

ESM Table 1. Selected SNPs used in the validation cohort for genotyping

| Candidate gene | Chr | SNP | OA, MA | BP | Associated glycan |
|----------------|-----|-----------|--------|-----------|---|
| <i>MGAT5</i> | 2 | rs2460382 | A, G | 135014116 | GP29 |
| <i>ST6GAL1</i> | 3 | rs3872724 | G, A | 186741221 | IGP16 |
| <i>ST6GAL1</i> | 3 | rs4686838 | A, G | 186743053 | IGP16 |
| <i>C3</i> | 19 | rs2230203 | C, A | 6710782 | GP19 |
| <i>C3</i> | 19 | rs1047286 | G, A | 6713262 | GP19 |
| <i>MGAT3</i> | 22 | rs137683 | G, C | 39738501 | IGP10 |
| <i>MGAT3</i> | 22 | rs137686 | G, C | 39739638 | IGP10, IGP15 |
| <i>MGAT3</i> | 22 | rs137690 | G, C | 39742825 | IGP10, IGP15 |
| <i>MGAT3</i> | 22 | rs9611156 | A, C | 39743170 | IGP10, IGP15 |
| <i>MGAT3</i> | 22 | rs137707 | G, A | 39751401 | IGP10, IGP15 |
| <i>MGAT3</i> | 22 | rs5757630 | A, C | 39754433 | IGP10 |
| <i>MGAT3</i> | 22 | rs2413588 | G, A | 39755175 | IGP10 |
| <i>MGAT3</i> | 22 | rs760742 | A, C | 39755190 | IGP10 |
| <i>MGAT3</i> | 22 | rs2413589 | G, A | 39755689 | IGP10, IGP15 |
| <i>MGAT3</i> | 22 | rs5757633 | G, A | 39756270 | IGP10 |
| <i>MGAT3</i> | 22 | rs4821887 | A, G | 39756985 | IGP10, IGP15 |
| <i>MGAT3</i> | 22 | rs1010169 | G, A | 39778167 | IGP10, IGP11, IGP15 |
| <i>MGAT3</i> | 22 | rs5757650 | G, A | 39778419 | IGP10, IGP11, IGP15 |
| <i>MGAT3</i> | 22 | rs5757678 | A, G | 39843409 | GP6, IGP6, IGP10, IGP11, IGP15, IGP19, IGP23, IGP24 |
| <i>MGAT3</i> | 22 | rs5757680 | G, A | 39844793 | GP6, IGP6, IGP10, IGP11, IGP15, IGP19, IGP23, IGP24 |
| <i>MGAT3</i> | 22 | rs137702 | G, A | 39750158 | IGP10, IGP15 |

The results are reported for the GRCh Build 37, and alleles are aligned to the TOP strand.

Chr, chromosome; BP, position of a SNP on a chromosome in base-pairs; MA, minor allele; OA, other allele; *MGAT5*, alpha-1,6-mannosylglycoprotein 6-beta-N-acetylglucosaminyltransferase gene; *MGAT3*, beta-1,4-mannosyl-glycoprotein 4-beta-N-acetylglucosaminyltransferase gene; *C3*, complement C3 gene; *ST6GAL1*, ST6 beta-galactoside alpha-2,6-sialyltransferase 1 gene

ESM Table 2. CVs (%) of the measured N-glycans among standard and duplicated samples obtained previously (Rudman N, Kifer D, Kaur S et al (2022) Children at onset of type 1 diabetes show altered N-glycosylation of plasma proteins and IgG. *Diabetologia* 65(8):1315–1327)

| Glycome | IgG | Plasma protein |
|----------------|------------|-----------------------|
| GP1 | 13.90 | 4.59 |
| GP2 | 8.98 | 2.01 |
| GP3 | 22.60 | 12.10 |
| GP4 | 3.48 | 3.68 |
| GP5 | 15.66 | 4.86 |
| GP6 | 3.08 | 3.87 |
| GP7 | 9.51 | 3.03 |
| GP8 | 1.45 | 7.98 |
| GP9 | 2.59 | 12.76 |
| GP10 | 3.62 | 3.11 |
| GP11 | 7.12 | 5.02 |
| GP12 | 10.15 | 4.92 |
| GP13 | 11.24 | 13.04 |
| GP14 | 2.78 | 3.22 |
| GP15 | 5.62 | 15.06 |
| GP16 | 3.11 | 2.59 |
| GP17 | 5.89 | 5.07 |
| GP18 | 3.08 | 2.53 |
| GP19 | 5.43 | 3.37 |
| GP20 | 12.61 | 2.60 |
| GP21 | 12.00 | 3.51 |
| GP22 | 16.46 | 2.93 |
| GP23 | 5.09 | 5.54 |
| GP24 | 6.36 | 4.64 |
| GP25 | | 22.82 |
| GP26 | | 4.42 |

| | |
|------|-------|
| GP27 | 6.68 |
| GP28 | 4.57 |
| GP29 | 18.94 |
| GP30 | 3.86 |
| GP31 | 8.69 |
| GP32 | 5.96 |
| GP33 | 5.04 |
| GP34 | 7.05 |
| GP35 | 9.52 |
| GP36 | 7.25 |
| GP37 | 8.60 |
| GP38 | 6.00 |
| GP39 | 7.72 |

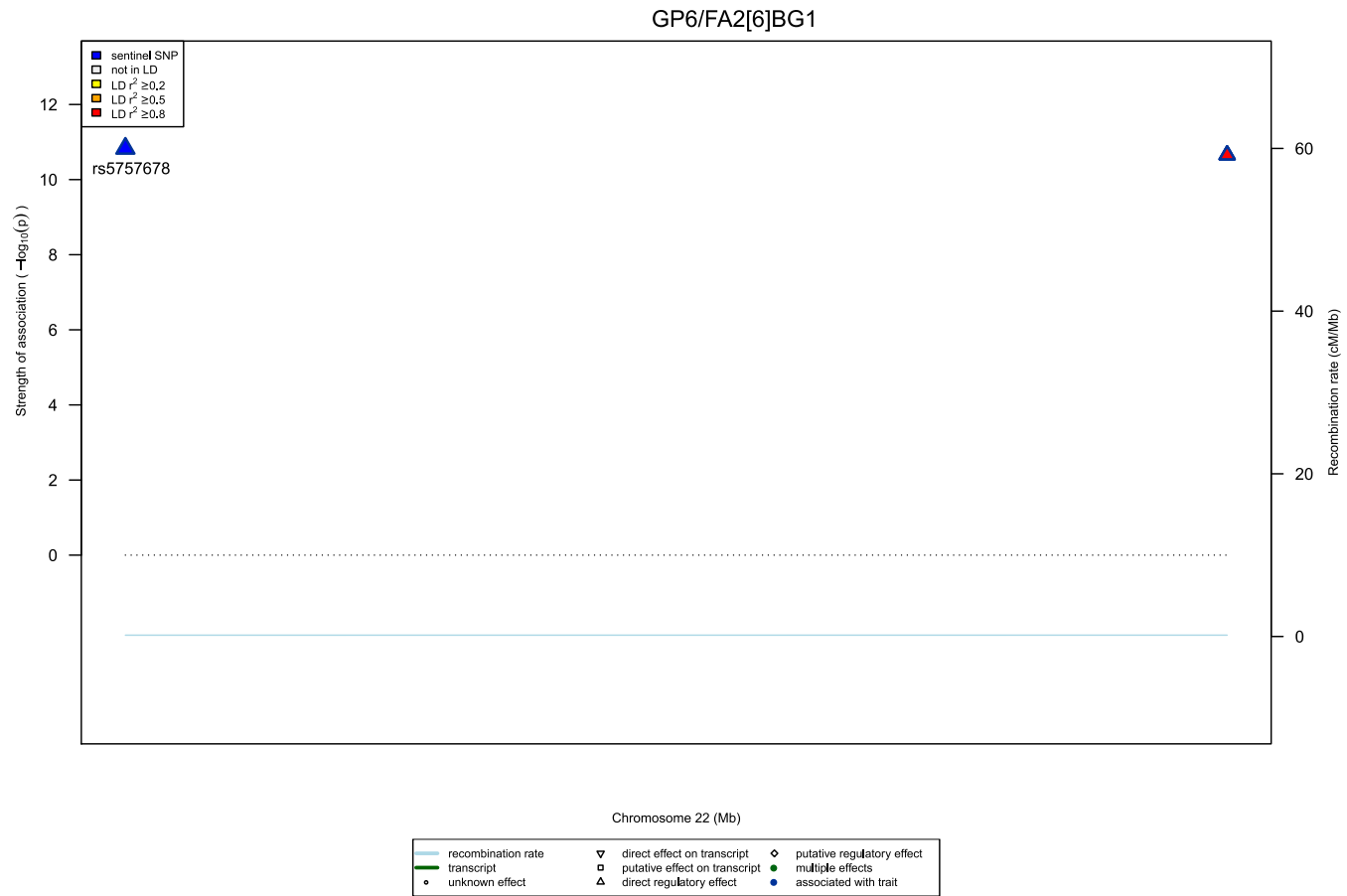
ESM Table 3. The complete list of genetic markers that reached significant genome-wide association ($p < 2.4 \times 10^{-9}$) with IgG N-glycans in the discovery cohort

| Chr | Candidate gene | N | Glycan | SNP | p | OA, MA (MAF) | β (SE) | R^2 | T | BP |
|-----|----------------|------|--------|-----------|------------------------|--------------|---------------|-------|-------|-----------|
| 3 | <i>ST6GALI</i> | 1056 | IGP16 | rs3872724 | 1.81×10^{-22} | G, A (0.37) | -0.16 (0.016) | 0.09 | -9.98 | 186741221 |
| 3 | <i>ST6GALI</i> | 1056 | IGP16 | rs4686838 | 1.09×10^{-15} | A, G (0.44) | -0.13 (0.016) | 0.06 | -8.14 | 186743053 |
| 22 | <i>MGAT3</i> | 1056 | IGP6 | rs5757678 | 1.57×10^{-13} | A, G (0.27) | 0.39 (0.052) | 0.05 | 7.48 | 39843409 |
| 22 | <i>MGAT3</i> | 1045 | IGP6 | rs5757680 | 2.03×10^{-13} | G, A (0.26) | 0.39 (0.053) | 0.05 | 7.45 | 39844793 |
| 22 | <i>MGAT3</i> | 1056 | IGP10 | rs1010169 | 6.39×10^{-21} | G, A (0.34) | 0.34 (0.036) | 0.08 | 9.59 | 39778167 |
| 22 | <i>MGAT3</i> | 1056 | IGP10 | rs137683 | 6.18×10^{-10} | G, C (0.23) | 0.26 (0.041) | 0.04 | 6.24 | 39738501 |
| 22 | <i>MGAT3</i> | 1052 | IGP10 | rs137686 | 5.30×10^{-13} | G, C (0.25) | 0.29 (0.04) | 0.05 | 7.31 | 39739638 |
| 22 | <i>MGAT3</i> | 1056 | IGP10 | rs137690 | 9.32×10^{-13} | G, C (0.25) | 0.29 (0.04) | 0.05 | 7.23 | 39742825 |
| 22 | <i>MGAT3</i> | 1048 | IGP10 | rs137702 | 5.95×10^{-14} | G, A (0.24) | 0.31 (0.041) | 0.05 | 7.61 | 39750158 |
| 22 | <i>MGAT3</i> | 1056 | IGP10 | rs137707 | 8.76×10^{-14} | G, A (0.24) | 0.31 (0.041) | 0.05 | 7.56 | 39751401 |
| 22 | <i>MGAT3</i> | 1036 | IGP10 | rs2413588 | 1.20×10^{-10} | G, A (0.29) | 0.25 (0.039) | 0.04 | 6.51 | 39755175 |
| 22 | <i>MGAT3</i> | 1056 | IGP10 | rs2413589 | 1.14×10^{-13} | G, A (0.24) | 0.31 (0.041) | 0.05 | 7.52 | 39755689 |
| 22 | <i>MGAT3</i> | 1056 | IGP10 | rs4821887 | 8.76×10^{-14} | A, G (0.24) | 0.31 (0.041) | 0.05 | 7.56 | 39756985 |
| 22 | <i>MGAT3</i> | 1056 | IGP10 | rs5757630 | 7.10×10^{-10} | A, C (0.30) | 0.24 (0.038) | 0.04 | 6.22 | 39754433 |
| 22 | <i>MGAT3</i> | 1056 | IGP10 | rs5757633 | 7.10×10^{-10} | G, A (0.30) | 0.24 (0.038) | 0.04 | 6.22 | 39756270 |
| 22 | <i>MGAT3</i> | 1056 | IGP10 | rs5757650 | 1.14×10^{-20} | G, A (0.35) | 0.34 (0.036) | 0.08 | 9.52 | 39778419 |
| 22 | <i>MGAT3</i> | 1056 | IGP10 | rs5757678 | 3.04×10^{-26} | A, G (0.27) | 0.41 (0.038) | 0.1 | 10.89 | 39843409 |
| 22 | <i>MGAT3</i> | 1045 | IGP10 | rs5757680 | 2.12×10^{-26} | G, A (0.26) | 0.41 (0.038) | 0.1 | 10.93 | 39844793 |
| 22 | <i>MGAT3</i> | 1056 | IGP10 | rs760742 | 7.10×10^{-10} | A, C (0.30) | 0.24 (0.038) | 0.04 | 6.22 | 39755190 |
| 22 | <i>MGAT3</i> | 1056 | IGP10 | rs9611156 | 5.09×10^{-12} | A, C (0.25) | 0.28 (0.04) | 0.04 | 6.98 | 39743170 |
| 22 | <i>MGAT3</i> | 1056 | IGP11 | rs1010169 | 2.82×10^{-11} | G, A (0.34) | 0.03 (0.004) | 0.04 | 6.73 | 39778167 |
| 22 | <i>MGAT3</i> | 1056 | IGP11 | rs5757650 | 7.00×10^{-11} | G, A (0.35) | 0.03 (0.004) | 0.04 | 6.59 | 39778419 |
| 22 | <i>MGAT3</i> | 1056 | IGP11 | rs5757678 | 3.40×10^{-13} | A, G (0.27) | 0.03 (0.005) | 0.05 | 7.37 | 39843409 |
| 22 | <i>MGAT3</i> | 1045 | IGP11 | rs5757680 | 1.63×10^{-13} | G, A (0.26) | 0.04 (0.005) | 0.05 | 7.48 | 39844793 |
| 22 | <i>MGAT3</i> | 1056 | IGP15 | rs1010169 | 1.51×10^{-11} | G, A (0.34) | 0.1 (0.014) | 0.04 | 6.82 | 39778167 |
| 22 | <i>MGAT3</i> | 1052 | IGP15 | rs137686 | 6.66×10^{-10} | G, C (0.25) | 0.1 (0.016) | 0.04 | 6.23 | 39739638 |
| 22 | <i>MGAT3</i> | 1056 | IGP15 | rs137690 | 6.07×10^{-10} | G, C (0.25) | 0.1 (0.016) | 0.04 | 6.25 | 39742825 |
| 22 | <i>MGAT3</i> | 1048 | IGP15 | rs137702 | 2.88×10^{-10} | G, A (0.24) | 0.1 (0.016) | 0.04 | 6.37 | 39750158 |

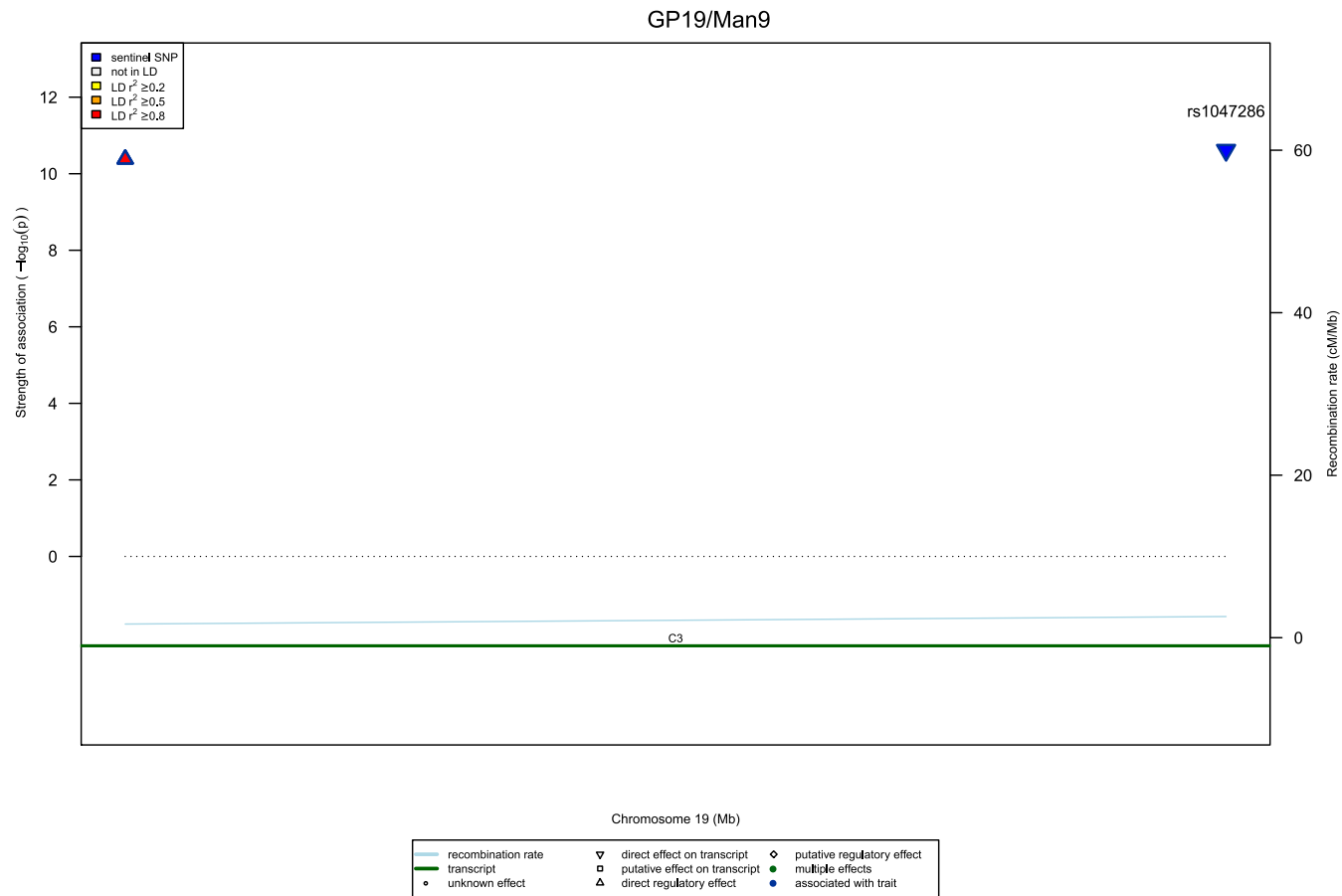
| | | | | | | | | | | |
|----|--------------|------|-------|-----------|------------------------|-------------|---------------|------|-------|----------|
| 22 | <i>MGAT3</i> | 1056 | IGP15 | rs137707 | 3.66×10^{-10} | G, A (0.24) | 0.1 (0.016) | 0.04 | 6.33 | 39751401 |
| 22 | <i>MGAT3</i> | 1056 | IGP15 | rs2413589 | 5.36×10^{-10} | G, A (0.24) | 0.1 (0.016) | 0.04 | 6.27 | 39755689 |
| 22 | <i>MGAT3</i> | 1056 | IGP15 | rs4821887 | 3.66×10^{-10} | A, G (0.24) | 0.1 (0.016) | 0.04 | 6.33 | 39756985 |
| 22 | <i>MGAT3</i> | 1056 | IGP15 | rs5757650 | 3.60×10^{-11} | G, A (0.35) | 0.09 (0.014) | 0.04 | 6.69 | 39778419 |
| 22 | <i>MGAT3</i> | 1056 | IGP15 | rs5757678 | 3.98×10^{-15} | A, G (0.27) | 0.12 (0.015) | 0.06 | 7.97 | 39843409 |
| 22 | <i>MGAT3</i> | 1045 | IGP15 | rs5757680 | 1.04×10^{-15} | G, A (0.26) | 0.12 (0.015) | 0.06 | 8.15 | 39844793 |
| 22 | <i>MGAT3</i> | 1056 | IGP15 | rs9611156 | 9.50×10^{-10} | A, C (0.25) | 0.1 (0.015) | 0.03 | 6.17 | 39743170 |
| 22 | <i>MGAT3</i> | 1056 | IGP19 | rs5757678 | 2.69×10^{-10} | A, G (0.27) | 0.1 (0.016) | 0.04 | 6.38 | 39843409 |
| 22 | <i>MGAT3</i> | 1045 | IGP19 | rs5757680 | 1.38×10^{-10} | G, A (0.26) | 0.1 (0.016) | 0.04 | 6.48 | 39844793 |
| 22 | <i>MGAT3</i> | 1056 | IGP23 | rs5757678 | 6.16×10^{-11} | A, G (0.27) | -0.19 (0.028) | 0.04 | -6.61 | 39843409 |
| 22 | <i>MGAT3</i> | 1045 | IGP23 | rs5757680 | 5.04×10^{-11} | G, A (0.26) | -0.19 (0.028) | 0.04 | -6.64 | 39844793 |
| 22 | <i>MGAT3</i> | 1056 | IGP24 | rs5757678 | 1.00×10^{-11} | A, G (0.27) | 0.12 (0.017) | 0.04 | 6.88 | 39843409 |
| 22 | <i>MGAT3</i> | 1045 | IGP24 | rs5757680 | 7.65×10^{-12} | G, A (0.26) | 0.12 (0.017) | 0.04 | 6.92 | 39844793 |

The results are reported for the GRCh Build 37, and alleles are aligned to the TOP strand. The β coefficient is reported for the minor allele and expressed as the relative glycan abundance (%).

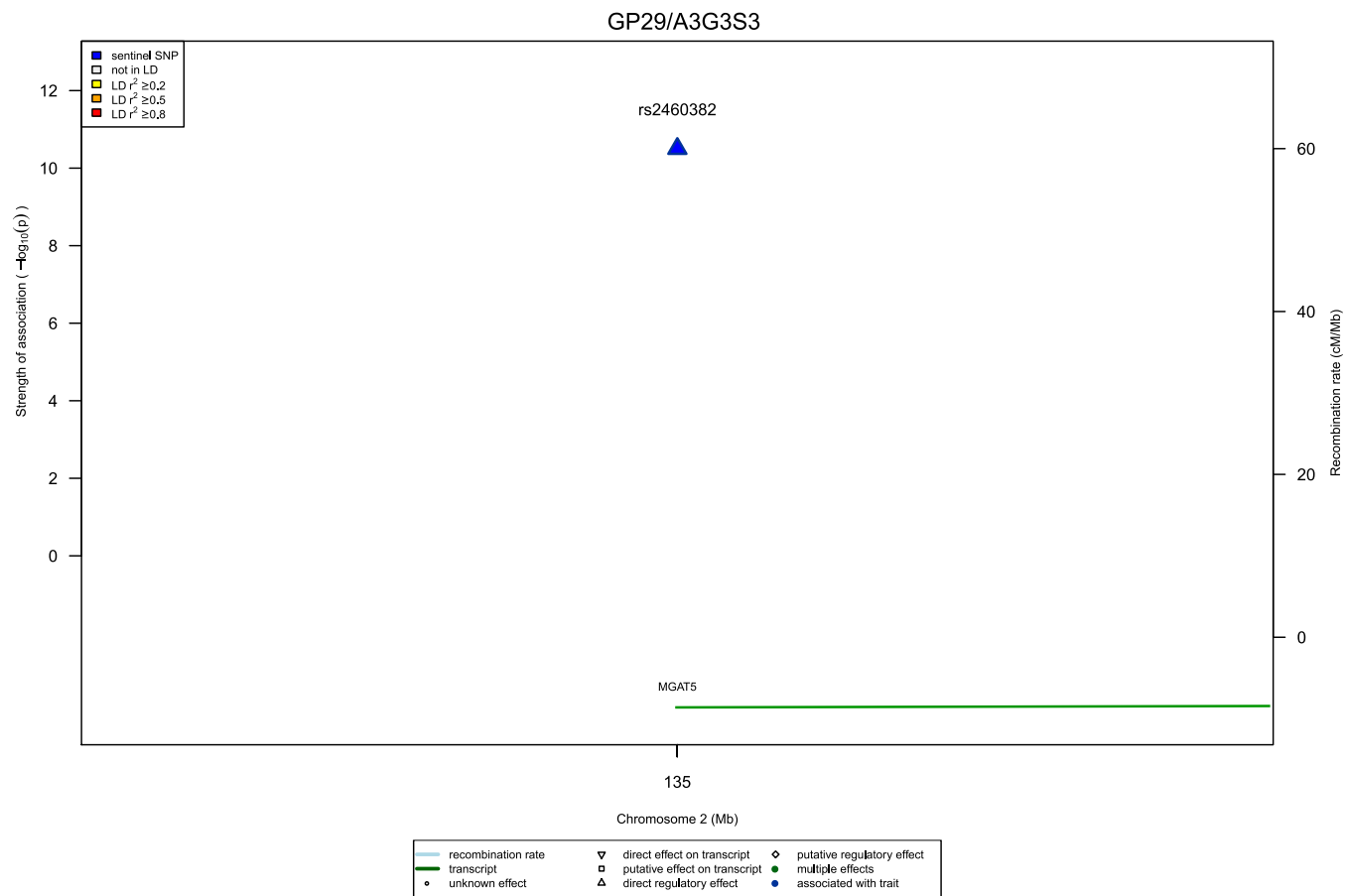
Chr, chromosome; N, sample size; MA, minor allele; OA, other allele; MAF, minor allele frequency; R^2 , percentage of explained glycan variance; BP, position of a SNP on a chromosome in base-pairs; *ST6GALI*, ST6 beta-galactoside alpha-2,6-sialyltransferase 1 gene; *MGAT3*, beta-1,4-mannosyl-glycoprotein 4-beta-N-acetylglucosaminyltransferase gene



ESM Fig. 1 Regional association plot for GP6 glycan. Figure was created using SNIQA v3.4 from November 2020, GRCh37.p13, Ensembl version 87, 1000 genomes phase 3 v5, European (Arnold M, Raffler J, Pfeufer A, Suhre K, Kastenmüller G (2015) SNIQA: an interactive, genetic variant-centered annotation browser. *Bioinforma* 31(8):1334–1336). The plot shows the strength of association ($-\log_{10}(P)$), recombination rate, genes, and regulatory elements. The variants' symbols depict the functional annotations, the colors depict the pairwise LD correlations to the sentinel variant



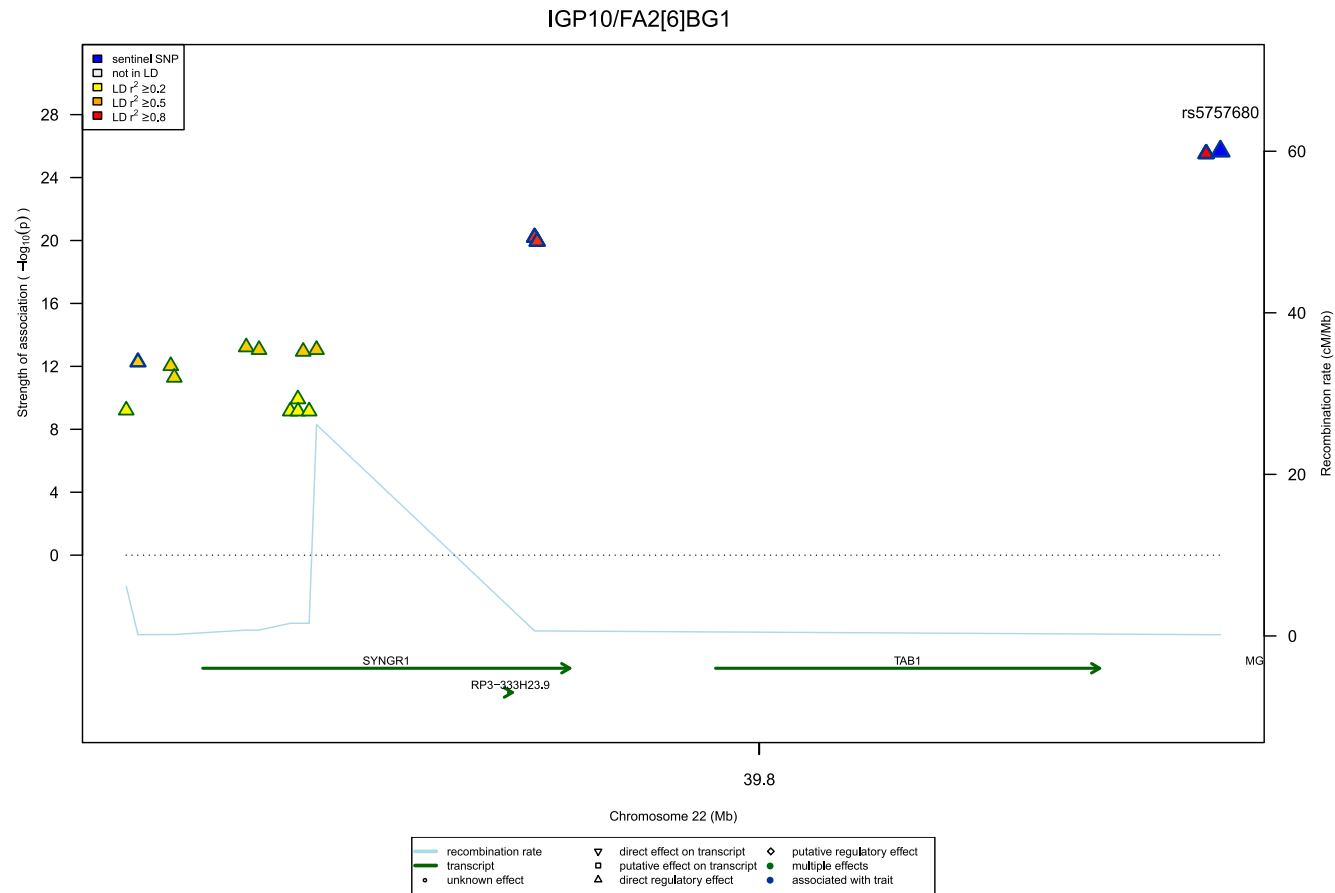
ESM Fig. 2 Regional association plot for GP19 glycan. Figure was created using SNI PA v3.4 from November 2020, GRCh37.p13, Ensembl version 87, 1000 genomes phase 3 v5, European (Arnold M, Raffler J, Pfeufer A, Suhre K, Kastenmüller G (2015) SNI PA: an interactive, genetic variant-centered annotation browser. *Bioinforma* 31(8):1334–1336). The plot shows the strength of association ($-\log_{10}(P)$), recombination rate, genes, and regulatory elements. The variants' symbols depict the functional annotations, the colors depict the pairwise LD correlations to the sentinel variant. C3, complement C3 gene



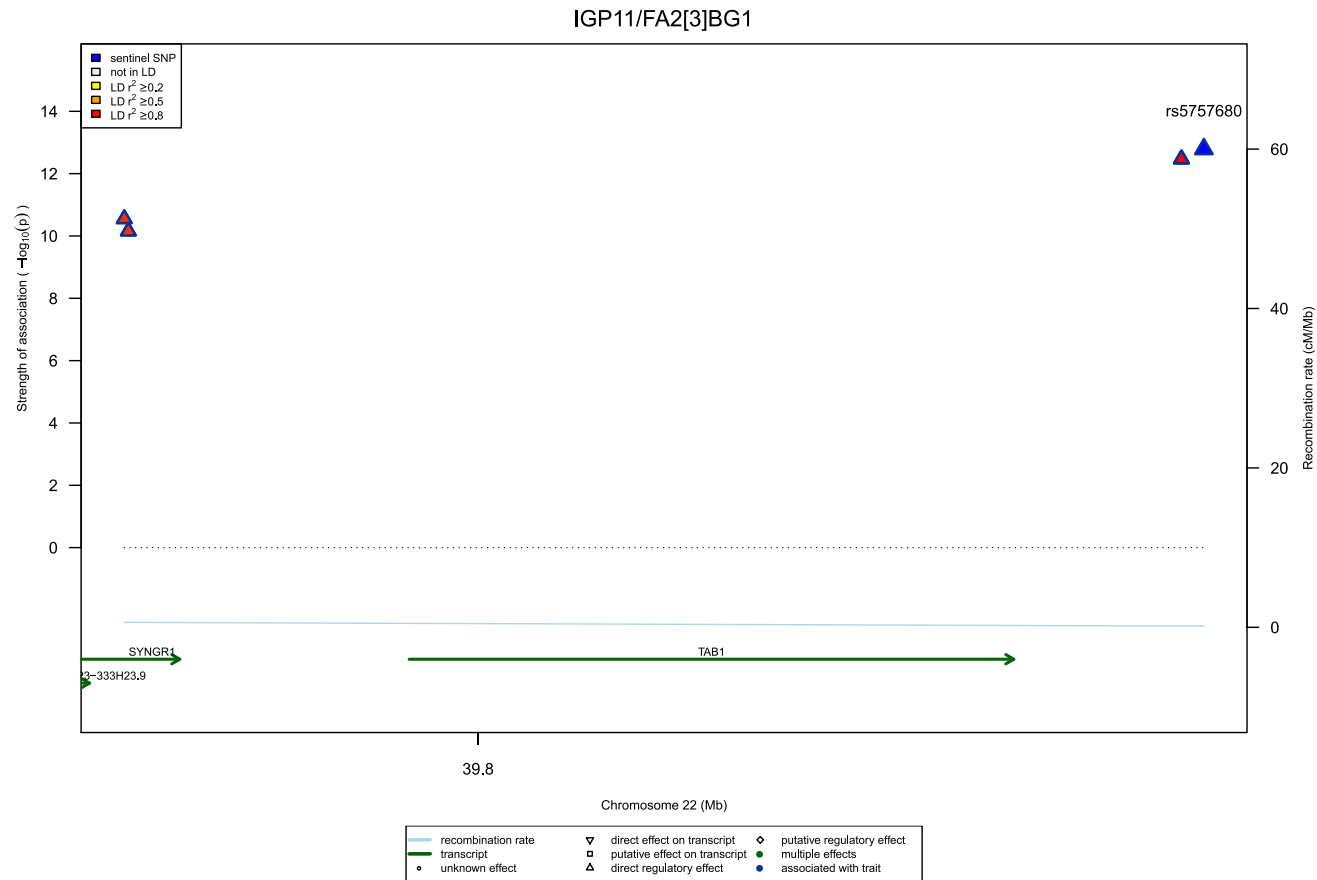
ESM Fig. 3 Regional association plot for GP29 glycan. Figure was created using SNIpa v3.4 from November 2020, GRCh37.p13, Ensembl version 87, 1000 genomes phase 3 v5, European (Arnold M, Raffler J, Pfeufer A, Suhre K, Kastenmüller G (2015) SNIpa: an interactive, genetic variant-centered annotation browser. *Bioinforma* 31(8):1334–1336). The plot shows the strength of association ($-\log_{10}(P)$), recombination rate, genes, and regulatory elements. The variants' symbols depict the functional annotations, the colors depict the pairwise LD correlations to the sentinel variant. *MGAT5*, alpha-1,6-mannosylglycoprotein 6-beta-*N*-acetylglucosaminyltransferase gene



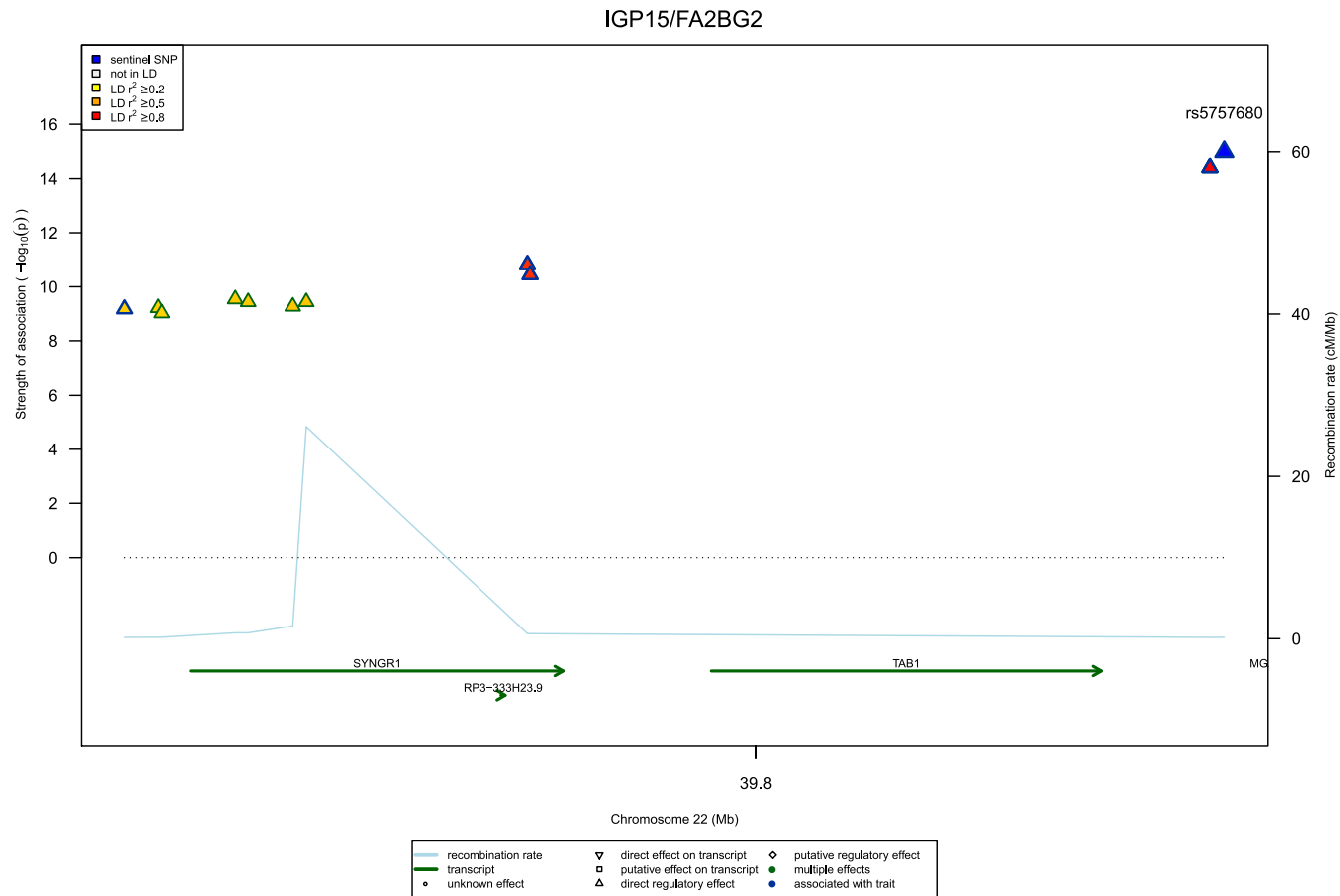
ESM Fig. 4 Regional association plot for IGP6 glycan. Figure was created using SNIPIA v3.4 from November 2020, GRCh37.p13, Ensembl version 87, 1000 genomes phase 3 v5, European (Arnold M, Raffler J, Pfeufer A, Suhre K, Kastenmüller G (2015) SNIPIA: an interactive, genetic variant-centered annotation browser. *Bioinforma* 31(8):1334–1336). The plot shows the strength of association ($-\log_{10}(P)$), recombination rate, genes, and regulatory elements. The variants' symbols depict the functional annotations, the colors depict the pairwise LD correlations to the sentinel variant



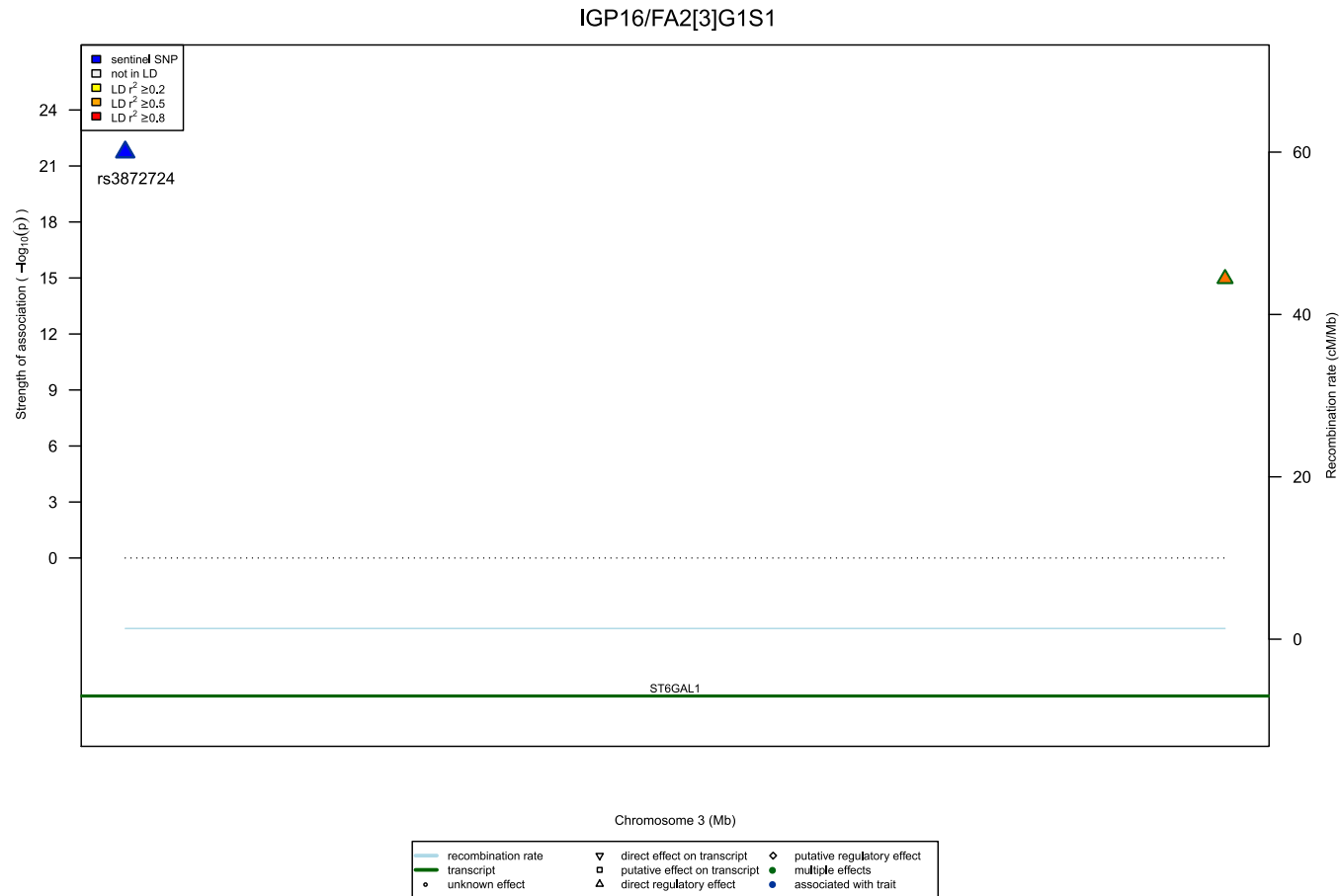
ESM Fig. 5 Regional association plot for IGP10 glycan. Figure was created using SNIQA v3.4 from November 2020, GRCh37.p13, Ensembl version 87, 1000 genomes phase 3 v5, European (Arnold M, Raffler J, Pfeufer A, Suhre K, Kastenmüller G (2015) SNIQA: an interactive, genetic variant-centered annotation browser. *Bioinforma* 31(8):1334–1336). The plot shows the strength of association ($-\log_{10}(P)$), recombination rate, genes, and regulatory elements. The variants' symbols depict the functional annotations, the colors depict the pairwise LD correlations to the sentinel variant. *SYNGR1*, synaptogyrin 1 gene; *TAB1*, TGF-beta activated kinase 1 (MAP3K7) binding protein 1 gene



ESM Fig. 6 Regional association plot for IGP11 glycan. Figure was created using SNIQA v3.4 from November 2020, GRCh37.p13, Ensembl version 87, 1000 genomes phase 3 v5, European (Arnold M, Raffler J, Pfeufer A, Suhre K, Kastenmüller G (2015) SNIQA: an interactive, genetic variant-centered annotation browser. *Bioinforma* 31(8):1334–1336). The plot shows the strength of association ($-\log_{10}(P)$), recombination rate, genes, and regulatory elements. The variants' symbols depict the functional annotations, the colors depict the pairwise LD correlations to the sentinel variant. *SYNGR1*, synaptogyrin 1 gene; *TAB1*, TGF-beta activated kinase 1 (MAP3K7) binding protein 1 gene



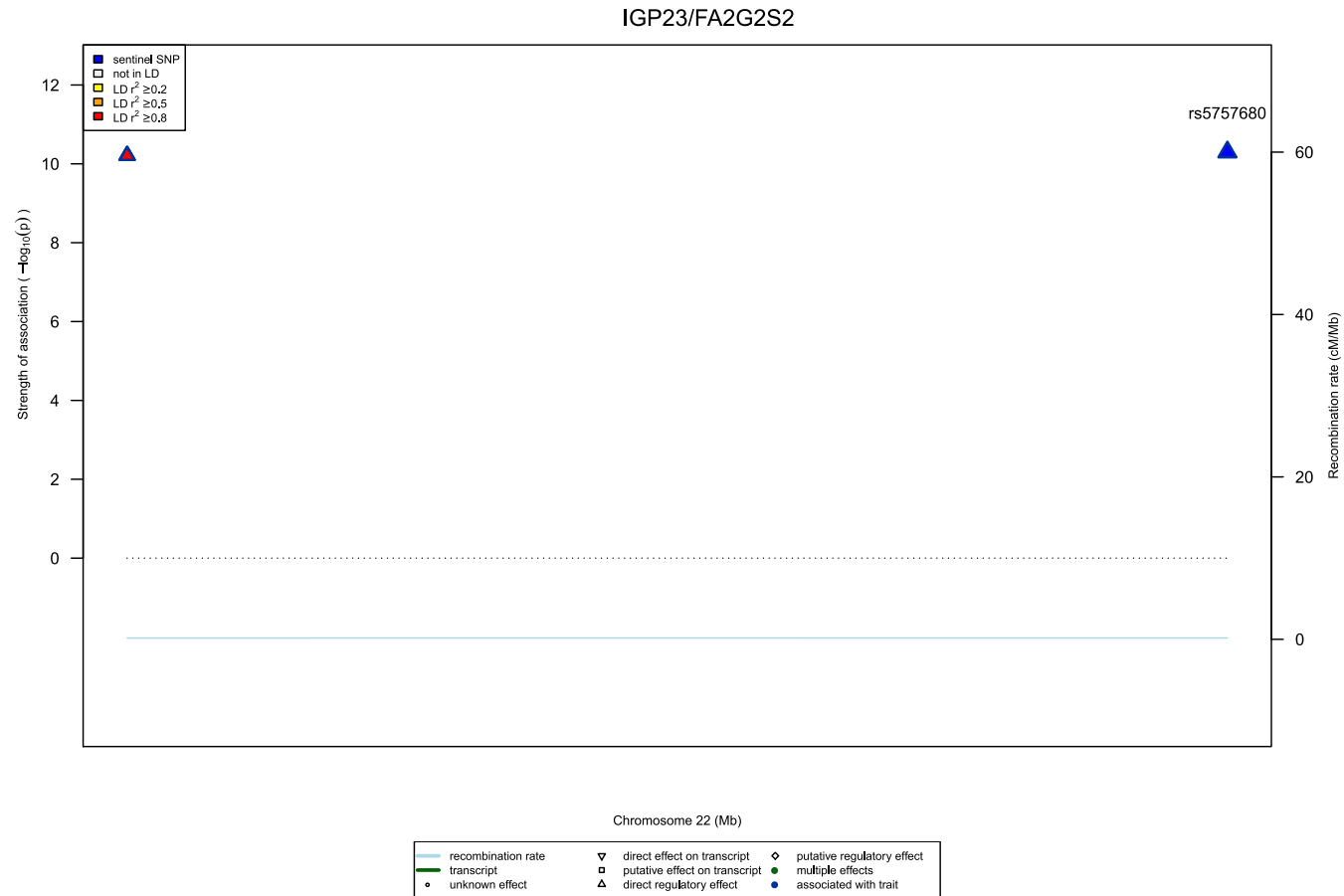
ESM Fig. 7 Regional association plot for IGP15 glycan. Figure was created using SNIQA v3.4 from November 2020, GRCh37.p13, Ensembl version 87, 1000 genomes phase 3 v5, European (Arnold M, Raffler J, Pfeufer A, Suhre K, Kastenmüller G (2015) SNIQA: an interactive, genetic variant-centered annotation browser. *Bioinforma* 31(8):1334–1336). The plot shows the strength of association ($-\log_{10}(P)$), recombination rate, genes, and regulatory elements. The variants' symbols depict the functional annotations, the colors depict the pairwise LD correlations to the sentinel variant. *SYNGR1*, synaptogyrin 1 gene; *TAB1*, TGF-beta activated kinase 1 (MAP3K7) binding protein 1 gene



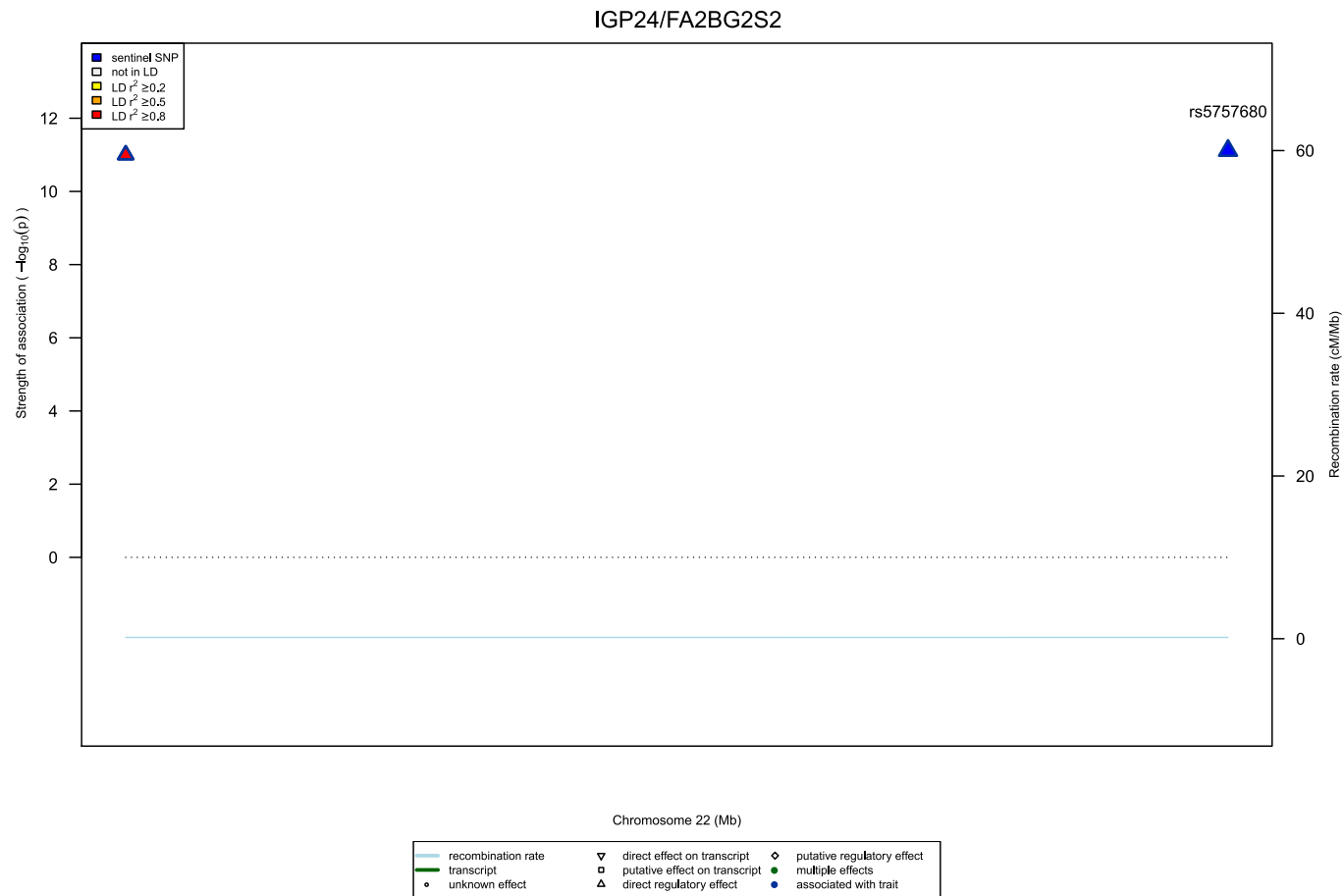
ESM Fig. 8 Regional association plot for IGP16 glycan. Figure was created using SNI_{PA} v3.4 from November 2020, GRCh37.p13, Ensembl version 87, 1000 genomes phase 3 v5, European (Arnold M, Raffler J, Pfeufer A, Suhre K, Kastenmüller G (2015) SNI_{PA}: an interactive, genetic variant-centered annotation browser. *Bioinforma* 31(8):1334–1336). The plot shows the strength of association ($-\log_{10}(P)$), recombination rate, genes, and regulatory elements. The variants' symbols depict the functional annotations, the colors depict the pairwise LD correlations to the sentinel variant. *ST6GAL1*, ST6 beta-galactoside alpha-2,6-sialyltransferase 1 gene



ESM Fig. 9 Regional association plot for IGP19 glycan. Figure was created using SNI_{PA} v3.4 from November 2020, GRCh37.p13, Ensembl version 87, 1000 genomes phase 3 v5, European (Arnold M, Raffler J, Pfeufer A, Suhre K, Kastenmüller G (2015) SNI_{PA}: an interactive, genetic variant-centered annotation browser. *Bioinforma* 31(8):1334–1336). The plot shows the strength of association ($-\log_{10}(P)$), recombination rate, genes, and regulatory elements. The variants' symbols depict the functional annotations, the colors depict the pairwise LD correlations to the sentinel variant



ESM Fig. 10 Regional association plot for IGP23 glycan. Figure was created using SNIpA v3.4 from November 2020, GRCh37.p13, Ensembl version 87, 1000 genomes phase 3 v5, European (Arnold M, Raffler J, Pfeufer A, Suhre K, Kastenmüller G (2015) SNIpA: an interactive, genetic variant-centered annotation browser. *Bioinforma* 31(8):1334–1336). The plot shows the strength of association ($-\log_{10}(P)$), recombination rate, genes, and regulatory elements. The variants' symbols depict the functional annotations, the colors depict the pairwise LD correlations to the sentinel variant



ESM Fig. 11 Regional association plot for IGP24 glycan. Figure was created using SNIIPA v3.4 from November 2020, GRCh37.p13, Ensembl version 87, 1000 genomes phase 3 v5, European (Arnold M, Raffler J, Pfeufer A, Suhre K, Kastenmüller G (2015) SNIIPA: an interactive, genetic variant-centered annotation browser. *Bioinforma* 31(8):1334–1336). The plot shows the strength of association ($-\log_{10}(P)$), recombination rate, genes, and regulatory elements. The variants' symbols depict the functional annotations, the colors depict the pairwise LD correlations to the sentinel variant