exploratory panel
rs10925039-R	ACAGGCCGCAAGAAGTAGT	SNPstream exploratory panel
rs10925039-GA-U18	AACATCCACGCAACTCATACTGGGGTAAAATGTACGTTATTCGG	SNPstream exploratory panel
rs4925654-F	TAAGGATAGGGACAGAAAGGAAG	SNPstream exploratory panel
rs4925654-R	AACAAAACTATACTTTATCCCTGTCA	SNPstream exploratory panel
rs4925654-GA-U19	CCACTCAACTCCACGAATACTAACAGGCTCCAGGACCTATGAACT	SNPstream exploratory panel

rs955328-F	AGGGACATTTGAGAGCAGTC	SNPstream exploratory panel
rs955328-R	CGTACAGTGTGTGTCCCTTG	SNPstream exploratory panel
rs955328-GA-U20	ACAACACTACCGACGACAAGACAACCCTGAGGACATTTGCTGAGTGC	SNPstream exploratory panel
rs12745508-F	TTAATTCTGGCTGAGTTCCCT	SNPstream exploratory panel
rs12745508-R	ATTGTGGTGGGATCACAGC	SNPstream exploratory panel
rs12745508-GA-U21	GATCCATCAACAGACATCACTCCTCATTCACTCTAGTTCAGCACC	SNPstream exploratory panel
rs4266924-F	GGGAGAAAAGGGAGAAGTTG	SNPstream exploratory panel
rs4266924-R	TGCTGCCGTGTAACCTAAGGT	SNPstream exploratory panel
rs4266924-GA-U22	GCAACATAAGACCGCTCAACGCCTTAATATCTCAGCAAGGTCCAT	SNPstream exploratory panel
rs12564791-F	AACATTCATTCAAGTGCCTGC	SNPstream exploratory panel
rs12564791-R	TAGACCATCAGCTCCCCG	SNPstream exploratory panel
rs12564791-GA-U23	AGTAGCCTAACAGCACTCGAATGTCTGTCCAGGCGTGGCAAAGAT	SNPstream exploratory panel
rs3806268-F	ATGATGAGCATTCTGAGCCT	SNPstream exploratory panel
rs3806268-R	ATATAGAACAGATAGTCAAACCTGTCTTG	SNPstream exploratory panel
rs3806268-GA-U24	CAACAAGACATAACAACGCACCAGGAAGATGATGTTGGACTGGGC	SNPstream exploratory panel
rs10754557-F	AAATCAGAAGTGTACATAGAGCTTGT	SNPstream exploratory panel
rs10754557-R	CAACCTTCCATAGAGATGGC	SNPstream exploratory panel
rs10754557-GA-U25	CCATAACAACCTACCAGCCAGCTTCCTTGTCCATGGTGGAGCGTG	SNPstream exploratory panel
rs7525979-F	ACATCATCTTCCTGGCCA	SNPstream exploratory panel
rs7525979-R	ATTAAGATGGAGTTGCTGTTTGA	SNPstream exploratory panel
rs7525979-GA-U26	AGACCGACAAGCAATCTACATCCCTGCCGCCCCCTGGAACACCAC	SNPstream exploratory panel
rs4317844-F	AGAACCTGGGGGTACAAAAG	SNPstream exploratory panel
rs4317844-R	CAGTTCCAGACTCTCGCTGT	SNPstream exploratory panel
rs4317844-GA-U27	GCAAGCCATCAGCTAATACAGGGGTACAAAAGGCATCGTGAACCT	SNPstream exploratory panel
rs12565738-F	GAGCAACTTGGAGGAAGTGA	SNPstream exploratory panel
rs12565738-R	AATTCTGTGTCTCCGTGCTT	SNPstream exploratory panel
rs12565738-GA-U28	CACTACATACGACCGCAGAAAGAATCAGGTTTCGGGTAGAAGAGA	SNPstream exploratory panel
rs10159239-F	GAGGAAAGCTGTGTGAGGAG	SNPstream exploratory panel
rs10159239-R	TGTCACAGGAGACACAAATGAT	SNPstream exploratory panel
rs10159239-GA-U29	AATAAGCTCACACCGTCAATCAGTTTGCCTTGGCTCTTTCTGTC	SNPstream exploratory panel

rs10732301-F	ATTTTACACTTGCTGCTTAATACGT	SNPstream exploratory panel
rs10732301-R	GCAGGATGGGCAGTATTAAC	SNPstream exploratory panel
rs10732301-GA-U30	CAGTCAACAATCCAGATCAACATCGACCCATCCATCCTCCACCTC	SNPstream exploratory panel
rs12070953-F	TTTATTTCTCTTCTATTCCATAATCAC	SNPstream exploratory panel
rs12070953-R	TACATCTCATGTCCTCATCATCC	SNPstream exploratory panel
rs12070953-GA-U31	CAGAACATCCTCAGAAGCAATTCACTACACCCTGAGAAATAAAG	SNPstream exploratory panel
rs12086048-F	TGCTCAGGATCCAGTCCTC	SNPstream exploratory panel
rs12086048-R	ATGTAAATCGCAGGTAGGTAGAAG	SNPstream exploratory panel
rs12086048-GA-U32	CAAGCAACGACCTACTACAAAGGGACGACACAAGGCCTTTGGGAC	SNPstream exploratory panel
rs12048215-F	AGGGTATTGCAGGATGATGA	SNPstream exploratory panel
rs12048215-R	CTGCACACTGCTGTCTGTTT	SNPstream exploratory panel
rs12048215-GA-U33	CGCAGAAGCAACTCACTTCTAAGGCAGGGCAGCAGTGTGGGTGTA	SNPstream exploratory panel
rs10399895-F	AAGTAGAAGGGTGGGGAGGT	SNPstream exploratory panel
rs10399895-R	GGCACATCCTGAATCAGTTC	SNPstream exploratory panel
rs10399895-GA-U34	CACTAGTCATAACGCAGCCTAAGGGTGGGGAGGTGGAGGTTGAAG	SNPstream exploratory panel
rs4925663-F	CCTTCTTCGTGTTGGTGC	SNPstream exploratory panel
rs4925663-R	TCCCTTGGAGGACTGGAT	SNPstream exploratory panel
rs4925663-GA-U35	CAGAATAGCCACGCCTAGATCTGGCTCTCATCCTTCTCTCCTATG	SNPstream exploratory panel
rs1106719-F	GCAGCTACAGTCAGTGGACAT	SNPstream exploratory panel
rs1106719-R	ACACCAAGCAGAGCAAGTCT	SNPstream exploratory panel
rs1106719-GA-U36	CACCGCTATCAACAGACTTGTTCCAGGCATTCTAGAATGAGAAAA	SNPstream exploratory panel
rs10925022-F	GATGCTTCCTCTGTTCTGGA	SNPstream exploratory panel
rs10925022-R	CTGGTTGCTGCTGAGGAC	SNPstream exploratory panel
rs10925022-GA-U37	ACCGCACTAAGCAATGTATCCTCTGTTCTGGAGCTCTCTGGTCAG	SNPstream exploratory panel
rs3738447-F	GCTTCCAGGTGCTTCCTC	SNPstream exploratory panel
rs3738447-R	ATACATCAATCTTTGCTCATGAAG	SNPstream exploratory panel
rs3738447-GA-U38	ACGTAAGACCACTCAAGACCGCTTCCTCGCCAGCTTCTTCTTGGC	SNPstream exploratory panel
rs12137901-F	AATAGAAGGAGAAGGCCAGG	SNPstream exploratory panel
rs12137901-R	TTCATCTCACTTCAATCCACTG	SNPstream exploratory panel
rs12137901-GA-U39	CACGACAAGACAACAGATACGGTGAGTAAGTGTGTTGATAACAGA	SNPstream exploratory panel

rs6673762_F	TGGCACTTTGTTACAGCAGA	SNPstream exploratory panel
rs6673762_R	TCATCATGTTGTCCAGGCTA	SNPstream exploratory panel
rs6673762-GA-U40	AAGTACCACGTCAACGTCACAGCATTGTTGGGAGGCCGAGGCGGGC	SNPstream exploratory panel
rs10925014-F	GGCATGGATTTTTACTGCAT	SNPstream exploratory panel
rs10925014-R	AGCTCATTGGCTGAACCTG	SNPstream exploratory panel
rs10925014-GA-U41	TACCTATGACCAGCAAGCACACTCCTGGGCTCAAGCTATCCTCCC	SNPstream exploratory panel
rs6677787-F	AGAAGGCAGACCATGTGG	SNPstream exploratory panel
rs6677787-R	ATCTCTTTTTGCTTTCTCATAAAGG	SNPstream exploratory panel
rs6677787-GA-U42	CTCACTATCTGACAAGCCACTGGGGAGGAGAAGGCGTGGGCCATG	SNPstream exploratory panel
rs12239046-F	AGTCGTGAAATCCCCAGAC	SNPstream exploratory panel
rs12239046-R	TCCTCTTTGGAAGCCTTCTT	SNPstream exploratory panel
rs12239046-GA-U44	CAAGACCGCAACTAGATACAGGGAGGGGGAAGCTATAACATTAGC	SNPstream exploratory panel
rs4378247-F	GAGCACCTCCAATGACAGAG	SNPstream exploratory panel
rs4378247-R	GAACCACATTGGGCACTTAG	SNPstream exploratory panel
rs4378247-GA-U43	AGCCGAACTACCACTGAGTACACGGCTCCCAATAAAAATGTGGGG	SNPstream exploratory panel
rs4925546-F	GTATCACCAAATAAGGTCACAATCT	SNPstream exploratory panel
rs4925546-R	TTTATATTATGGTTCTAGTTTCAATAGATAGG	SNPstream exploratory panel
rs4925546-GA-U45	CTAACTAAGCTACGCCGACACTAGGACTTCCACATATAAAGTCTT	SNPstream exploratory panel
rs12128790_F	CCTGATAAGGGGTAAACACTCA	SNPstream exploratory panel
rs12128790_R	TTTGCATTTCCCTGATGACT	SNPstream exploratory panel
rs12128790-GA-U46	ACAGATCACTACCGACTAAACTCTTACAACCTCAAACTAAGAGA	SNPstream exploratory panel
rs6700719-F	AAGCTATACAGTGGTGAAATCCTAGT	SNPstream exploratory panel
rs6700719-R	ATTTCAACAGAATCAGATAACTGGA	SNPstream exploratory panel
rs6700719-GA-U47	ACAAGAACTCCATGACTCAACATGGCAGTGATTTTCAGTGTGAAAC	SNPstream exploratory panel
rs4356092-F	AAATGTTTTTCATTTGTTCCACAT	SNPstream exploratory panel
rs4356092-R	AGTTTTTTCAGCCTTAAGAAATTATG	SNPstream exploratory panel
rs4356092-GA-U48	CGATCACCTCACTAGAACAAGAACTTTTAATCTCACCCAGGGGA	SNPstream exploratory panel
rs10157379_F	ACGTTGGATGTGCTGGTCATCTGTTTCATGC	Sequenom exploratory panel
rs10157379_R	ACGTTGGATGTGCCAGAGTCCTTGGCAATG	Sequenom exploratory panel
rs10157379_F_CT	GTATTTCTATTTTTCCCTGCCT	Sequenom exploratory panel

rs10399895_F	ACGTTGGATGTACAAGTGCAGGTTTCTGAAAAG	Sequenom exploratory panel
rs10399895_R	ACGTTGGATGACGCAGAGTGGAGGAATAGATA	Sequenom exploratory panel
rs10399895_F_CT	TCGTACCCAACAGGTAAT	Sequenom exploratory panel
rs10732301_F	ACGTTGGATGCTTAATACGTGGCCATTGCT	Sequenom exploratory panel
rs10732301_R	ACGTTGGATGAACCCTGGAGGTGAGTGATT	Sequenom exploratory panel
rs10732301_F_AG	ATCCATCCTCCACCTC	Sequenom exploratory panel
rs10737805_F	ACGTTGGATGTGTGATCTTCATTTCTGGAGACT	Sequenom exploratory panel
rs10737805_R	ACGTTGGATGTTGTCTATCACATGTAAGGGTCTG	Sequenom exploratory panel
rs10737805_R_CT	GGGTTGGACGACACAGGCAA	Sequenom exploratory panel
rs10754555_F	ACGTTGGATGGAAACAGACAGCAGTGTGCA	Sequenom exploratory panel
rs10754555_R	ACGTTGGATGTAAGTACTGACACAATGATAATTGC	Sequenom exploratory panel
rs10754555_F_CG	GATGGGAGGTCAGAAACCA	Sequenom exploratory panel
rs10754558_F	ACGTTGGATGAGCTTGGGCATCTCCTTTAC	Sequenom exploratory panel
rs10754558_R	ACGTTGGATGGAACATCCTCTAACTGAGGC	Sequenom exploratory panel
rs10754558_F_CG	ACAATGACAGCATCGGGTGTTGTT	Sequenom exploratory panel
rs10802496_F	ACGTTGGATGAGTCAAGCCATGTATGCCTCA	Sequenom exploratory panel
rs10802496_R	ACGTTGGATGGGTTTCACCATATTGGTCAGG	Sequenom exploratory panel
rs10802496_F_AT	TACTATTGGCTGGGCG	Sequenom exploratory panel
rs10802510_F	ACGTTGGATGATTTGAGGTGATGGATATGCT	Sequenom exploratory panel
rs10802510_R	ACGTTGGATGTAAATACTGTAACATTTTTAAAGTTCCA	Sequenom exploratory panel
rs10802510_F_CT	ACAATGTATACACATATATCAAAATAT	Sequenom exploratory panel
rs10925014_F	ACGTTGGATGATAAAGGCATGGATTTTTACTGC	Sequenom exploratory panel
rs10925014_R	ACGTTGGATGCTGTAATCCCAGCTCTCAGG	Sequenom exploratory panel
rs10925014_R_CT	AAAATCAGGGAGGCAAGAGG	Sequenom exploratory panel
rs10925019_F	ACGTTGGATGCCATGGAGACTGGTTGTTTG	Sequenom exploratory panel
rs10925019_R	ACGTTGGATGGCCTCTCCAGAATCATACAG	Sequenom exploratory panel
rs10925019_F_CT	TGGTTGTTTGGGACATTTAAC	Sequenom exploratory panel
rs10925026_F	ACGTTGGATGGATCACAACCTCAAGATGGG	Sequenom exploratory panel
rs10925026_R	ACGTTGGATGTCCATCTAAGAAGCTCCTAC	Sequenom exploratory panel
rs10925026_R_GT	CCTCAAGATGGGAATGTTA	Sequenom exploratory panel

rs10925039_F	ACGTTGGATGCGCAAGAAGTAGTGACATT	Sequenom exploratory panel
rs10925039_R	ACGTTGGATGAGGGAGGAGAAATTACGTGG	Sequenom exploratory panel
rs10925039_F_CT	TGGGCATTTAGCGTAACTATCA	Sequenom exploratory panel
rs12048215_F	ACGTTGGATGGGGAAGGAGGAGTACAAATG	Sequenom exploratory panel
rs12048215_R	ACGTTGGATGTGGTTTCTGACCTCCCCCG	Sequenom exploratory panel
rs12048215_F_AG	GCAGCAGTGTGGGTGTA	Sequenom exploratory panel
rs12062001_F	ACGTTGGATGGTGACAGAGCGAGATTCCAT	Sequenom exploratory panel
rs12062001_R	ACGTTGGATGACAGAGCAGGGAATGAAACA	Sequenom exploratory panel
rs12062001_R_AT	GAGAAAGCAAGCACATTT	Sequenom exploratory panel
rs12070953_F	ACGTTGGATGCATGTCCTCATCATCCACAG	Sequenom exploratory panel
rs12070953_R	ACGTTGGATGAATCACCCCCACTCTCAATC	Sequenom exploratory panel
rs12070953_F_CT	CAGAGCCCCCTTCATA	Sequenom exploratory panel
rs12089794_F	ACGTTGGATGATTCCAGCTTGGGTTTCATC	Sequenom exploratory panel
rs12089794_R	ACGTTGGATGAAGATCATGCCACAGCACTC	Sequenom exploratory panel
rs12089794_F_AG	TCATCTAGTTCCACCTCA	Sequenom exploratory panel
rs1539019_F	ACGTTGGATGCTACCTTCTCTCTGAGTGTC	Sequenom exploratory panel
rs1539019_R	ACGTTGGATGGCTATAGGGTAGGGTATCTG	Sequenom exploratory panel
rs1539019_F_GT	TCTCTGAGTGTCCTTGGACAAAG	Sequenom exploratory panel
rs2027432_F	ACGTTGGATGACCAAGCACTACATCAACCC	Sequenom exploratory panel
rs2027432_R	ACGTTGGATGGAGCATTCTCTCTGCAGTTC	Sequenom exploratory panel
rs2027432_F_CT	AGTTGGTTCCGATGAC	Sequenom exploratory panel
rs4353135_F	ACGTTGGATGGAGAGAATGAAGGAAGCAAG	Sequenom exploratory panel
rs4353135_R	ACGTTGGATGTATTACAGTACCTGGCTCAC	Sequenom exploratory panel
rs4353135_F_GT	AAGATAGAGGGGTAAATGTAT	Sequenom exploratory panel
rs4356092_F	ACGTTGGATGGTCTGGATACACAGCAAATG	Sequenom exploratory panel
rs4356092_R	ACGTTGGATGGCCTTAAGAAATTATGTTTCC	Sequenom exploratory panel
rs4356092_F_AG	TTAATCTCACCCAGGGGA	Sequenom exploratory panel
rs4925546_F	ACGTTGGATGCAATAGATAGGGTGTTATGG	Sequenom exploratory panel
rs4925546_R	ACGTTGGATGCCTGTGAAAGAACAAGTC	Sequenom exploratory panel
rs4925546_R_CT	ATGGATTGAATTGTTTCCTC	Sequenom exploratory panel

rs4925671_F	ACGTTGGATGCATGAGCTACAATTCATGTG	Sequenom exploratory panel
rs4925671_R	ACGTTGGATGGAGTCAAACCTAGAGAGGG	Sequenom exploratory panel
rs4925671_F_CT	CATCATGTGATTAATGCTGCTA	Sequenom exploratory panel
rs6673459_F	ACGTTGGATGCCCAAGTCTTGGCAATTGA	Sequenom exploratory panel
rs6673459_R	ACGTTGGATGCTTTGCTCTCCTCCTACTC	Sequenom exploratory panel
rs6673459_R_CA	TCAGGAATATTAATGGTTTAGTTG	Sequenom exploratory panel
rs6673762_F	ACGTTGGATGTCATCATGTTGTCCAGGCTAGT	Sequenom exploratory panel
rs6673762_R	ACGTTGGATGGTTACAGCAGAAACCACACCA	Sequenom exploratory panel
rs6673762_F_CT	AGTCCTGACCTCAGGTGATC	Sequenom exploratory panel
rs6700719_F	ACGTTGGATGCCTCAAGCTATACAGTGGTG	Sequenom exploratory panel
rs6700719_R	ACGTTGGATGAGAGCCCAGAGTAAAACCAG	Sequenom exploratory panel
rs6700719_F_AG	GGAAAGTGATTCAGTGTGAAAC	Sequenom exploratory panel
rs7528887_F	ACGTTGGATGCCTGAAATTTGCTAAGAGAG	Sequenom exploratory panel
rs7528887_R	ACGTTGGATGCATGAGTTAACATAGCCACC	Sequenom exploratory panel
rs7528887_R_CA	AAGAGATTTTAGATGTTTTTACCAC	Sequenom exploratory panel
9kb_ss107635120_GA-F	ACGTTGGATAGAAAGGGGCAGGGATTAGA	Sequenom Phase II panel
9kb_ss107635120_GA-R	ACGTTGGATCCATTGAGAAACCGTGTGTG	Sequenom Phase II panel
9kb_ss107635120_GA-Pa	ACAAGAGAAACCGTGTGTGTGTG	Sequenom Phase II panel
9kb_ss107635122_CT-F	ACGTTGGATGATACCTTGGCTCTTCCACTC	Sequenom Phase II panel
9kb_ss107635122_CT-R	ACGTTGGATGTCATGACCACACACGCACAG	Sequenom Phase II panel
9kb_ss107635122_CT-P	ACACGCACAGGCAGCCCTGTCACTACA	Sequenom Phase II panel
9kb_ss107635124_CT-F	ACGTTGGATGTGGGA ACTACTGTGTCCATC	Sequenom Phase II panel
9kb_ss107635124_CT-R	ACGTTGGATGGCACTCCTTGACCTTCTTC	Sequenom Phase II panel
9kb_ss107635124_CT-P	ATCTTTCATCTTCCC ACTAC	Sequenom Phase II panel
9kb_ss107635126_GA-F	ACGTTGGATTGAATCCCGCAGTTTCTTC	Sequenom Phase II panel
9kb_ss107635126_GA-R	ACGTTGGATGCAAATGTCAGGGATAAGAGGT	Sequenom Phase II panel
9kb_ss107635126_GA-Pa	GCGGAATGATATATATCTAAGGGTG	Sequenom Phase II panel
9kb_ss107635130_TA-F	ACGTTGGATGCCTCAACTCCACCTCTTCA	Sequenom Phase II panel
9kb_ss107635130_TA-R	ACGTTGGATCTATTCCCAGCAGGAGGATG	Sequenom Phase II panel
9kb_ss107635130_TA-Pa	TCTGGCACAGGATGAGAAAGG	Sequenom Phase II panel

9kb_ss107635144_CT-F	ACGTTGGATGCACAAGTGAGGCACAGATAG	Sequenom Phase II panel
9kb_ss107635144_CT-R	ACGTTGGATGAAGCATGAGACCTGAACTGG	Sequenom Phase II panel
9kb_ss107635144_CT-P	CTGAACTGGCTTCAACACCAGGCT	Sequenom Phase II panel
rs55646866_CT-F	ACGTTGGATGAAAAAGGCGATGACGTGTGG	Sequenom Phase II panel
rs55646866_CT-R	ACGTTGGATGAGTGATGGGCCTATGGGAG	Sequenom Phase II panel
rs55646866_CT-P	CTATGGGAGGGAGGATA	Sequenom Phase II panel
rs10925032_AG-F	ACGTTGGATGATTCCTCCATTGAAACCCTG	Sequenom Phase II panel
rs10925032_AG-R	ACGTTGGATGCATGTTGCAACAGGTGTTCC	Sequenom Phase II panel
rs10925032_AG-P	TTCCCTGCTGCCCCAGTTGAT	Sequenom Phase II panel
rs10925034_rs10925035-F	ACGTTGGATGGTATCACAGCCTGCGTGTTCC	Sequenom Phase II panel
rs10925034_rs10925035-R	ACGTTGGATGCGCTCAAGAGTTACCTGCTG	Sequenom Phase II panel
rs10925034_AG-P	CTCAAGAGTTACCTGCTGATTGTATC	Sequenom Phase II panel
rs10925035_GA-Pa	GGAAACTGCGGGAATTCAG	Sequenom Phase II panel
rs10925040_CT-F	ACGTTGGATGAAGCCAAACAACACTGAGGAAC	Sequenom Phase II panel
rs10925040_CT-R	ACGTTGGATGCTTACTCCATCCTCTGCATC	Sequenom Phase II panel
rs10925040_CT-P	ATTTAGCTCCCACTTGTA	Sequenom Phase II panel
rs11583410_CA-F	ACGTTGGATGATGAGAACGGCATAGTGCAG	Sequenom Phase II panel
rs11583410_CA-R	ACGTTGGATGATATGCAGTCTTCCACTGGC	Sequenom Phase II panel
rs11583410_CA-Pa	ATCCCACCCTGGACCGCTACGTGGCCA	Sequenom Phase II panel
rs11802680_GA-F	ACGTTGGATCATCACCGTCAGAGTGTTGA	Sequenom Phase II panel
rs11802680_GA-R	ACGTTGGATGCCCTTCTGCTTGCTTTATG	Sequenom Phase II panel
rs11802680_GA-Pa	CGTTATGCTTGCTTTATGTCAC	Sequenom Phase II panel
rs12028142_rs35305980-F	ACGTTGGATGCTCAATTTGCCACAAGTGCC	Sequenom Phase II panel
rs12028142_rs35305980-R	ACGTTGGATGACACACCCAGAAGGATGAAG	Sequenom Phase II panel
rs12028142_AG-P	AATTGTGAAGGCTTTAGGGGA	Sequenom Phase II panel
rs35305980_-A-Pa	GCAACATGAAAAGTGACAACCATAGCT	Sequenom Phase II panel
rs12135709_GC-F	ACGTTGGATGCAATGTTGCATCGTTGCAGG	Sequenom Phase II panel
rs12135709_GC-R	ACGTTGGATGCAGGTAGCAAGTTCCAAGAG	Sequenom Phase II panel
rs12135709_GC-Pa	TCGTTTCTGCCAGGAC	Sequenom Phase II panel
rs12406394_AT-F	ACGTTGGATGGCTGCTCGGCAAAGAAATTG	Sequenom Phase II panel

rs12406394_AT-R	ACGTTGGATGCTACGGAAAGATCAGACTGC	Sequenom Phase II panel
rs12406394_AT-P	GCTTGAGTGACATTCCA	Sequenom Phase II panel
rs12756328_GC-F	ACGTTGGATGTCTCATAATGCTCTCCCTCC	Sequenom Phase II panel
rs12756328_GC-R	ACGTTGGATGTTCCCTCATGCTGTGAATGAC	Sequenom Phase II panel
rs12756328_GC-Pa	ATTATCGGGGGCCCATCAGGGAGTG	Sequenom Phase II panel
rs4269805_CT-F	ACGTTGGATCCACTCTTCCTTTCCCAGGT	Sequenom Phase II panel
rs4269805_CT-R	ACGTTGGATGCAAAGACACAGAGGCTGCT	Sequenom Phase II panel
rs4269805_CT-P	TTCAGAACCAGGAGCCCCAG	Sequenom Phase II panel
rs4301663_AG-F	ACGTTGGATCCTCCTTCAATTGCCAAGAC	Sequenom Phase II panel
rs4301663_AG-R	ACGTTGGATTCAAACACTCTGACGGTGATG	Sequenom Phase II panel
rs4301663_AG-P	GCATTTCTAGAGCGAAGCGTGCT	Sequenom Phase II panel
rs4362022_CT-F	ACGTTGGATGGAAGGTGTGCAATGCTTGAG	Sequenom Phase II panel
rs4362022_CT-R	ACGTTGGATGTGCTGTTAGGAAGCAACTGG	Sequenom Phase II panel
rs4362022_CT-P	CCTTTCGACTGCACCA	Sequenom Phase II panel
rs6665526_CT-F	ACGTTGGATGTGCGTGTGTGGTCATGACAG	Sequenom Phase II panel
rs6665526_CT-R	ACGTTGGATGGGCTGTATTGATAGGACCAC	Sequenom Phase II panel
rs6665526_CT-P	GCTTGCATCCAGCTCCCGGATTCA	Sequenom Phase II panel
rs6672995_AG-F	ACGTTGGATGAGCCCATCAGAGGAAATGTG	Sequenom Phase II panel
rs6672995_AG-R	ACGTTGGATGAGTCTGTGTTGGCCTTAGTC	Sequenom Phase II panel
rs6672995_AG-P	CCGCGGAGGGACATTTAA	Sequenom Phase II panel
rs9988620_CA-F	ACGTTGGATGCCTCAAACCCCTTTGTA CTG	Sequenom Phase II panel
rs9988620_CA-R	ACGTTGGATGTTTCAGGACAGCCCGGTTTC	Sequenom Phase II panel
rs9988620_CA-P	ATGCCCTCACTAATTTAACTATTC	Sequenom Phase II panel

Supplementary Table 2: Primers used for the 9kb sequencing experiment

ID	Primer Sequence
9kb_set1_F	ATGCACCGTGCTCTCTGTC
9kb_set1_R	GAATCAGGAAATTGGAAGTGAAA
9kb_set2_F	GCAAAGACACAGAGGCTGCT
9kb_set 2_R	CGGCACCTCACAGAAAAAGT
9kb_set3_F	CTGCTCGGCAAAGAAATTGT
9kb_set 3_R	TCCCAGGTGATAGCCTGTTT
9kb_set4_F	GCCACAGCTCACTGTTTTGA
9kb_set 4_R	AAGCTCTTGATTGGCGTGAG
9kb_set5_F	TCTCCTCCAGATTCTATCAACA
9kb_set5_R	CCATTGAGAAACCGTGTGTG
9kb_set6_F	AGAAAGGGGCAGGGATTAGA
9kb_set6_R	TTCGTGTGAGGGTGAGTGAG
9kb_set7_F	CTTGCTACCTGCCTCTCTGC
9kb_set7_R	GTGCCAGCTAACGTCTCGAT
9kb_set8_F	TTTGCAGTCCTGGTTCAATG
9kb_set8_R	GCAAGACCCCATCTCTATTTATTTT
9kb_set9_F	CCTCTGGATGTCATAATCTGTCAC
9kb_set9_R	CCAGCTCCTTCTCCTCCTCT
9kb_set10_F	AGAGTCCTCAGCCTCGTCAG
9kb_set10_R	TTCCTGGAATATGAAGAGCATT
9kb_set11_F	ATCCTGCACCTCCACTGC
9kb_set11_R	CACACACACACACACAGAGTTCTT
9kb_set12_F	TGAGGTGGTGTGAGAGCTTG
9kb_set12_R	TCTGTGCCACTCATTGTTCTG
9kb_set13_F	TCTGTGCCTCACTTGTGTTTTC
9kb_set13_R	CATGACTCACCTGTGTCCA

Supplementary Table 3: SNPs uncovered while sequencing the 9kb region

#	SNP ID	dbSNP129	Frequency ^e
1	rs4925663 ^a	245,681,240	0.417
2	rs11583410 ^c	245,681,519	0.354
3	rs12028142 ^c	245,681,875	0.25
4	rs35305980 ^c	245,681,886	0.417
5	rs4269805 ^c	245,682,093	0.063
6	rs6673459 ^a	245,682,135	0.071
7	rs6698597 ^a	245,682,218	0.045
8	rs4301663 ^c	245,682,292	0.136
9	rs10802505	245,682,403	0.432
10	rs11802680 ^d	245,682,407	0.333
11	rs6665526 ^c	245,682,510	0.432
12	ss107635122 ^{b,d}	245,682,563	0.024
13	rs10925031	245,682,666	0.024
14	rs6674091	245,682,723	0.024
15	rs12406394 ^c	245,682,804	0.026
16	rs4362022 ^d	245,682,942	0.043
17	rs4372298	245,683,069	0.457
18	rs10925032 ^c	245,683,202	0.022
19	rs4333884	245,683,346	0.457
20	rs4593864	245,683,356	0.457
21	rs4518943	245,683,389	0.457
22	rs4436424	245,683,425	0.478
23	rs55903505 ^b	245,683,462	0.435
24	rs4353135 ^a	245,683,659	0.413
25	rs56310736 ^b	245,683,709	0.022
26	rs4266924 ^a	245,683,757	0.457
27	rs10802506	245,683,999	0.478
28	rs6677999	245,684,020	0.478
29	ss107635120 ^{b,c}	245,684,132	0.022
30	ss107635124 ^{b,d}	245,684,289	0.048
31	rs6669625	245,684,356	0.022
32	rs10802507	245,684,374	0.477
33	rs10802508	245,684,378	0.477
34	ss107635146 ^b	245,684,452	0.021
35	rs12745508	245,684,602	0.477
36	rs12135709 ^c	245,684,694	0.406
37	rs10925033	245,684,862	0.438
38	rs10925034 ^d	245,684,892	0.042
39	rs10925035 ^d	245,684,900	0.438
40	ss107635126 ^{b,d}	245,684,966	0.021
41	rs6672845	245,685,068	0.5
42	rs10925036	245,685,254	0.438
43	rs9700400	245,685,366	0.438

44	ss107635128 ^b	245,685,521	0.438
45	rs10925038	245,685,641	0.479
46	ss107635130 ^{b,d}	245,685,647	0.042
47	rs9988617	245,685,669	0.479
48	rs9988501	245,685,739	0.479
49	rs9287213	245,685,750	0.042
50	rs9988571	245,685,778	0.479
51	rs9988620 ^c	245,685,814	0.479
52	ss107635132 ^b	245,685,884	0.438
53	rs9988621	245,685,903	0.479
54	rs9988572	245,685,933	0.042
55	ss107635133 ^b	245,685,965	0.438
56	ss107635136 ^b	245,686,061	0.438
57	ss107635138 ^b	245,686,130	0.438
58	ss107635140 ^b	245,686,136	0.438
59	rs4925664	245,686,610	0.043
60	rs12756328 ^d	245,686,690	0.143
61	rs4925666	245,686,879	0.476
62	rs55646866 ^{b,c}	245,687,008	0.457
63	rs4925667	245,687,277	0.5
64	rs10732301	245,687,457	0.043
65	ss107635142 ^b	245,687,462	0.457
66	rs6672995 ^c	245,687,656	0.479
67	rs4925669	245,687,946	0.479
68	rs11267736	245,688,318	0.475
69	ss107635144 ^{b,d}	245,688,775	0.295
70	rs10732302	245,688,851	0.479
71	rs55775744 ^b	245,688,902	0.435
72	rs10737807	245,688,941	0.5
73	rs34837390	245,688,958	0.479
74	rs10733113 ^a	245,688,980	0.479
75	rs10925039 ^a	245,689,184	0.146
76	rs10925040 ^d	245,689,321	0.417
77	rs10925041	245,689,331	0.417
78	rs10754561 ^a	245,689,423	0.083
79	rs4925671	245,689,497	0.438

^a SNPs ($n=8$) observed in the sequencing experiment that had already been genotyped in the exploratory phase.

^b Novel SNPs ($n=18$) uncovered in the sequencing experiment as of dbSNP Build 126; 4 of these SNPs are now part of dbSNP Build 129.

^c SNPs ($n=13$) that were prioritized for the second phase of the genotyping experiments.

^d SNPs ($n=11$) observed in the sequencing experiment that were selected as tag for the second phase of the genotyping experiments using a pairwise tagging approach.

^e The minor allele frequency (MAF) was estimated using the 24 samples sequenced for the 9kb region.

Supplementary Table 4: Association results between *NLRP3* gene expression levels and associated genotypes

SNP ID	Unstimulated Monocytes			Unstimulated Peripheral Blood Cells		
	Slope	R ²	P value	Slope	R ²	P value
rs4353135	0.856 ± 0.321	0.1968	0.0124	0.677 ± 0.203	0.2833	0.00246
rs4266924	0.356 ± 0.578	0.01292	0.543	0.753 ± 0.450	0.09112	0.105
rs55646866	0.356 ± 0.578	0.01292	0.543	0.800 ± 0.442	0.1080	0.0817
rs6672995	-0.011 ± 0.466	0.0000207	0.980	0.301 ± 0.357	0.02577	0.405
ss107635144	-0.134 ± 0.491	0.002545	0.787	0.603 ± 0.415	0.07025	0.157
rs10733113	-0.134 ± 0.491	0.002545	0.787	0.603 ± 0.415	0.07025	0.157

Supplementary Table 5: Association results between IL-1β levels and associated genotypes

SNP ID	Unstimulated			LPS 1.0 µg/ml		
	Slope	R ²	P value	Slope	R ²	P value
rs4353135	-0.0916 ± 0.102	0.02786	0.378	-0.623 ± 2.85	0.001767	0.829
rs4266924	0.0045 ± 0.166	0.0000260	0.979	4.44 ± 4.485	0.0350	0.331
rs55646866	0.0568 ± 0.178	0.00363	0.752	6.51 ± 4.733	0.06554	0.180
rs6672995	0.2610 ± 0.127	0.1346	0.0502	9.85 ± 3.285	0.2569	0.00591
ss107635144	0.0784 ± 0.149	0.00971	0.604	4.62 ± 4.041	0.04618	0.263
rs10733113	0.0784 ± 0.149	0.00971	0.604	4.62 ± 4.041	0.04618	0.263

Supplementary Table 6: Linkage disequilibrium between SNPs from Table 1 and SNPs genotyped in the *NLRP3* region in recently published genome-wide association studies (GWAS) for CD

		<i>NLRP3</i> replicated SNPs ^{a, b}			
		rs4353135	rs4266924	rs6672995	rs10733113
GWAS ^a	rs7529058	0.015	0.006	0	0.027
	rs3738448	0.052	0.023	0.003	0.010
	rs4612666	0.020	0.033	0	0.009
	rs12143966	0.048	0.027	0.103	0.070
	rs4925659	0.034	0.014	0.078	0.049
	rs12065526	0.035	0.002	0.163	0.068

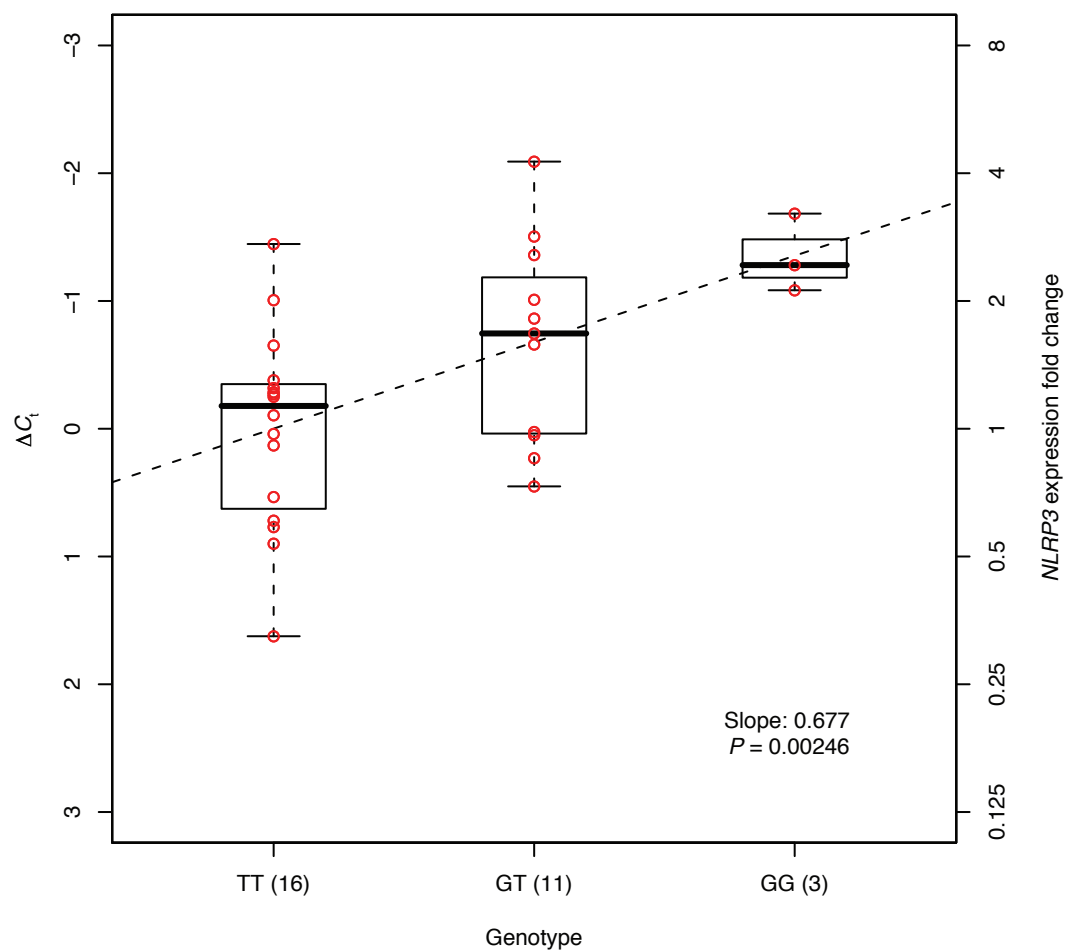
^a r^2 measure of linkage disequilibrium between the 4 replicated SNPs and SNPs present on the Affymetrix 500k and HumanHap300 arrays. SNPs are restricted to the region shown in **Fig.1** and that were not genotyped in the present study.

^b rs55646866 and ss107635144 were excluded from this table because these 2 SNPs were uncovered as part of the resequencing effort in this project. There are thus no genotypes available from the HapMap project for these 2 SNPs.

LEGEND SUPPLEMENTARY FIGURE 1: *Association results between NLRP3 gene expression levels and associated genotypes.* Linear regression analysis of *NLRP3* mRNA level versus the genotypes of the six SNPs from **Table 1** (rs4353135, rs4266924, rs55646866, rs6672995, ss107635144, and rs10733113) in DNA-RNA matched freshly isolated peripheral blood cells (**a,c,e,g,i,k**; PBCs; $n=30$) and monocytes (**b,d,f,h,j,l**; $n=31$) obtained from healthy individuals. Genotypes of the six Crohn's disease (CD)-associated SNPs (**Table 1**) were obtained by sequencing. Mean threshold cycle (C_t) was calculated for each sample from three replicates and then used to calculate relative expression levels (ΔC_t), which is the difference between *NLRP3* C_t and endogenous control 18S RNA C_t . Fold change in *NLRP3* expression was calculated using the ABI's comparative C_t method (see Methods), using as a reference the average ΔC_t of the homozygous for the risk allele of each SNP. ΔC_t (**a-l**) for each individual is shown in red; regression lines are shown as dashed lines (**a-l**).

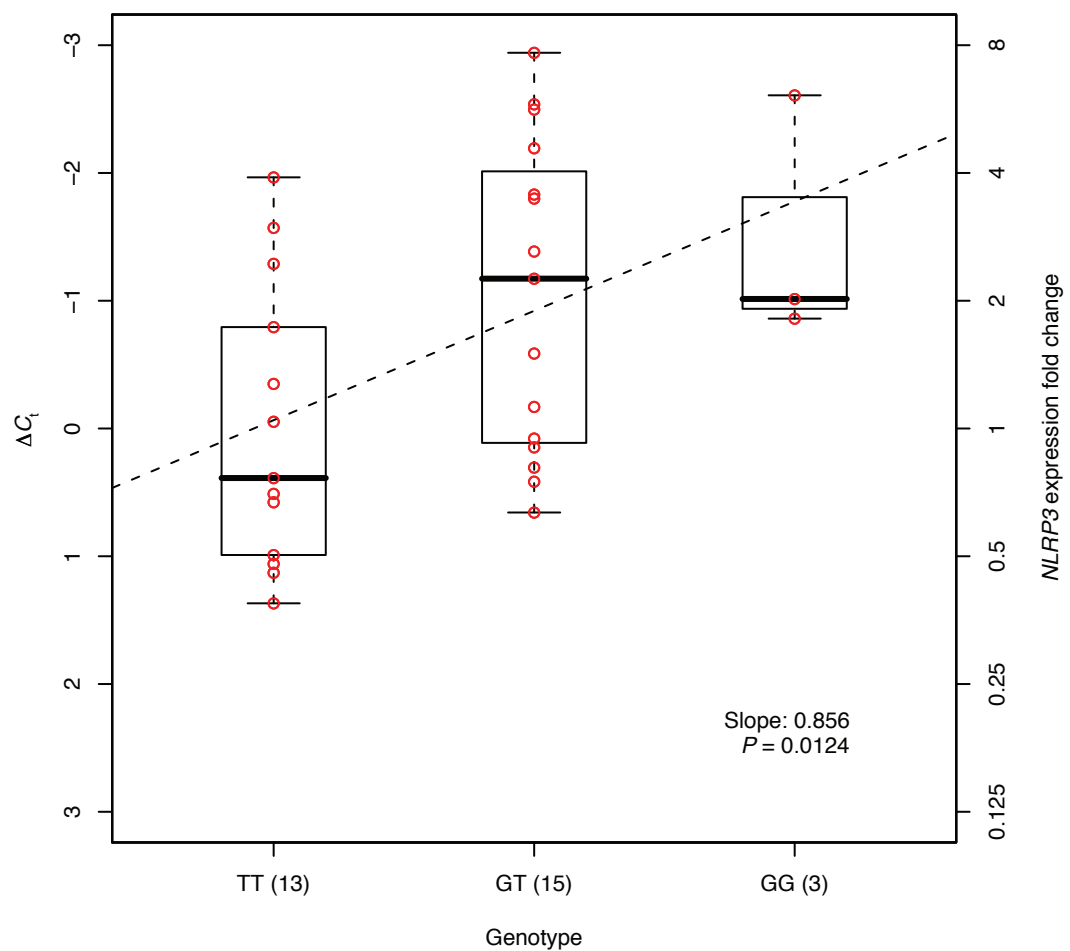
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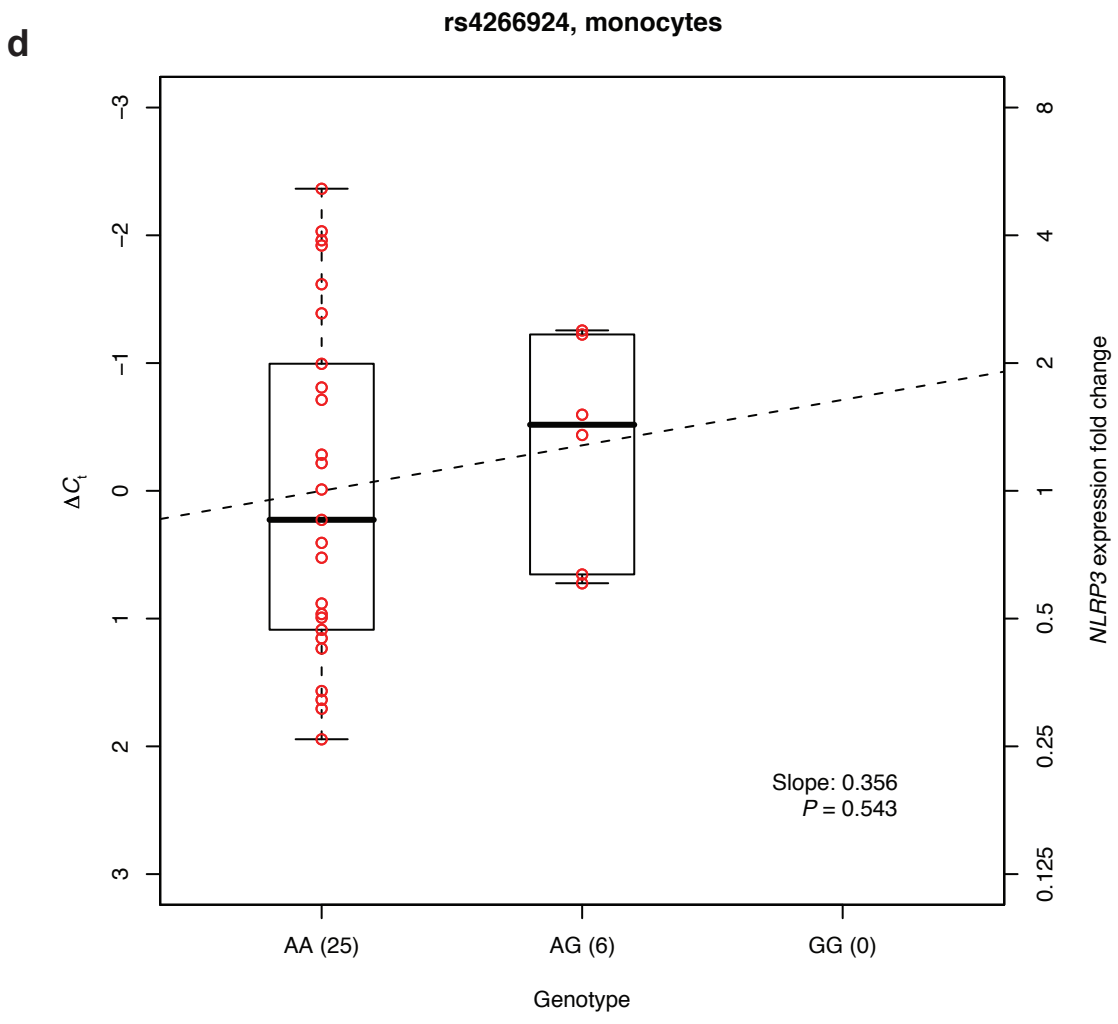
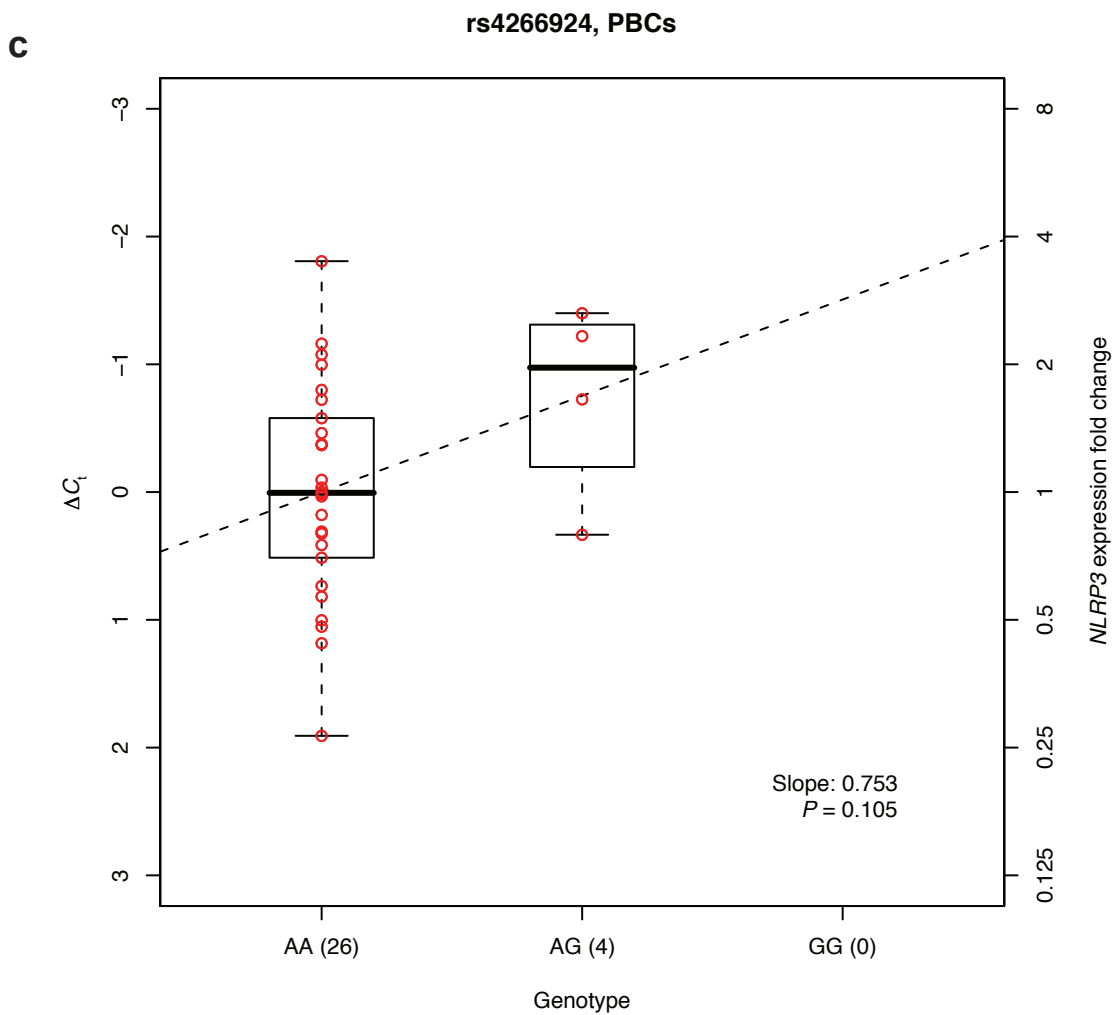
rs4353135, PBCs

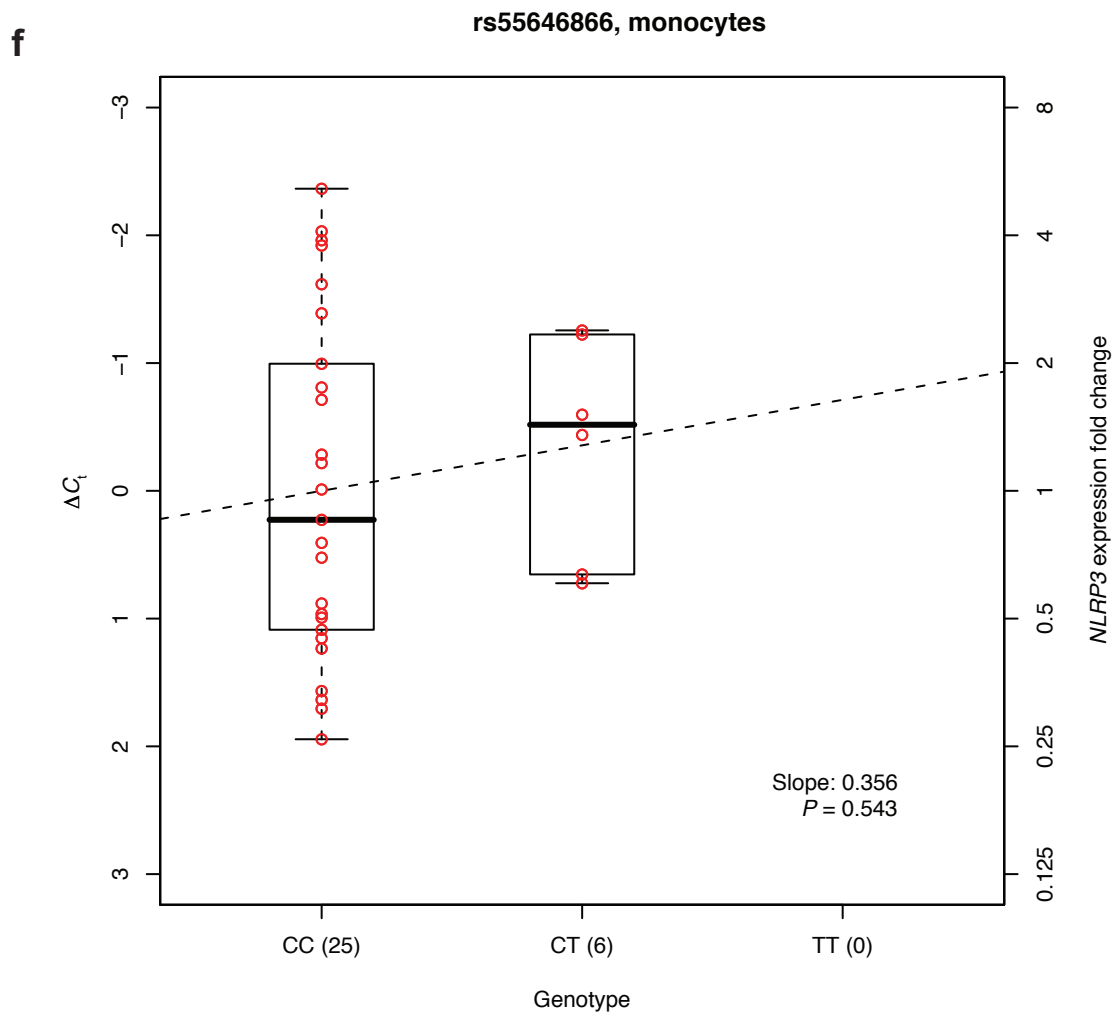
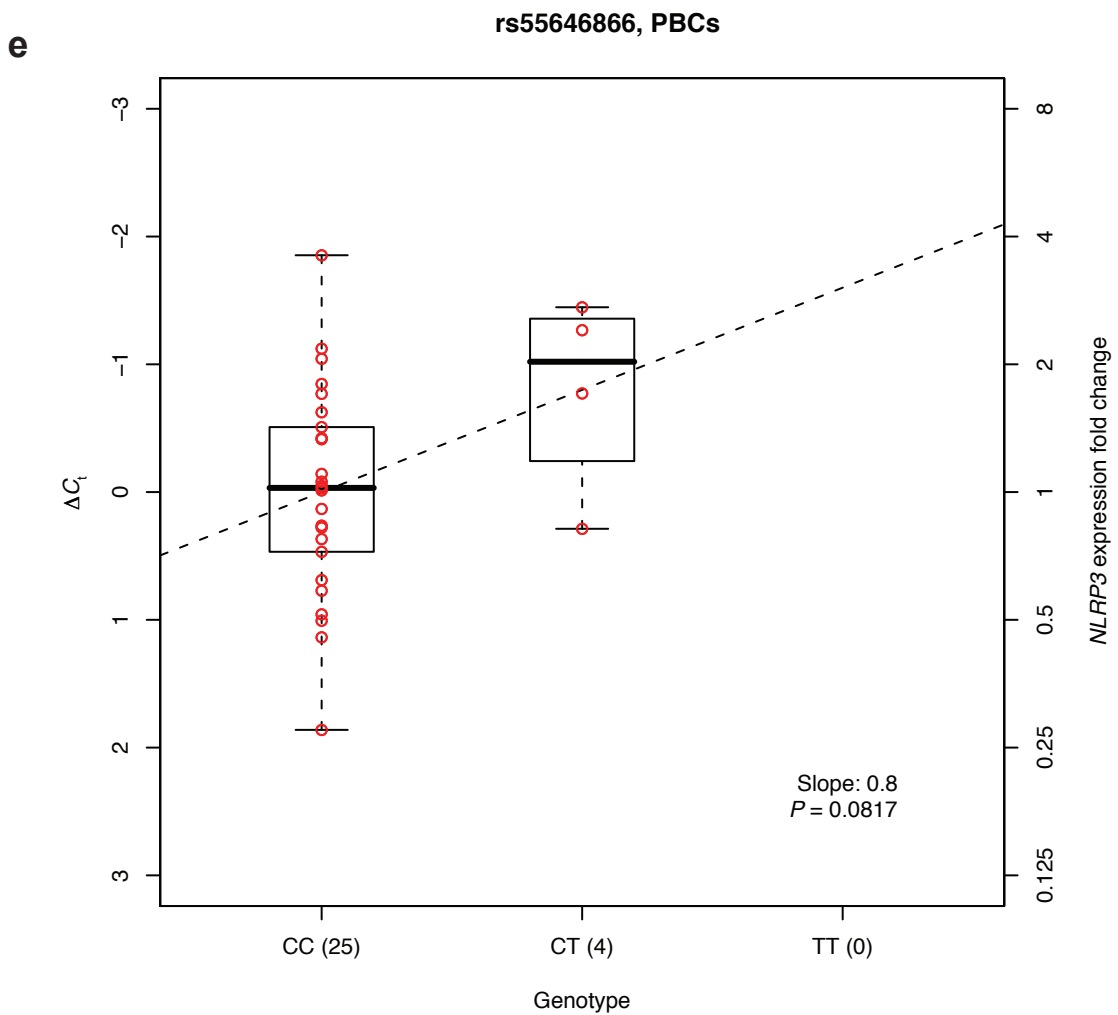


b

rs4353135, monocytes

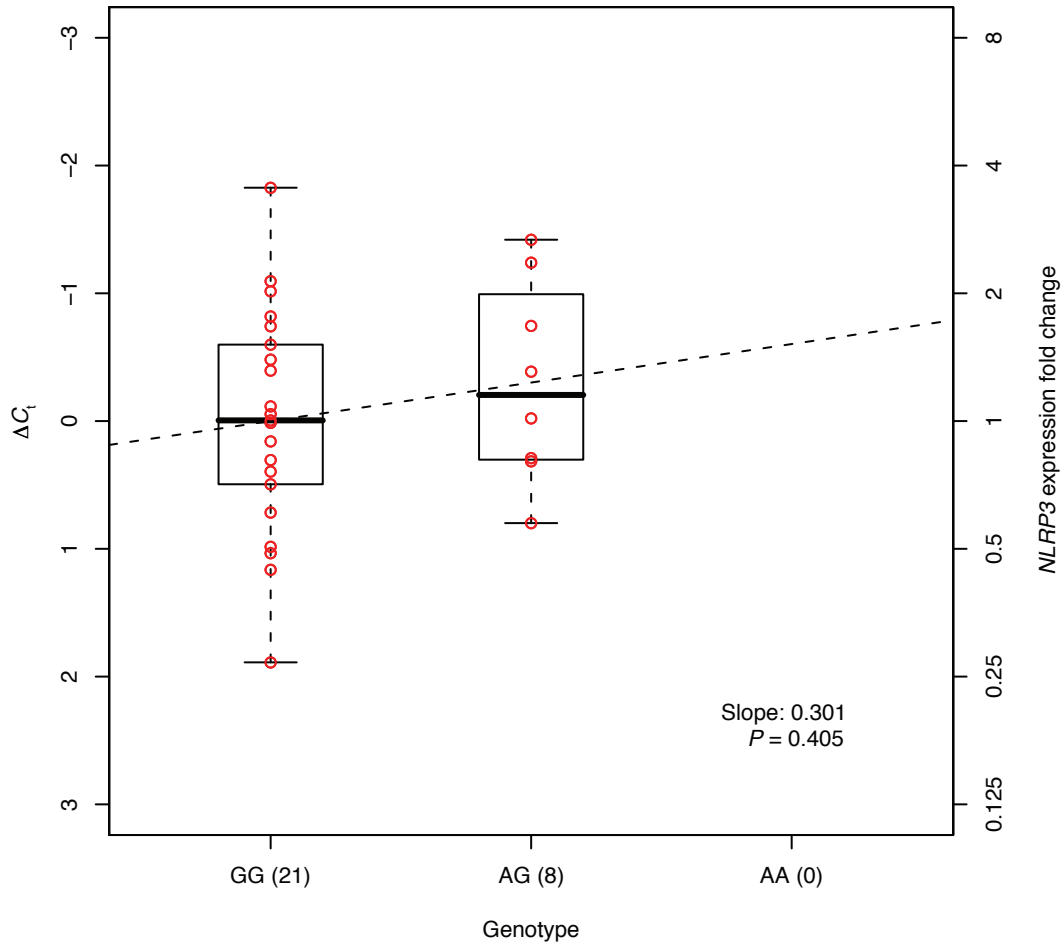






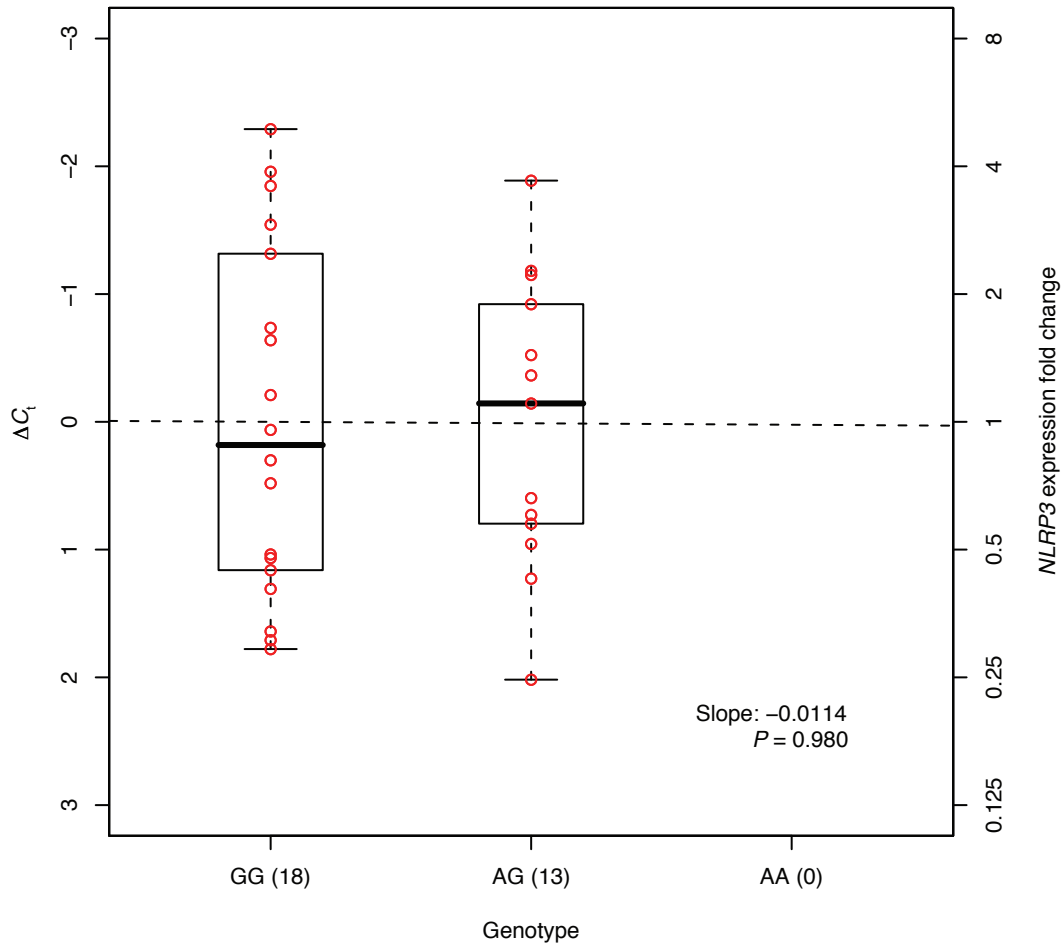
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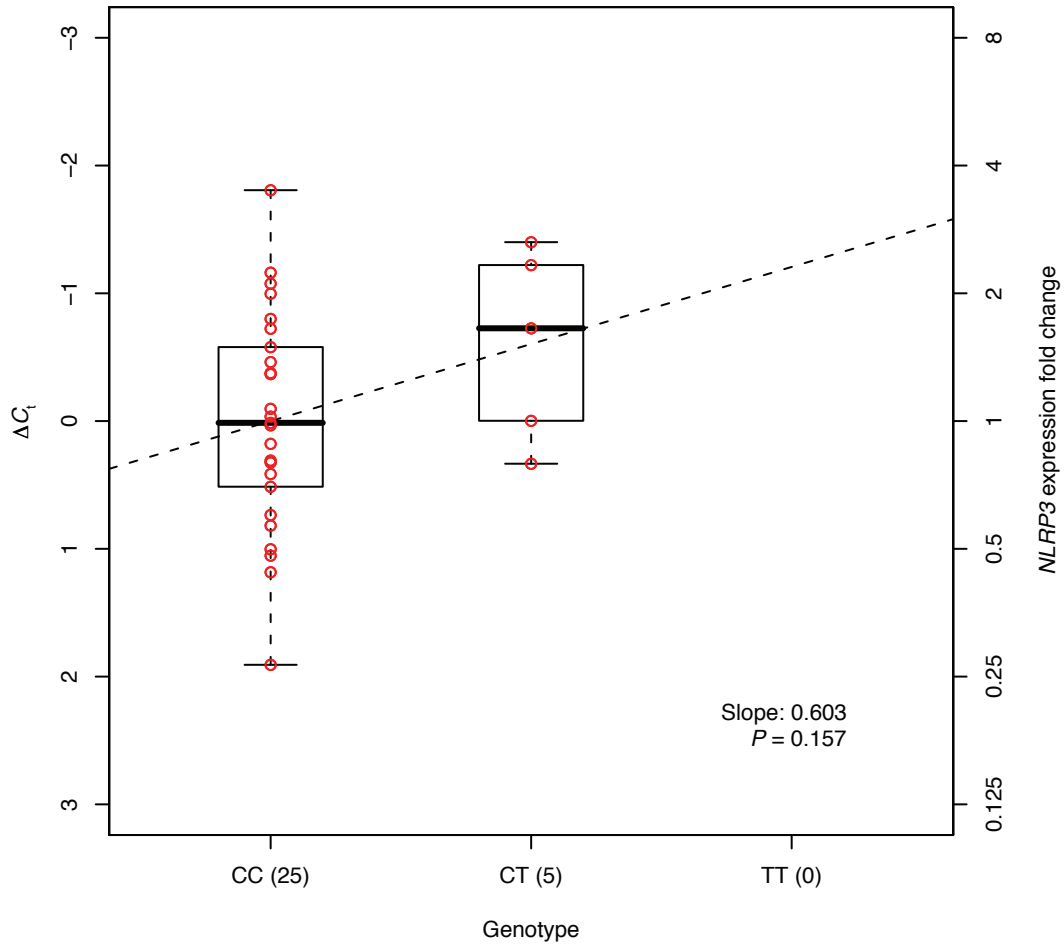
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rs6672995, monocytes



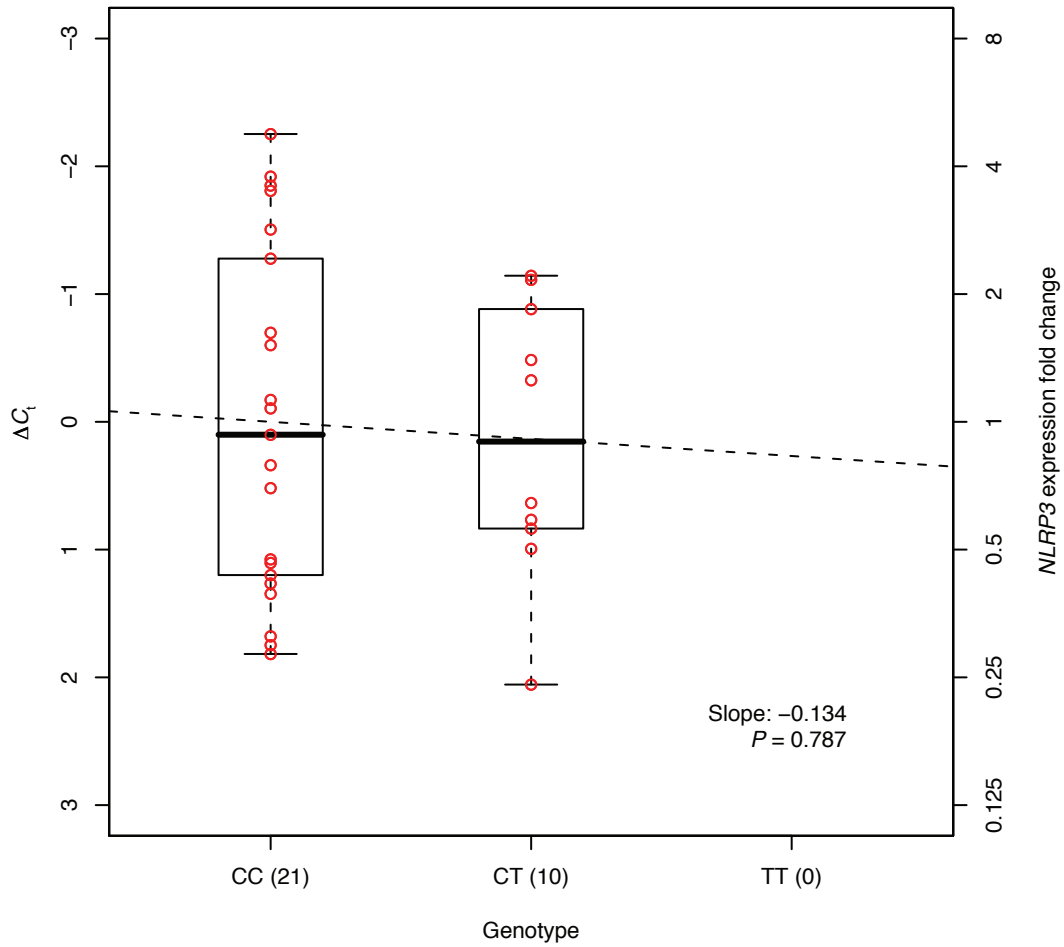
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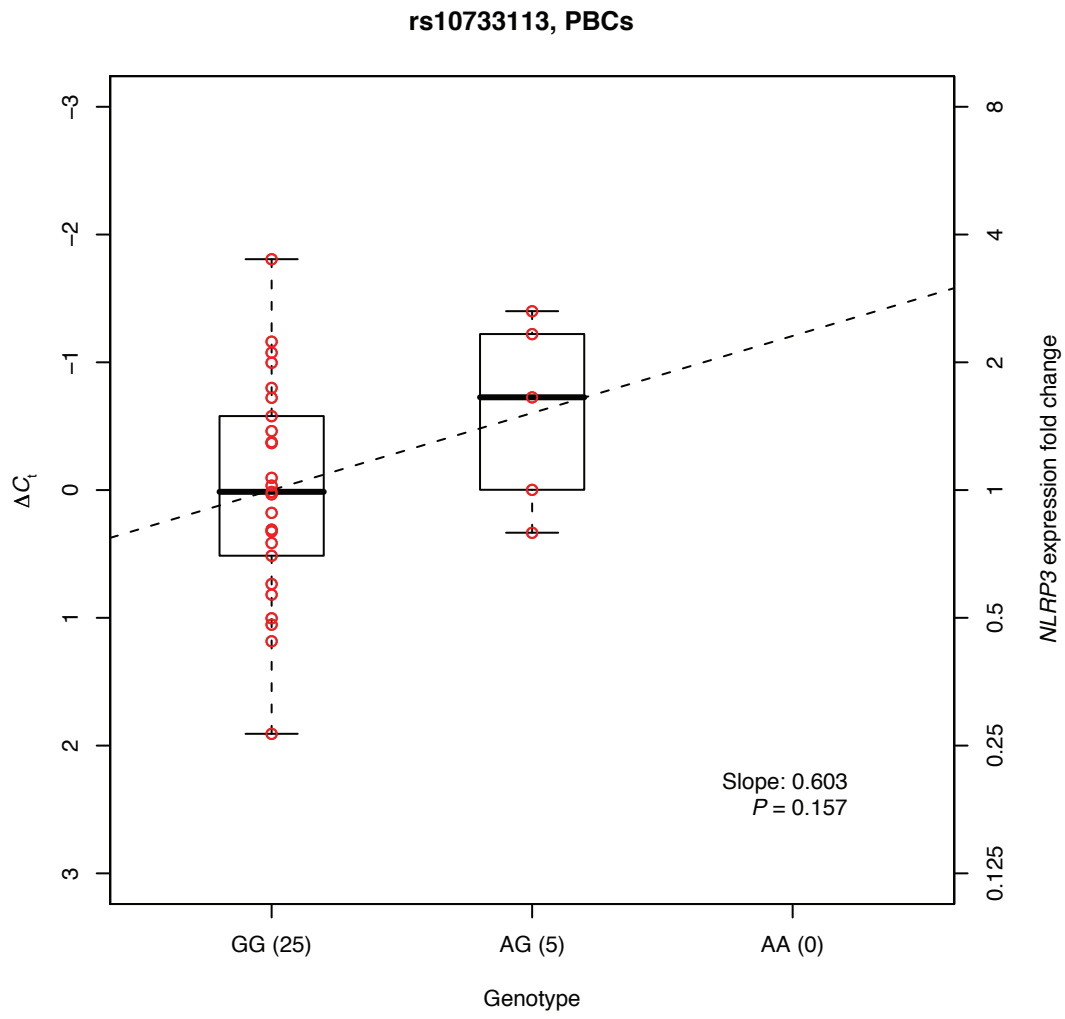
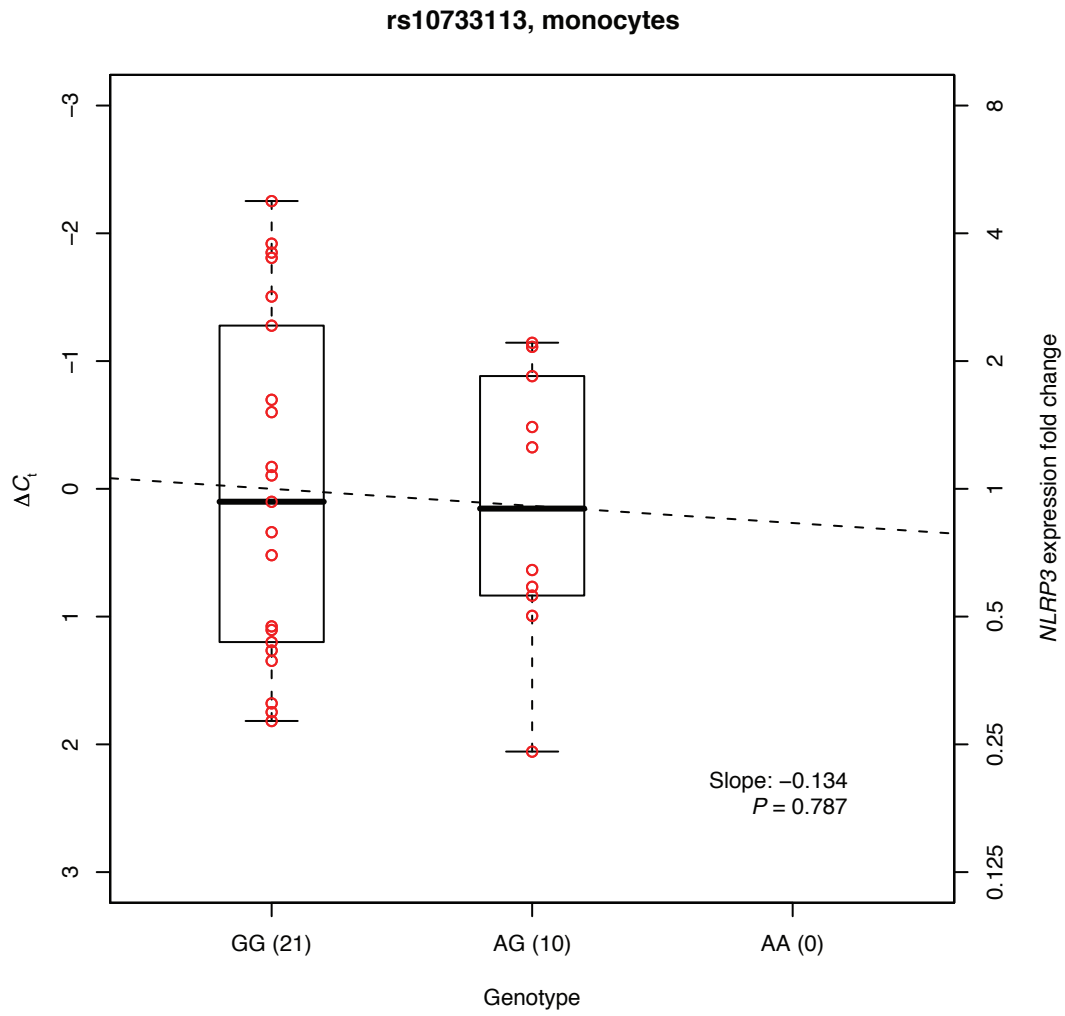
ss107635144, PBCs



j

ss107635144, monocytes

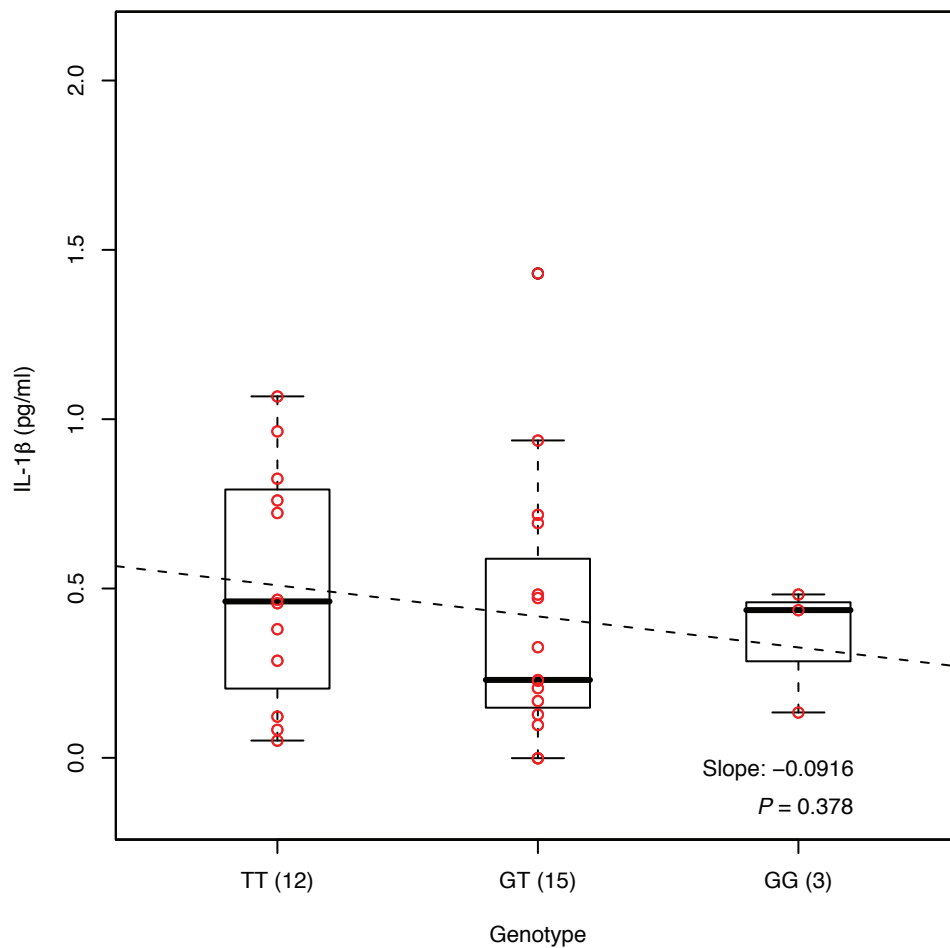


k**l**

LEGEND SUPPLEMENTARY FIGURE 2: *Association results between IL-1 β levels and associated genotypes.* Linear regression analysis of IL-1 β production ($\mu\text{g/ml}$) versus the genotypes of the six SNPs from **Table 1** (rs4353135, rs4266924, rs55646866, rs6672995, ss107635144, and rs10733113), obtained from sequencing, for unstimulated (**a,c,e,g,i,k**) and the LPS-stimulated (**b,d,f,h,j,l**; 1.0 $\mu\text{g/ml}$) conditions after 3 h of incubation. The IL-1 β level (**a-l**) for each individual is shown in red; regression lines are shown as dashed lines (**a-l**).

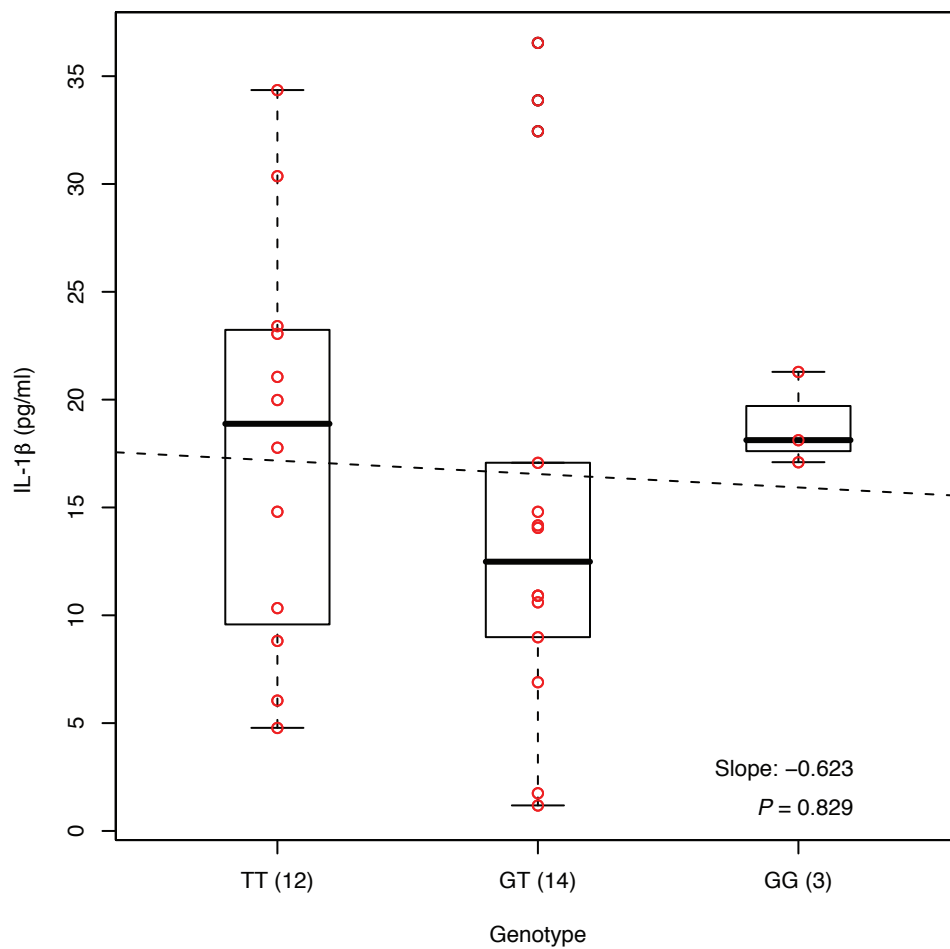
a

rs4353135, unstimulated



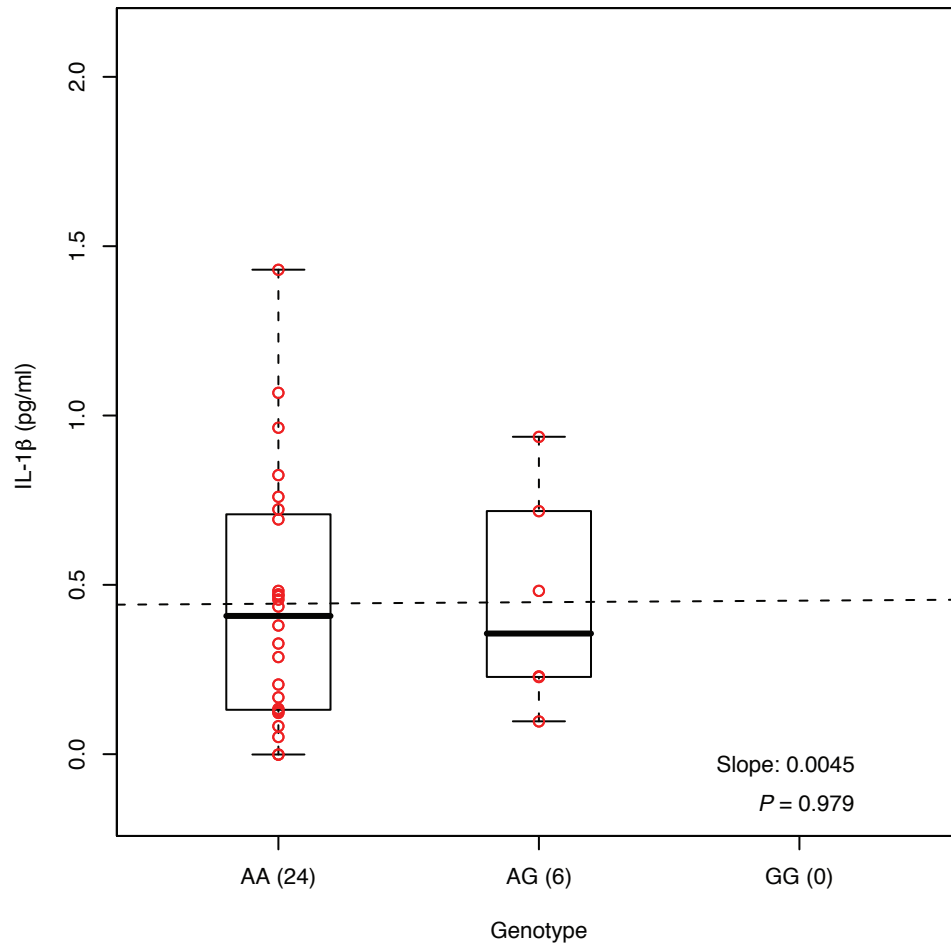
b

rs4353135, LPS



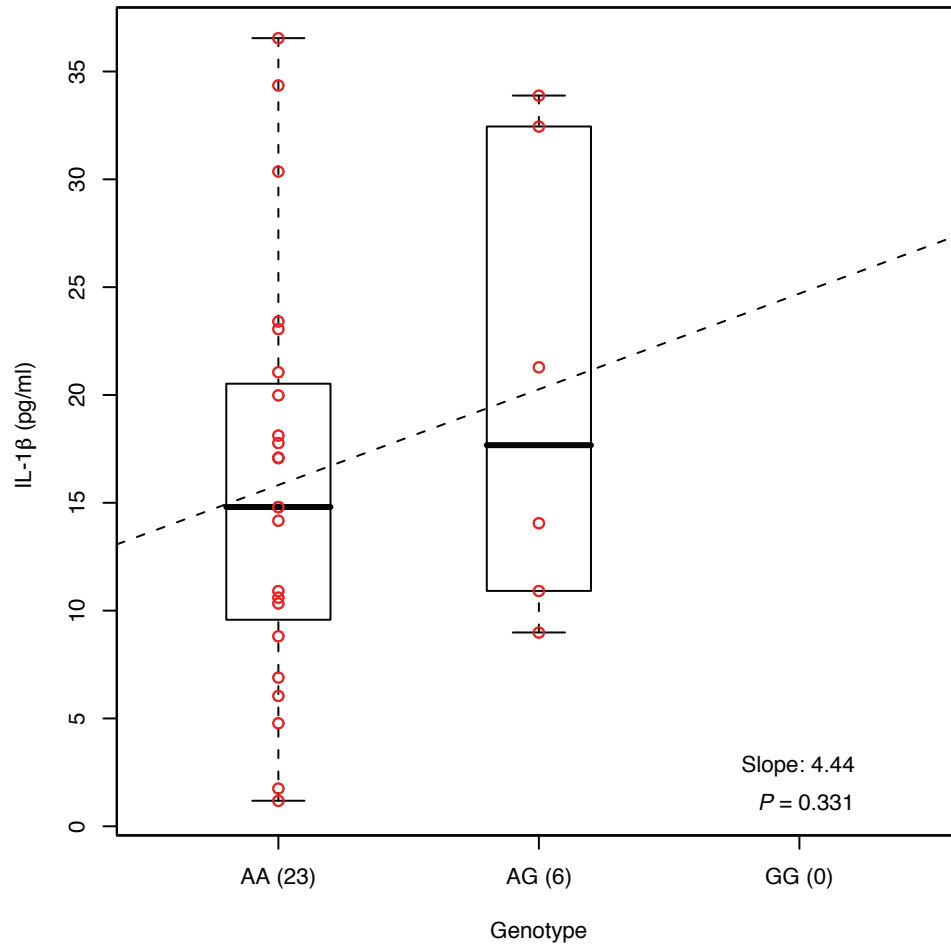
rs4266924, unstimulated

c



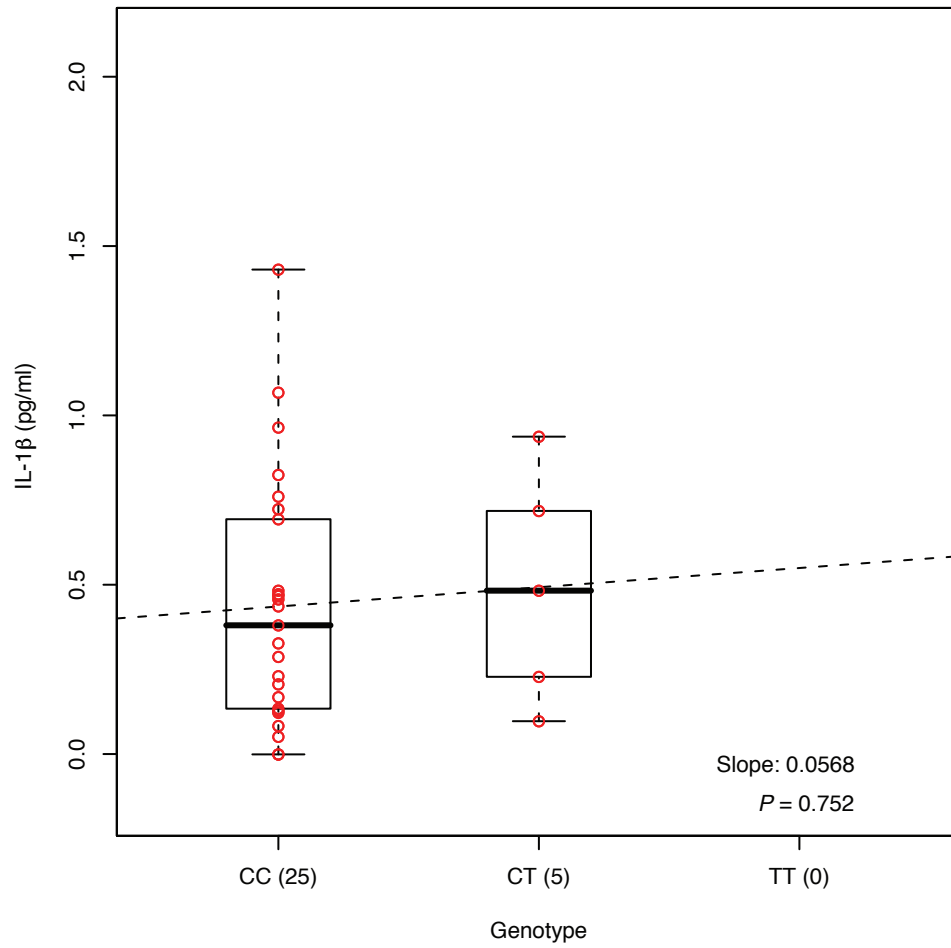
rs4266924, LPS

d



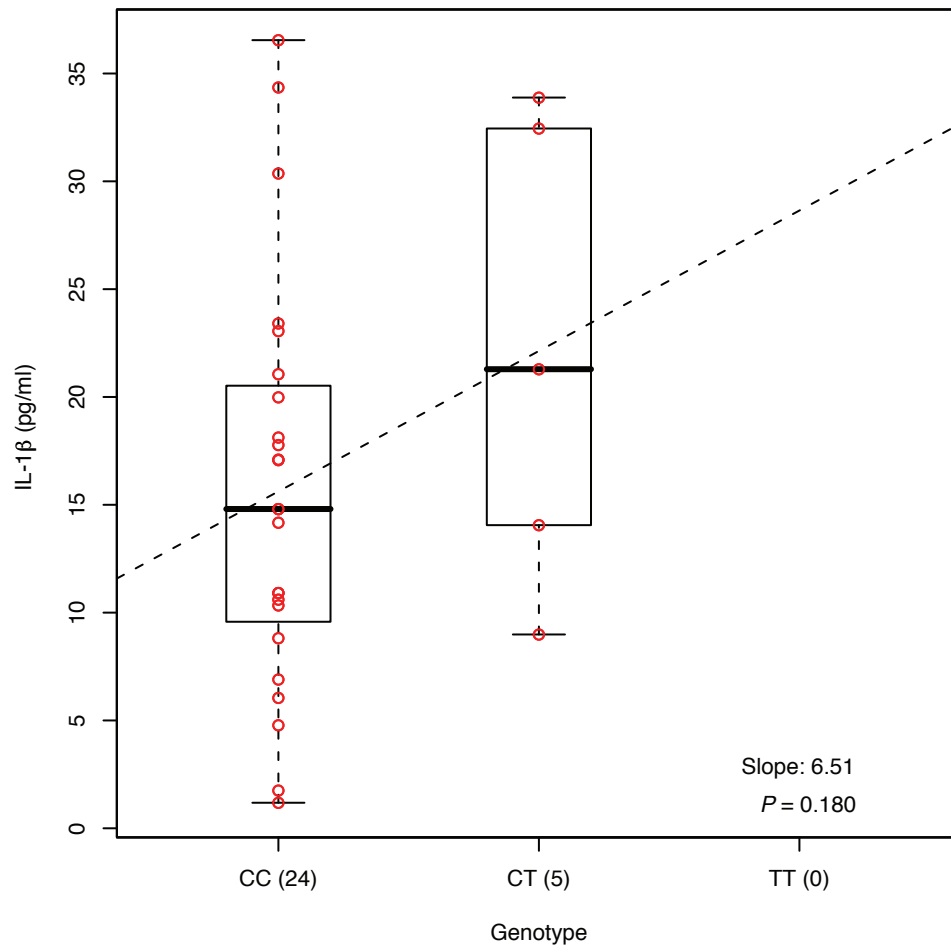
e

rs55646866, unstimulated



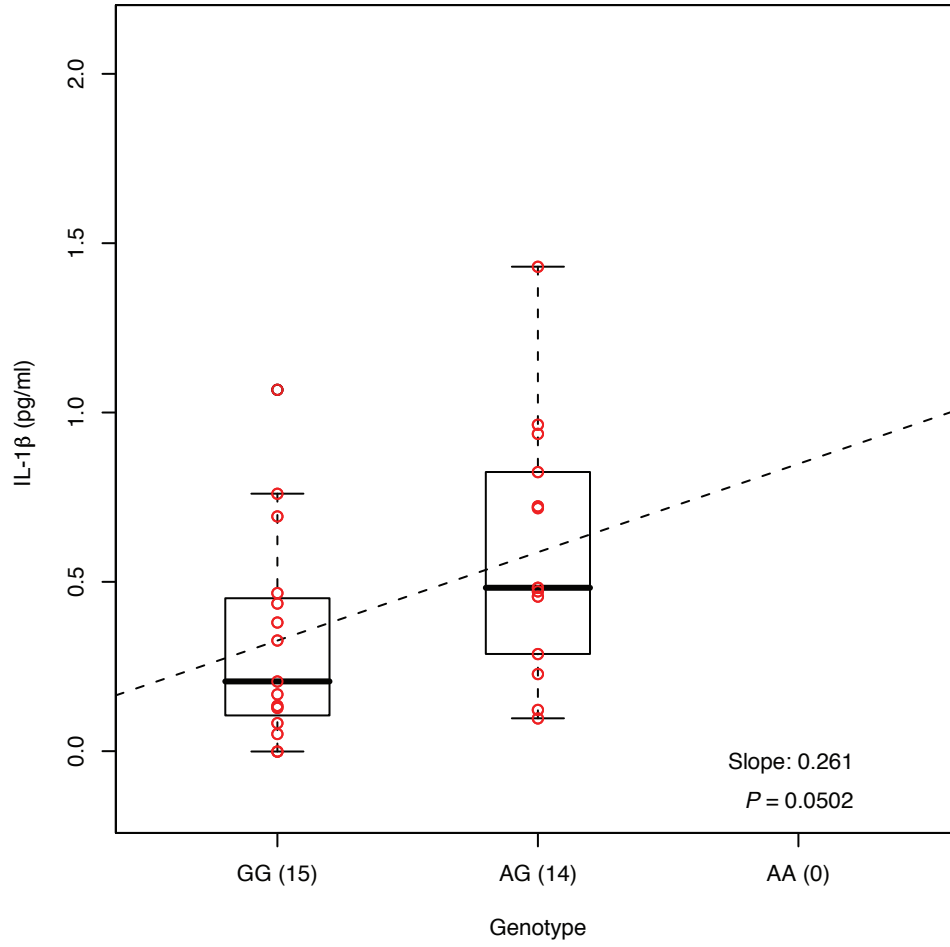
f

rs55646866, LPS



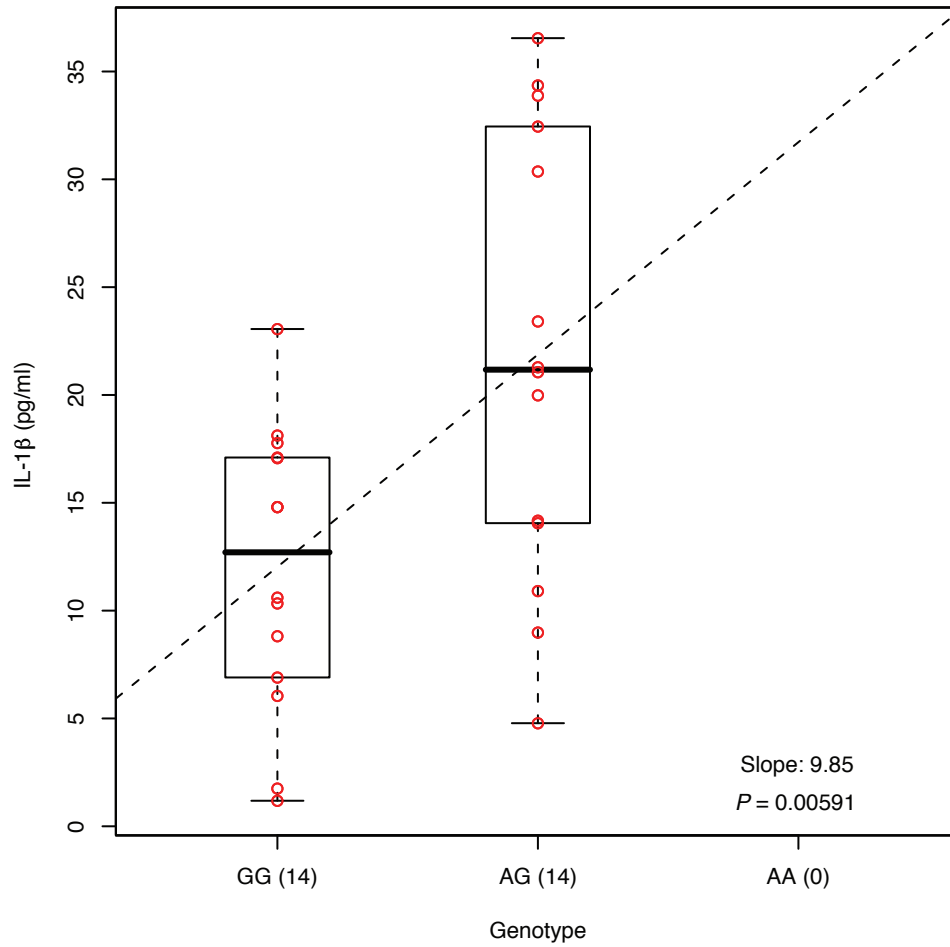
g

rs6672995, unstimulated



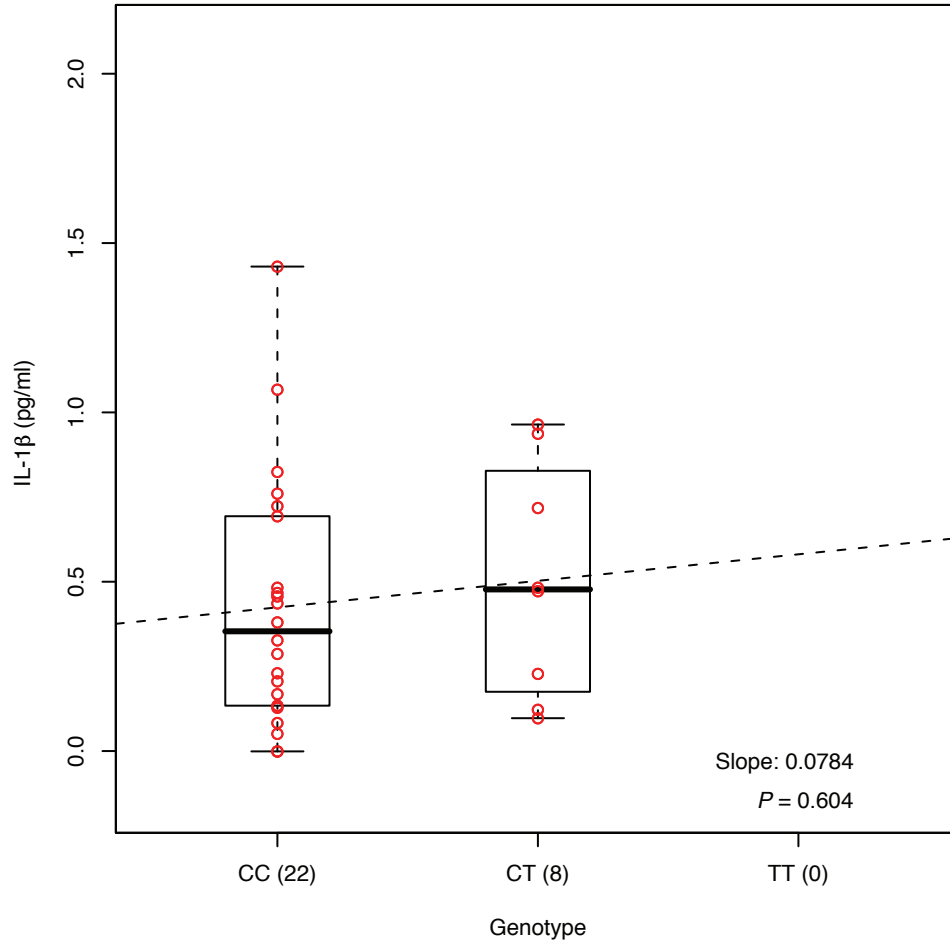
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rs6672995, LPS



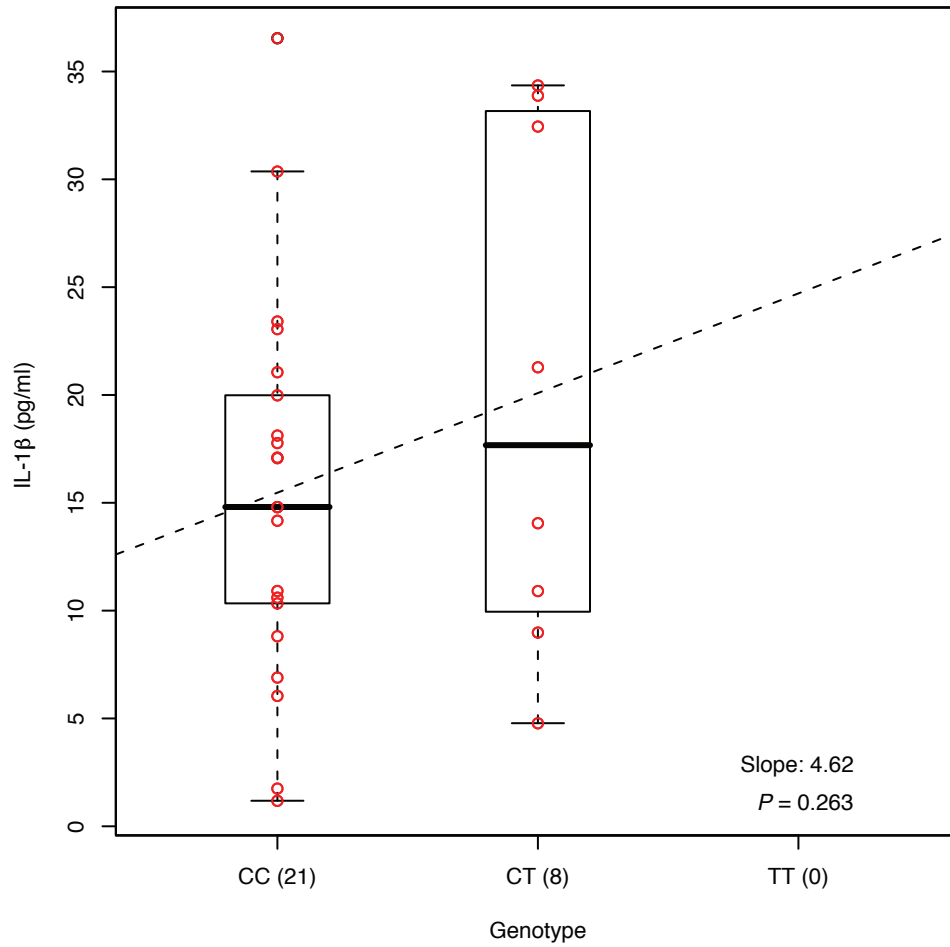
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ss107635144, unstimulated



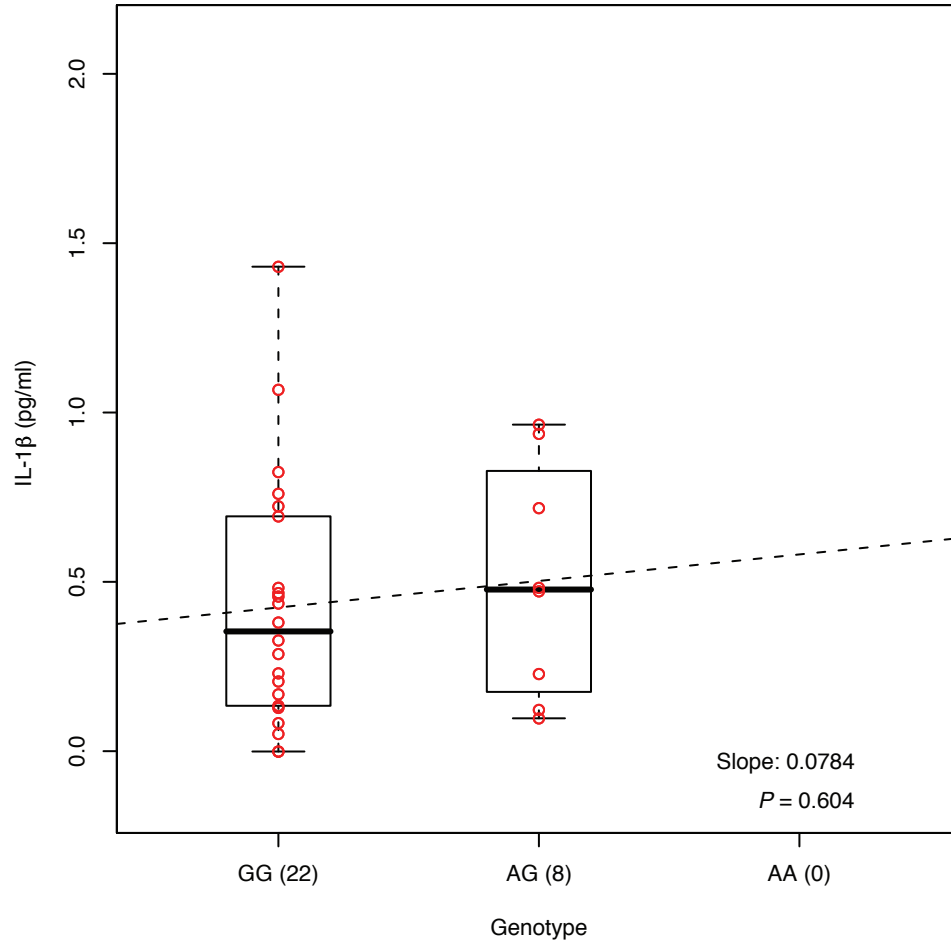
j

ss107635144, LPS



k

rs10733113, unstimulated



l

rs10733113, LPS

