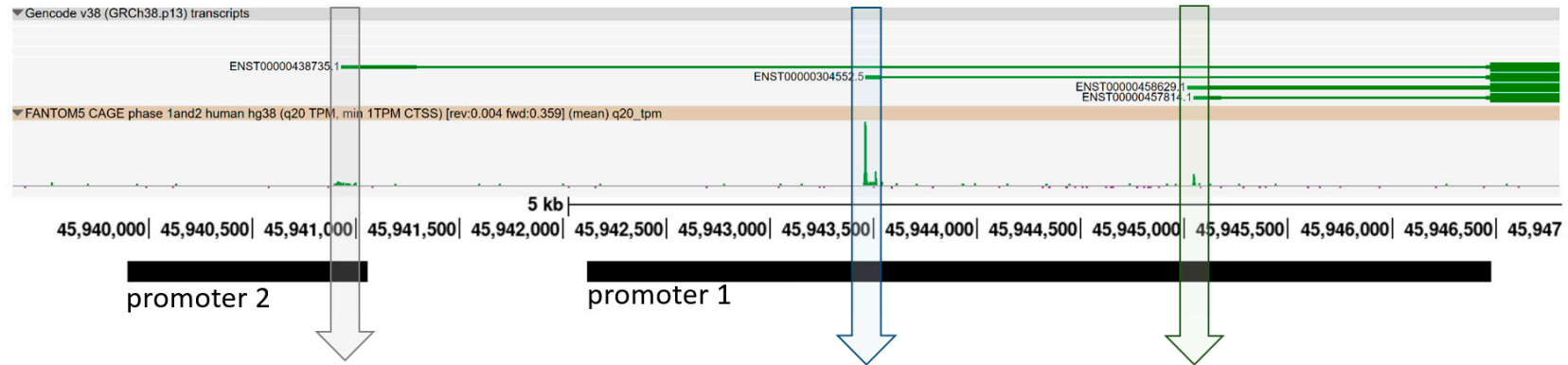(legend is on the next page)

**Figure S1.** Schematic representation of the regulatory elements in the 3p21.31 locus around rs71327024 and *CXCR6* promoter based on the UCSC Genome Browser visualization (GRCh38/hg38). In the top section, light gray and light blue areas highlight the putative *CXCR6* promoter regions. In the bottom section, the light red area marks the putative enhancer in the 3p21.31 locus and the vertical red line shows the location of the rs71327024. Histograms indicate the location of histone modifications in T cells typical of regulatory elements (H3K4 mono/tri-methylation, H3K27 acetylation; Roadmap epigenomic data). Chromatin state segmentation in different subsets of T cells represents ChromHMM model (Roadmap): red and orange denote a state with a promoter-like signature, yellow denote states with an enhancer-like signature, green denotes a signature for transcribed region. Rectangles mark regulatory elements positions according to ENCODE, DNase I hypersensitivity clusters (DNase I) in T cells (Roadmap) and transcription factor ChIP-seq (TF clusters; ENCODE).

# a

Gencode v38 (GRCh38.p13) transcripts

ENST00000438735.1

ENST00000304552.5

ENST00000458629.1
ENST00000457814.1

FANTOM5 CAGE phase 1and2 human hg38 (q20 TPM, min 1TPM CTSS) [rev:0.004 fwd:0.359] (mean) q20_tpm

5 kb

45,940,000| 45,940,500| 45,941,000| 45,941,500| 45,942,000| 45,942,500| 45,943,000| 45,943,500| 45,944,000| 45,944,500| 45,945,000| 45,945,500| 45,946,000| 45,946,500| 45,947

promoter 2

promoter 1

| Cell type | CAGE tag counts |
|---|---|
| chorionic membrane cells, donor3 | 50.115 |
| chorionic membrane cells, donor1 | 47.645 |
| choriocarcinoma cell line:SCH | 22.292 |
| chorionic membrane cells, donor2 | 15.826 |
| choriocarcinoma cell line:T3M-3 | 14.057 |
| amniotic membrane cells, donor1 | 9.967 |
| placenta, adult, pool1 | 9.273 |
| pancreatic carcinoma cell line:NOR-P1 | 3.202 |
| choriocarcinoma cell line:BeWo | 2.495 |
| Universal RNA - Human Normal Tissues | 1.808 |

| Cell type | CAGE tag counts |
|---|---|
| CD4+CD25-CD45RA- memory conventional T cells expanded, donor2 | 219.676 |
| CD4+CD25-CD45RA- memory conventional T cells expanded, donor3 | 157.987 |
| CD4+CD25+CD45RA- memory regulatory T cells expanded, donor1 | 144.358 |
| gamma delta positive T cells, donor1 | 142.637 |
| CD4+CD25-CD45RA+ naive conventional T cells expanded, donor2 | 138.766 |
| CD4+CD25-CD45RA+ naive conventional T cells expanded, donor3 | 123.578 |
| CD4+CD25-CD45RA- memory conventional T cells expanded, donor1 | 87.047 |
| CD4+CD25+CD45RA- memory regulatory T cells expanded, donor3 | 80.933 |
| CD4+CD25+CD45RA- memory regulatory T cells expanded, donor2 | 68.653 |
| CD4+CD25-CD45RA+ naive conventional T cells expanded, donor1 | 64.083 |

| Cell type | CAGE tag counts |
|---|---|
| CD4+CD25+CD45RA- memory regulatory T cells, donor1 | 17.723 |
| gamma delta positive T cells, donor1 | 15.333 |
| CD4+CD25-CD45RA- memory conventional T cells, donor1 | 12.087 |
| CD8+ T Cells, donor1 | 11.455 |
| CD4+CD25+CD45RA- memory regulatory T cells expanded, donor1 | 10.852 |
| CD4+CD25+CD45RA- memory regulatory T cells, donor2 | 16316 |
| Natural Killer Cells, donor1 | 7.435 |
| CD4+CD25+CD45RA- memory regulatory T cells expanded, donor3 | 6.206 |
| CD8+ T Cells (pluriselect), donor090325, donation2 | 5.667 |
| CD8+ T Cells, donor2 | 5.586 |

# b
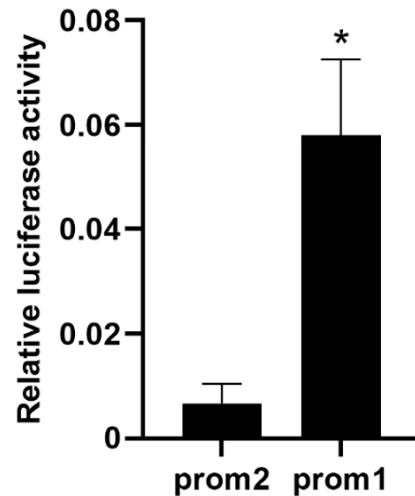


**Figure S2.** The activity of *CXCR6* promoter variants. (**a**) Schematic representation of the promoters and corresponding CAGE tag counts for three TSSs based on FANTOM5 hg38 human promoterome collection. Arrows highlight areas of TSSs and point to corresponding tables with specific CAGE tag counts for different cell types. (**b**) Relative luciferase activity in Jurkat cells transfected with constructs containing *CXCR6* promoter variants. All data were normalized to Renilla luciferase internal reference. Data represent five (promoter 1) and three (promoter 2) independent experiments with mean values ± SEM, * $p < 0.05$, as calculated by unpaired Student's t-test.
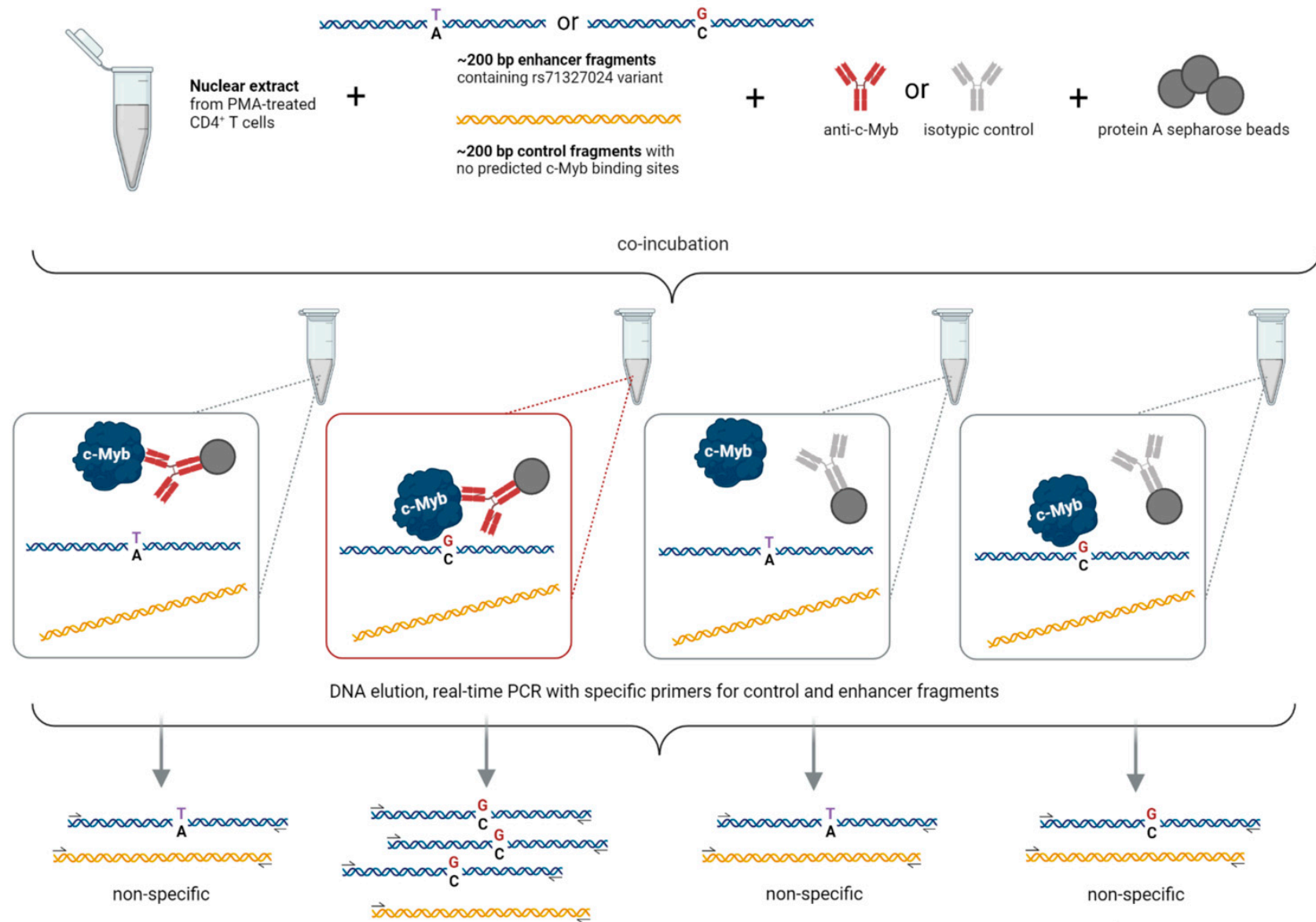
**Figure S3.** Scheme of the DNA pull-down assay used in the study (created with BioRender.com).

**Table S1.** rs71327024(T) minor allele frequencies for different populations (NCBI dbSNP database).

| Minor allele frequencies | Global | American | African | East Asian | European | South Asian |
|---|---|---|---|---|---|---|
| **1000Genomes_30x** | 0.1087 | 0.061 | 0.0034 | 0.0462 | 0.1161 | 0.3569 |
| **gnomAD** | 0.081548 | 0.06780 | 0.01863 | 0.0441 | 0.11609 | no data |
| **ALFA** | 0.10439 | no data | 0.0187 | 0.06 | 0.12537 | 0.32 |

**Table S2.** Oligonucleotides utilized in the study.

| Primer | Nucleotide sequence 5′- 3′ |
|---|---|
| prom1CXCR6-KpnI-Fw | TTAAGGTACCAAAGGCCTGCAAACCTACTAGAG |
| prom1CXCR6-XhoI-Rev | TTAACTCGAGGGTGTCTGTTCTGATGAACACCT |
| prom2CXCR6-KpnI-Fw | TTAAGGTACCAAGTGCTCAATTCAAGTGGCACTA |
| prom2CXCR6-XhoI-Rev | TTAACTCGAGAGGATGAGCTGAGAGATCATCTG |
| 3p21.31-enh-BamHI-Fw | TTTTGGATCCTTCAGTTTAGAATCTGGAACTGACC |
| 3p21.31-enh-SalI-Rev | TTTTGTCGACGTGGCTCAACATTTACATTGCAGG |
| contr-nonenh-BamHI-Fw | TTTTGGATCCCACATTAATGCCCTTGGGATAGTC |
| contr-nonenh-SalI-Rev | TTTTGTCGACCAAGGGCAATAGTGACTGGTTCC |
| real-time_c-Myb-Fw | ATCTCCCGAATCGAACAGATGT |
| real-time_c-Myb-Rev | TGCTTGGCAATAACAGACCAAC |
| real-time_CXCR6-Fw | CAGTTCAGCAAGGTCTTTCTGCC |
| real-time_CXCR6-Rev | AGGTTCACCAGGAACACATCCG |
| siRNA-323_c-Myb-sense | GAAAUACGGUCCGAAACGUdTdT |
| siRNA-323_c-Myb-antisense | ACGUUUCGGACCGUAUUUCdAdG |
| scrambled_c-Myb-sense | GCAUACCACGGAGUUAGAAdTdT |
| scrambled_c-Myb-antisense | UUCUAACUCCGUGGUAUGCdAdG |
| pull-down-Fw | TGGGTTCCTGGTGGTGAATG |
| pull-down-Rev | TGCTCCAGCCCTTGAAGAAG |
| pull-down-control-Fw | AGCCATGGCCTTCTGTTTT |
| pull-down-control-Rev | GTGTACAAGACCTGGGTGGA |
| overlap_rs71327024(T)-Fw | GATGTGGCATTTTTTGCTGTGGTTATGA |
| overlap_rs71327024(T)-Rev | GCAAAAAAATGCCACATCAAACTGAGA |