

## SUPPLEMENTARY INFORMATION

### Variants in the *DDX6-CXCR5* autoimmune disease risk locus influence the regulatory network in immune cells and salivary gland

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### Consortium Acknowledgments and Funding\*:

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The study was approved by the following ethic committees: Comitato Etico Area 2 (Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano and University of Milan); approval no. 425bis Nov 19, 2014, and no. 671\_2018 Sep 19, 2018; Klinikum der Universitaet zu Koeln, Cologne, Germany. Geschäftsstelle Ethikkommission; Pôle de pathologies rhumatismales systémiques et inflammatoires, Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, Brussels, Belgium. Comité d'Éthique Hospitalo-Facultaire; University of Szeged, Szeged, Hungary. Csongrad Megyei Kormányhivatal; Hospital Clinic I Provincia, Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona, Spain. Comité Ética de Investigación Clínica del Hospital Clínic de Barcelona. Hospital Clínic del Barcelona; Servicio Andaluz de Salud, Hospital Universitario Reina Sofía Córdoba, Spain. Comité de Ética e la Investigación de Centro de Granada (CEI – Granada); Centro Hospitalar do Porto, Portugal.

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PRECISESADS Study was funded by the Innovative Medicines Initiative of the European Union with grant number 115565 partly supported by the EFPIA Companies (Aларcon-Riquelme).

**B. Sjögren's International Collaborative Clinical Alliance (SICCA) is composed of the following members:** Cox D<sup>1</sup>, Jordan R<sup>1</sup>, Lee D<sup>1</sup>, DeSouza Y<sup>1</sup>, Drury D<sup>1</sup>, Do A<sup>1</sup>, Scott L<sup>1</sup>, Nespeco J<sup>1</sup>, Whiteford J<sup>1</sup>, Margaret M<sup>1</sup>, Sack S<sup>1</sup>, Adler I<sup>2</sup>, Smith AC<sup>2</sup>, Bisio AM<sup>2</sup>, Gandolfo MS<sup>2</sup>, Chirife AM<sup>2</sup>, Keszler A<sup>2</sup>, Daverio S<sup>2</sup>, Kambo V<sup>2</sup>, Dong Y<sup>3</sup>, Jiang Y<sup>3</sup>, Xu D<sup>3</sup>, Su J<sup>3</sup>, Du D<sup>3</sup>, Wang H<sup>3</sup>, Li Z<sup>3</sup>, Xiao J<sup>3</sup>, Wu Q<sup>3</sup>, Zhang C<sup>3</sup>, Meng W<sup>3</sup>, Zhang J<sup>3</sup>, Johansen S<sup>4</sup>, Hamann S<sup>4</sup>, Schiødt J<sup>4</sup>, Holm H<sup>4</sup>, Ibsen P<sup>4</sup>, Manniche AM<sup>4</sup>, Kreutzmann SP<sup>4</sup>, and Villadsen J<sup>4</sup>, Sugai S<sup>5</sup>, Masaki Y<sup>5</sup>, Sakai T<sup>5</sup>, Shibata N<sup>5</sup>, Honjo M<sup>5</sup>, Kurose N<sup>5</sup>, Nojima T<sup>5</sup>, Kawanami T<sup>5</sup>, Sawaki T<sup>5</sup>, Fujimoto K<sup>5</sup>, Odell E<sup>6</sup>, Morgan P<sup>6</sup>, Fernandes-Naglik L<sup>6</sup>, Varghese-Jacob B<sup>6</sup>, Ali S<sup>6</sup>, Adamson M<sup>6</sup>, Seghal S<sup>7</sup>, Mishra R<sup>7</sup>, Bunya V<sup>7</sup>, Massaro-Giordano M<sup>7</sup>, Abboud SK<sup>7</sup>, Pinto A<sup>7</sup>, Sia YW<sup>7</sup>, Dow K<sup>7</sup>, Akpek E<sup>8</sup>, Ingrodi S<sup>8</sup>, Henderson W<sup>8</sup>, Gourin C<sup>8</sup>, Keyes A<sup>8</sup>, Srinivasan M<sup>9</sup>, Mascarenhas J<sup>9</sup>, Das M<sup>9</sup>, Kumar A<sup>9</sup>, Joshi P<sup>9</sup>, Banushree R<sup>9</sup>, Kim U<sup>9</sup>, Babu B<sup>9</sup>, Ram A<sup>9</sup>, Saravanan R<sup>9</sup>, Kannappan KN<sup>9</sup>, Kalyani N<sup>9</sup>, Criswell LA<sup>1</sup>, Shiboski SC<sup>1</sup>, Baer A<sup>8</sup>, Challacombe S<sup>6</sup>, Lanfranchi H<sup>2</sup>, Schiødt M<sup>4</sup>, Umehara H<sup>5</sup>, Vivino F<sup>7</sup>, Zhao Y<sup>3</sup>, Dong Y<sup>3</sup>, Greenspan D<sup>1</sup>, Heidenreich AM<sup>2</sup>, Helin P<sup>4</sup>, Kirkham B<sup>6</sup>, Kitagawa K<sup>5</sup>, Larkin G<sup>6</sup>, Li M<sup>3</sup>, Lietman T<sup>1</sup>, Lindegaard J<sup>4</sup>, McNamara N<sup>1</sup>, Sack K<sup>1</sup>, Shirlaw P<sup>6</sup>, Sugai S<sup>5</sup>, Vollenweider C<sup>2</sup>, Whitcher J<sup>1</sup>, Wu A<sup>1</sup>, Zhang S<sup>3</sup>, Zhang W<sup>3</sup>, Greenspan JS<sup>1</sup>, Daniels TE<sup>1</sup>, **Shiboski CH**<sup>1</sup>, Criswell LA<sup>10</sup>.

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SICCA Study was funded by the National Institutes of Health (NIH): N01DE32636 (SICCA), HHSN26S201300057C (SICCA), U01DE028891 (SICCA), R03DE029800 (SICCA), U01HG004446 (SICCA-GWAS), P30AR070155 (SICCA-GWAS).

Genotype data from the Sjögren's International Collaborative Clinical Alliance (SICCA) Registry was obtained through **dbGAP accession number phs000672.v1.p1**. This study was supported by the National Institute of Dental and Craniofacial Research (NIDCR), the National Eye Institute, and the Office of Research on Women's Health through contract number N01-DE-32636. Genotyping services were provided by the Center for Inherited Disease Research (CIDR). CIDR is fully funded through a federal contract from the National Institutes of Health (NIH) to the Johns Hopkins University (contract numbers HHSN268200782096C, HHSN268201100011I, HHSN268201200008I). Funds for genotyping were provided by the NIDCR through CIDR's NIH contract. Assistance with data cleaning and imputation was provided by the University of Washington. SICCA thanks investigators from the following studies that provided DNA samples for genotyping: the Genetic Architecture of Smoking and Smoking Cessation, Collaborative

Genetic Study of Nicotine Dependence (phs000404.v1.p1); Age-Related Eye Disease Study (AREDS) - Genetic Variation in Refractive Error Substudy (phs000429.v1.p1); and National Institute of Mental Health's Human Genetics Initiative (phs000021.v3.p2, phs000167.v1.p1). SICCA thanks the many clinical collaborators and research participants who contributed to this research.

**C. The UK Primary Sjögren's Syndrome Registry is composed of the following members:** Wan-Fai Ng<sup>1</sup>, Simon J. Bowman<sup>2</sup>, Bridget Griffiths<sup>3</sup>, Frances Hall<sup>4</sup>, Elaline C. Bacabac<sup>5</sup>, Robert Moots<sup>5</sup>, Kuntal Chadravarty<sup>6</sup>, Shamin Lamabadusuriya<sup>6</sup>, Michele Bombardieri<sup>7</sup>, Constantino Pitzalis<sup>7</sup>, Nurhan Sutcliffe<sup>7</sup>, Nagui Gendi<sup>8</sup>, Rashidat Adeniba<sup>8</sup>, John Hamburger<sup>9</sup>, Andrea Richards<sup>9</sup>, Saaeha Rauz<sup>10</sup>, Sue Brailsford<sup>1</sup>, Joanne Logan<sup>11</sup>, Diamuid Mulherin<sup>11</sup>, Paul Emery<sup>12</sup>, Alison McManus<sup>12</sup>, Colin Pease<sup>12</sup>, Alison Booth<sup>13</sup>, Marian Regan<sup>13</sup>, Theodoros Dimitroulas<sup>14</sup>, Lucy Kadiki<sup>14</sup>, Daljit Kaur<sup>14</sup>, George Kitas<sup>14</sup>, Mark Lloyd<sup>15</sup>, Lisa Moore<sup>15</sup>, Esther Gordon<sup>16</sup>, Cathy Lawson<sup>16</sup>, Monica Gupta<sup>17</sup>, John Hunter<sup>17</sup>, Lesley Stirton<sup>17</sup>, Gill Ortiz<sup>18</sup>, Elizabeth Price<sup>18</sup>, Gavin Clunie<sup>19</sup>, Ginny Rose<sup>19</sup>, Sue Cuckow<sup>19</sup>, Susan Knight<sup>20</sup>, Deborah Symmons<sup>20</sup>, Beverley Jones<sup>20</sup>, Shereen Al-Ali<sup>1</sup>, Andrew Carr<sup>1</sup>, Katherine Collins<sup>1</sup>, Andini Natasari<sup>1</sup>, Philip Stocks<sup>1</sup>, Jessica Tarn<sup>1</sup>, Ian Corbett<sup>3</sup>, Christine Downie<sup>3</sup>, Suzanne Edgar<sup>3</sup>, Marco Carrozzo<sup>3</sup>, Francisco Figueredo<sup>3</sup>, Heather Foggo<sup>3</sup>, Dennis Lendrem<sup>3</sup>, Iain Macleod<sup>3</sup>, Philip Mawson<sup>3</sup>, Sheryl Mitchell<sup>3</sup>, Adrian Jones<sup>21</sup>, Peter Lanyon<sup>21</sup>, Alice Muir<sup>21</sup>, Paula White<sup>22</sup>, Steven Young-Min<sup>22</sup>, Susan Pugmire<sup>23</sup>, Saravanan Vadivelu<sup>23</sup>, Annie Cooper<sup>24</sup>, Marianne Watkins<sup>24</sup>, Anne Field<sup>25</sup>, Stephen Kaye<sup>25</sup>, Devesh Mewar<sup>25</sup>, Patricia Medcalf<sup>25</sup>, Pamela Tomlinson<sup>25</sup>, Debbie Whiteside<sup>25</sup>, Neil McHugh<sup>26</sup>, John Pauling<sup>26</sup>, Julie James<sup>26</sup>, Nike Olaitan<sup>26</sup>, Mohammed Akil<sup>27</sup>, Jayne McDermott<sup>27</sup>, Olivia Godia<sup>27</sup>, David Coady<sup>28</sup>, Elizabeth Kidd<sup>28</sup>, Lynne Palmer<sup>28</sup>, Bhaskar Dasgupta<sup>29</sup>, Victoria Katsande<sup>29</sup>, Pamela Long<sup>29</sup>, Charles Li<sup>30</sup>, Usha Chandra<sup>31</sup>, Kirsten MacKay<sup>31</sup>, Stefano Fedele<sup>32</sup>, Ada Ferenkey-Koroma<sup>32</sup>, Ian Giles<sup>32</sup>, David Isenberg<sup>32</sup>, Helena Maconnell<sup>32</sup>, Stephen Porter<sup>32</sup>, Paul Allcoat<sup>33</sup>, John McLaren<sup>33</sup>.

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The UK Primary Sjögren's Syndrome Registry was funded by the Medical Research Council (G080062; W-F.N.), and the British Sjögren's Syndrome Association (W-F.N.). This work also received infra-structure support from the NIHR Newcastle Biomedical Research Centre, Newcastle and NIHR Newcastle Clinical Research Facility.

SNP Name	Reference Allele	Alternative Allele	Non-Risk	Risk	Notes
rs57494551	C (major)	T (minor)	T	C	Reference is risk allele
rs10892294	G (major)	C (minor)	C	G	Reference is risk allele
rs4936443	C (minor)	T (major)	C	T	
rs4938572	C (minor)	T (major)	C	T	
rs7117261	T (minor)	C (major)	T	C	
rs4938573	C (minor)	T (major)	C	T	
rs12365699	G (major)	A (minor)	G	A	

**Supplemental Table 2: Patient-Derived EBV B Cell Genotypes**

Cell Line	Haplotype	Allele	Application Used
p1000068-2	Heterozygous		Luciferase & EMSA (pooled)
p1000069-5	Heterozygous		Luciferase & EMSA (pooled)
p1000334-2	Heterozygous		Luciferase & EMSA (pooled)
p1000181-5	Homozygous	Minor allele (1) Non-Risk	Luciferase & EMSA (pooled), 3C
p1000370-0	Homozygous	Minor allele (1) Non-Risk	3C
p1000373-7	Homozygous	Major allele (2) Risk	Luciferase & EMSA (pooled)
p1000333-5	Homozygous	Major allele (2) Risk	Luciferase & EMSA (pooled), 3C
p1000161-0	Homozygous	Major allele (2) Risk	3C



**Supplemental Table 3: EMSA Probes**

EMSA Probe Name		Sequence
rs57494551-altT-F	Non-Risk	TTCCTCCTGCCGACCCTGCTGCGCACCACATT <b>T</b> CTATATTGCCTCCTCTCAGGCGCTCC
rs57494551-altT-R	Non-Risk	GGAGCGCCTGAGAGGAGGCGAATATAG <b>A</b> AATGTGGTGCAGCAGGGTCGGCAGGAGGAA
rs57494551-refC-F	Risk	TTCCTCCTGCCGACCCTGCTGCGCACCACATT <b>C</b> CTATATTGCCTCCTCTCAGGCGCTCC
rs57494551-refC-R	Risk	GGAGCGCCTGAGAGGAGGCGAATATAG <b>G</b> AATGTGGTGCAGCAGGGTCGGCAGGAGGAA
rs10892294-altC-F	Non-Risk	GGTTTCCTGCCACTAGTCAATCTGCAGAG <b>C</b> ACTTTTATTGATTCTTGAAAAACAACCTGTG
rs10892294-altC-R	Non-Risk	CACAGTTGATTTTCAAGAATCAATAAAAGT <b>G</b> TCTGCAGATTGACTAGTGGCAGGAAACC
rs10892294-refG-F	Risk	GGTTTCCTGCCACTAGTCAATCTGCAGAG <b>G</b> ACTTTTATTGATTCTTGAAAAACAACCTGTG
rs10892294-refG-R	Risk	CACAGTTGATTTTCAAGAATCAATAAAAGT <b>C</b> TCTGCAGATTGACTAGTGGCAGGAAACC
rs4936443-refC-F	Non-Risk	AGGTTTAGTTTGCCTGGAGAGAAACAGGC <b>C</b> GGAGAGAGACTGCGGCCTCCCTAGGGTCTT
rs4936443-refC-R	Non-Risk	AAGACCCTAGGGAGGCCGAGTCTCTCTCC <b>G</b> GCCTGTTTCTCTCCAGGCAAACCTAACCT
rs4936443-altT-F	Risk	AGGTTTAGTTTGCCTGGAGAGAAACAGGC <b>T</b> GGAGAGAGACTGCGGCCTCCCTAGGGTCTT
rs4936443-altT-R	Risk	AAGACCCTAGGGAGGCCGAGTCTCTCTCC <b>A</b> GCCTGTTTCTCTCCAGGCAAACCTAACCT
rs4938572-refC-F	Non-Risk	CGGCAAATTCCTCCAGCTCAGTGGCTGCTGGG <b>C</b> AGCAGCACAGCCGTTTCTCTCAAGGG
rs4938572-refC-R	Non-Risk	CCCTTGAGAGAAACCGGCTGTGCTGCT <b>G</b> CCCAGCAGCCACTGAGCTGGAGGAATTTGCCG
rs4938572-altT-F	Risk	CGGCAAATTCCTCCAGCTCAGTGGCTGCTGGG <b>T</b> AGCAGCACAGCCGTTTCTCTCAAGGG
rs4938572-altT-R	Risk	CCCTTGAGAGAAACCGGCTGTGCTGCT <b>A</b> CCCAGCAGCCACTGAGCTGGAGGAATTTGCCG
rs7117261-refT-F	Non-Risk	CCCTTCTTCTGTCCCTGGGCACCTCC <b>T</b> GGCTGCTCTTTCCCACTGCCAGCCCA
rs7117261-refT-R	Non-Risk	TGGGCTGGGCAGTGGGAAAGAGAGCAGCC <b>A</b> GGGAAGTGCCAGGGACAGGAAAGAAGGG
rs7117261-altC-F	Risk	CCCTTCTTCTGTCCCTGGGCACCTCC <b>C</b> GGCTGCTCTTTCCCACTGCCAGCCCA
rs7117261-altC-R	Risk	TGGGCTGGGCAGTGGGAAAGAGAGCAGCC <b>G</b> GGGAAGTGCCAGGGACAGGAAAGAAGGG
rs4938573-refC-F	Non-Risk	TCACTTGTGTAATTCATCAACAACTTTA <b>C</b> TGAGCACCTAATAGGCACTGAGTGTTCG
rs4938573-refC-R	Non-Risk	CGAAAACACTCAGTGCCTATTAGGTGCTCA <b>G</b> TAAAGTTTGTGATGAATTACACAAGTGA
rs4938573-altT-F	Risk	TCACTTGTGTAATTCATCAACAACTTTA <b>T</b> TGAGCACCTAATAGGCACTGAGTGTTCG
rs4938573-altT-R	Risk	CGAAAACACTCAGTGCCTATTAGGTGCTCA <b>A</b> TAAAGTTTGTGATGAATTACACAAGTGA
rs12365699-refG-F	Non-Risk	TCATTTGAAACCTCTCTCGGAGGAGCTCC <b>G</b> TGATCAAGGTGCAGATGCGGCAGGTGGGC
rs12365699-refG-R	Non-Risk	GCCACCTGCCGATCTGCACCTTGATCA <b>C</b> GGAGCTCCTCCGAGAGAGGTTTCAAATGA
rs12365699-altA-F	Risk	TCATTTGAAACCTCTCTCGGAGGAGCTCC <b>A</b> TGATCAAGGTGCAGATGCGGCAGGTGGGC
rs12365699-altA-R	Risk	GCCACCTGCCGATCTGCACCTTGATCA <b>T</b> GGAGCTCCTCCGAGAGAGGTTTCAAATGA

**Supplemental Table 4: Luciferase Reporter Assay gBlocks**

rs57494551-refC	<p>ACCCTCTGGTACCTGTTATTGACCCGCAAGGCCTACTGCAATCAAGCAGCGGCCGGT                  TTGCTTCTAAACCGAGCCCTCCAATACAGCATGTCCCTGCCGCCCCCTATAGGGCCG                  CCTCGTACCCTATAACCTCCACCATCATCCCCCTAAGTCCTTGCCGCCCCCTTCGGCC                  TCATATTCCCTCATCTTCGATAAAGCTACTCCGAGTACTTAGCCTGTTCTCCTGCCGA                  CCCTGCTGCGCACCACATT<b>C</b>CTATATTGCCTCCTCTCAGGCGCTCCCACCCACAC                  AGCTGCCGACCGCCTTCTCCCCAGGCCCGGCCAGGCCTTAGGCCTCCGCCCCGAGA                  GTCCCCCAGAGCCGGCCCGGGGGGCTCCCCACAGCCCCAAAGCACCGCTGACCT                  CGACCCACACCTCACCCAAAGCCTCGCGACTCGGGCCCGTGTCTACCAACGAG                  GCCACTCCCGCTCGGCACCCTCGGTCCTTTATAAGCTTTGTTGAC</p>
rs57494551-altT	<p>ACCCTCTGGTACCTGTTATTGACCCGCAAGGCCTACTGCAATCAAGCAGCGGCCGGT                  TTGCTTCTAAACCGAGCCCTCCAATACAGCATGTCCCTGCCGCCCCCTATAGGGCCG                  CCTCGTACCCTATAACCTCCACCATCATCCCCCTAAGTCCTTGCCGCCCCCTTCGGCC                  TCATATTCCCTCATCTTCGATAAAGCTACTCCGAGTACTTAGCCTGTTCTCCTGCCGA                  CCCTGCTGCGCACCACATT<b>T</b>CTATATTGCCTCCTCTCAGGCGCTCCCACCCACACA                  GCTGCCGACCGCCTTCTCCCCAGGCCCGGCCAGGCCTTAGGCCTCCGCCCCGAGAG                  TCCCCCAGAGCCGGCCCGGGGGGCTCCCCACAGCCCCAAAGCACCGCTGACCTC                  GACCCACACCTCACCCAAAGCCTCGCGACTCGGGCCCGTGTCTACCAACGAGG                  CCACTCCCGCTCGGCACCCTCGGTCCTTTATAAGCTTTGTTGAC</p>
rs10892294-refG	<p>TTCTCCTTGGTACCGGGTATTTTCCAAGTTAGTTCAGGGGCAGTTGCCGAGGAATAAC                  ACTGATGGGGGTTACACTATGGCGATCTTGTTGAACTGCCTGATGTTGGTTTGTGTA                  ATCTGCCCCCTTTGTGCCAAGAACCTGTGACAAGATTCTGCTTCTGACAACCTTCTG                  TGCAGGGGTAGCGACAGGAGTCTGAACAATCATTAAAGTGCCAGCCCTGGTTTCCTG                  CCACTAGTCAATCTGCAGA<b>G</b>ACTTTTATTGATTCTTGAAAATACAACGTGATTGTAGG                  TTTGGGCCCTGGGAATGTAATTTATAGCTAAAGAATGGGCAATGTCTTCTGTCCTGAG                  TGCCATGGTTGGATTGTGAACATCTGTGGCTACCAGGACAAGGAAGGAACAAAGGA                  AGACAAAAGTATTTTCAGTGCAGAGATCTTCTCAGTGACCCTCCTTGCTTTTCATCTGCC                  TGATGAATTTTAAAGACTACTTAAGCTTGTGCATCAT</p>
rs10892294-altC	<p>TTCTCCTTGGTACCGGGTATTTTCCAAGTTAGTTCAGGGGCAGTTGCCGAGGAATAAC                  ACTGATGGGGGTTACACTATGGCGATCTTGTTGAACTGCCTGATGTTGGTTTGTGTA                  ATCTGCCCCCTTTGTGCCAAGAACCTGTGACAAGATTCTGCTTCTGACAACCTTCTG                  TGCAGGGGTAGCGACAGGAGTCTGAACAATCATTAAAGTGCCAGCCCTGGTTTCCTG                  CCACTAGTCAATCTGCAGA<b>C</b>ACTTTTATTGATTCTTGAAAATACAACGTGATTGTAGG                  TTTGGGCCCTGGGAATGTAATTTATAGCTAAAGAATGGGCAATGTCTTCTGTCCTGAG                  TGCCATGGTTGGATTGTGAACATCTGTGGCTACCAGGACAAGGAAGGAACAAAGGA                  AGACAAAAGTATTTTCAGTGCAGAGATCTTCTCAGTGACCCTCCTTGCTTTTCATCTGCC                  TGATGAATTTTAAAGACTACTTAAGCTTGTGCATCAT</p>
rs4936443-refC	<p>GCTGGAGGGTACCAAAGGCCTGGAGAGCTCCCAGCGCCCTCTGAGACATGGCTCCA                  GGTCACACAGCCCAAAGCCTTGGCCTGTTTTGTACGTGGACGGGGCAAAGAGAACAC                  CCTCGCCGCTTCTCTCTGCCTTTAGCAGGGCTGTAGGAAACCCCAACAGAGACCTC                  CAGCTTGGAGAGGAAAGAGTGGAACAGCCCTCTGGAAGCAAGTTACCCACAGGTTTA                  GTTTGCCTGGAGAGAAACAGGC<b>C</b>GGAGAGAGACTGCGGCCTCCCTAGGGTCTTCTG                  ACGGCAAATTCCTCCAGCTCAGTGGCTGCTGGG<b>C</b>AGCAGCACAGCCGGTTTCTCTCA                  AGGGCACACCCACACACCGCGTCACTGTGCACTAGCCTCAGATGACAGACAAGCCT                  TTCACAAGACTTTTGTGGCACTGTTTCTTTCTGAGACCTTCTCTATGATGAGCTCAAAC                  TGCTTACCTCAGAGAAGAACTGCGTGCACAAGCTTAGAAAGC                  Green=rs4938572</p>

Supplementary Table 4 Continued

rs4936443-altT	<p>GCTGGAGGGTACCAAAGGCCTGGAGAGCTCCCAGCGCCCTCTGAGACATGGCTCCA  GGTCACACAGCCCAAAGCCTTGGCCTGTTTTGTACGTGGACGGGGCAAAGAGAACAC  CCTCGCCGCTTCTCTCTGCCTTTAGCAGGGCTGTAGGAAACCCACCAGAGACCTC  CAGCTTGGAGAGGAAAGAGTGGAACAGCCCTCTGGAAGCAAGTTACCCACAGGTTTA  GTTTGCCTGGAGAGAAACAGGC<b>T</b>GGAGAGAGACTGCGGCCTCCCTAGGGTCTTCTGA  CGGCAAATTCCTCCAGCTCAGTGGCTGCTGGG<b>C</b>AGCAGCACAGCCGGTTTCTCTCAA  GGGCACACCCACACACCGCGTCACTGTGCACTAGCCTCAGATGACAGACAAGCCTT  TCACAAGACTTTTTGTGGCACTGTTCAATTTCTGAGACCTTCTCTATGATGAGCTCAAAC  GCTTACCTCAGAGAAGAACTGCGTGCACAAGCTTAGAAAGC</p> <p><b>Green</b>=rs4938572</p>
rs4938572-refC	<p>GCCTTGGCGGTACCCTGTTTTGTACGTGGACGGGGCAAAGAGAACACCCTCGCCGCT  TCTCTCTGCCTTTAGCAGGGCTGTAGGAAACCCACCAGAGACCTCCAGCTTGGAG  AGGAAAGAGTGGAACAGCCCTCTGGAAGCAAGTTACCCACAGGTTTAGTTTGCCTGG  AGAGAAACAGGC<b>C</b>GGAGAGAGACTGCGGCCTCCCTAGGGTCTTCTGACGGCAAATT  CCTCCAGCTCAGTGGCTGCTGGG<b>C</b>AGCAGCACAGCCGGTTTCTCTCAAGGGCACAC  CCCACACCCGCGTCACTGTGCACTAGCCTCAGATGACAGACAAGCCTTTTACAAGA  CTTTTGTGGCACTGTTCAATTTCTGAGACCTTCTCTATGATGAGCTCAAACCTGCTTACCT  CAGAGAAGAAACTGCGTGCACAGAAAGCTGCTGAGGCCAGCTTGGGGCCCCTTCTTT  CCTGTCCCTGGGCACTTCCCT<b>T</b>GGCTGCTCTAAGCTTCTTTCCCC</p> <p><b>Red</b>=rs4936443  <b>Blue</b>=rs7117261</p>
rs4938572-altT	<p>GCCTTGGCGGTACCCTGTTTTGTACGTGGACGGGGCAAAGAGAACACCCTCGCCGCT  TCTCTCTGCCTTTAGCAGGGCTGTAGGAAACCCACCAGAGACCTCCAGCTTGGAG  AGGAAAGAGTGGAACAGCCCTCTGGAAGCAAGTTACCCACAGGTTTAGTTTGCCTGG  AGAGAAACAGGC<b>C</b>GGAGAGAGACTGCGGCCTCCCTAGGGTCTTCTGACGGCAAATT  CCTCCAGCTCAGTGGCTGCTGGG<b>T</b>AGCAGCACAGCCGGTTTCTCTCAAGGGCACACC  CCACACACCCGCGTCACTGTGCACTAGCCTCAGATGACAGACAAGCCTTTTACAAGAC  TTTTGTGGCACTGTTCAATTTCTGAGACCTTCTCTATGATGAGCTCAAACCTGCTTACCTC  AGAGAAGAAACTGCGTGCACAGAAAGCTGCTGAGGCCAGCTTGGGGCCCCTTCTTTC  CTGTCCCTGGGCACTTCCCT<b>T</b>GGCTGCTCTAAGCTTCTTTCCCC</p> <p><b>Red</b>=rs4936443  <b>Blue</b>=rs7117261</p>
rs7117261-refT	<p>GCTCAGTGGTACCGGCTGCTGGG<b>C</b>AGCAGCACAGCCGGTTTCTCTCAAGGGCACAC  CCCACACACCGCGTCACTGTGCACTAGCCTCAGATGACAGACAAGCCTTTTACAAGA  CTTTTGTGGCACTGTTCAATTTCTGAGACCTTCTCTATGATGAGCTCAAACCTGCTTACCT  CAGAGAAGAAACTGCGTGCACAGAAAGCTGCTGAGGCCAGCTTGGGGCCCCTTCTTT  CCTGTCCCTGGGCACTTCCCT<b>T</b>GGCTGCTCTCTTTCCCACTGCCAGCCCAAGGAGT  CCCCTCTGCAGCTGACCCGGGTTTCCAGCCTCCAGAACAGCGAGTTCCACAGCCCTGAA  GCCTGGCCATCGTCCCTTTTCTGGACACTGGACTGGTTTATAGGGCTCAGTGCCCTG  CGGCTTTCTCCTCCCACCACAGGCCTGGGAGGGGCAAGAAGCACCAGTTTGTTTTC  TGGTTCAGCCTGCAGCAAAGAGCGACTGCAAGCTTCTCACC</p> <p><b>Green</b>=rs4938572</p>
rs7117261-altC	<p>GCTCAGTGGTACCGGCTGCTGGG<b>C</b>AGCAGCACAGCCGGTTTCTCTCAAGGGCACAC  CCCACACACCGCGTCACTGTGCACTAGCCTCAGATGACAGACAAGCCTTTTACAAGA  CTTTTGTGGCACTGTTCAATTTCTGAGACCTTCTCTATGATGAGCTCAAACCTGCTTACCT  CAGAGAAGAAACTGCGTGCACAGAAAGCTGCTGAGGCCAGCTTGGGGCCCCTTCTTT  CCTGTCCCTGGGCACTTCCCT<b>C</b>GGCTGCTCTCTTTCCCACTGCCAGCCCAAGGAGT  CCCCTCTGCAGCTGACCCGGGTTTCCAGCCTCCAGAACAGCGAGTTCCACAGCCCTGAA  GCCTGGCCATCGTCCCTTTTCTGGACACTGGACTGGTTTATAGGGCTCAGTGCCCTG  CGGCTTTCTCCTCCCACCACAGGCCTGGGAGGGGCAAGAAGCACCAGTTTGTTTTC  TGGTTCAGCCTGCAGCAAAGAGCGACTGCAAGCTTCTCACC</p> <p><b>Green</b>=rs4938572</p>

Supplementary Table 4 Continued

rs4938573-refC	<p>ACTACTGGTACCGATTTACATATCACACATGTGCTCATCCATCCATTACCAAACCTCT                  GTTGACTGCTCGCGCTGCCCTGCGTTCCTGGCACTGTGCAGGGTTATAATCTAGTAG                  GAAAGACCTGACAAGGTCACAGATGTCAGTACTGAAAGGAAGAGTAGGGTAGATGGC                  CACCCACACCCACCCCAACCTCAAAAAAGAGACTAAAAAATTACTGTCACCTTGTGTA                  ATTCATCAACAAACTTTA<b>C</b>TGAGCACCTAATAGGCACTGAGTGTTCGTGTATTGATC                  ACGCATTGATCCTACAATAACCTTTGAGATGGGTTGTGCCATTTACACAGGGCGAAG                  AAGAGAGACTGGCCACTGTACACAGCTACTGATATCCAAGCTGAGATCCAAAGCTC                  CTCTGCTTCTCCTGATGAGAATGAGCACCACAGGCAGGCCACAGAAAAACACCCAGG                  AGAGCCAAACTCAGACCCACCCAGAAGCTTATTTCC</p>
rs4938573-altT	<p>ACTACTGGTACCGATTTACATATCACACATGTGCTCATCCATCCATTACCAAACCTCT                  GTTGACTGCTCGCGCTGCCCTGCGTTCCTGGCACTGTGCAGGGTTATAATCTAGTAG                  GAAAGACCTGACAAGGTCACAGATGTCAGTACTGAAAGGAAGAGTAGGGTAGATGGC                  CACCCACACCCACCCCAACCTCAAAAAAGAGACTAAAAAATTACTGTCACCTTGTGTA                  ATTCATCAACAAACTTTA<b>T</b>TGAGCACCTAATAGGCACTGAGTGTTCGTGTATTGATC                  ACGCATTGATCCTACAATAACCTTTGAGATGGGTTGTGCCATTTACACAGGGCGAAG                  AAGAGAGACTGGCCACTGTACACAGCTACTGATATCCAAGCTGAGATCCAAAGCTC                  CTCTGCTTCTCCTGATGAGAATGAGCACCACAGGCAGGCCACAGAAAAACACCCAGG                  AGAGCCAAACTCAGACCCACCCAGAAGCTTATTTCC</p>
rs12365699-refG	<p>CACAAGAGGTACCGCCGTTGGCGGGATTTCCATTGTCCCCCTTGGGTAGGTAAGGC                  CAGGTGGCTGCTCCATCTCTGCCACCTCCAGCGCCGGTCCCCTGTGTCAGCAGCC                  CTGTCCCCTACTGCTGTGTCATCAATTACTCTCAGGTGCCTGGCCCCACCCAGTGG                  CCCCACCTTGCAGCCCCGAAGGCTTCCTTCTGGGGCAGCAGGGCCGAGTCATTT                  GGAAACCTCTCTCGGAGGAGCTCC<b>G</b>TGATCAAGGTGCAGATGCGGCAGGTGGGCCG                  GCCTCAATCATGTCTCCAATTGCGACGGTGAATGCGGTGAGGAGTTTCGTTGGCCCA                  TCACCTCTGCCTTGGGCCTGGCTCACTTTCACTGCTGAGTTAGTTCCACGGCCGCCTT                  TGATGATGCCGCTTCAGCATCTTTTTTCTTCGGCGTTTCTGCTCCTTTGTTTTCAAGG                  TCACTCTGTCTGCTGCCCTGCCCACTCTGGGCCAAGCTTACCCAAG</p>
rs12365699-altA	<p>CACAAGAGGTACCGCCGTTGGCGGGATTTCCATTGTCCCCCTTGGGTAGGTAAGGC                  CAGGTGGCTGCTCCATCTCTGCCACCTCCAGCGCCGGTCCCCTGTGTCAGCAGCC                  CTGTCCCCTACTGCTGTGTCATCAATTACTCTCAGGTGCCTGGCCCCACCCAGTGG                  CCCCACCTTGCAGCCCCGAAGGCTTCCTTCTGGGGCAGCAGGGCCGAGTCATTT                  GGAAACCTCTCTCGGAGGAGCTCC<b>A</b>TGATCAAGGTGCAGATGCGGCAGGTGGGCCG                  GCCTCAATCATGTCTCCAATTGCGACGGTGAATGCGGTGAGGAGTTTCGTTGGCCCA                  TCACCTCTGCCTTGGGCCTGGCTCACTTTCACTGCTGAGTTAGTTCCACGGCCGCCTT                  TGATGATGCCGCTTCAGCATCTTTTTTCTTCGGCGTTTCTGCTCCTTTGTTTTCAAGG                  TCACTCTGTCTGCTGCCCTGCCCACTCTGGGCCAAGCTTACCCAAG</p>
All Non-Risk	<p>TCTGAGAGGTACCCATGGCTCCAGGTCACACAGCCCAAAGCCTTGGCCTGTTTTGTA                  CGTGGACGGGGCAAAGAGAACACCCTCGCCGCTTCTCTCTGCCCTTAGCAGGGCTGT                  AGGAAACCCCAACAGAGACCTCCAGCTTGGAGAGGAAAGAGTGGAAACAGCCCTCT                  GGAAGCAAGTTACCCACAGGTTTAGTTTGCCTGGAGAGAAACAGGC<b>R</b>GGAGAGAGAC                  TGCGGCCTCCCTAGGGTCTTCTGACGGCAAATTCCTCCAGCTCAGTGGCTGCTGGG<b>C</b>                  AGCAGCAGACCCGGTTTCTCTCAAGGGCACACCCACACACCCGCTCACTGTGCACT                  AGCCTCAGATGACAGACAAGCCTTTCAACAAGACTTTTGTGGCACTGTTCAATTTCTGAG                  ACCTTCTCTATGATGAGCTCAAACCTTACCTCAGAGAAGAAACTGCGTGCACAGAA                  AGCTGCTGAGGCCAGCTTGGGGCCCTTCTTCTGTCCTGGGCACTTCCCT<b>T</b>GGCT                  GCTCTCTTTCCCACTGCCAGCCAAAGGAGTCCCCTCTGCAGCTGACCCGGGTTCA                  GCCTCCAGAACAGCGAGTTCCACAGCCCTGAAGCCTGGCCATCGTCCCTTTTCTGGA                  CACTGGACTGGTTCATAGGGCTCAGTGCCCTGCGGCTTCTCCTCCCACACAGGC                  CTGGGAGGGGCAAGAAGCAAGCTTACCAAGT  <b>Red</b>=rs4936443_Non-risk (C)  <b>Green</b>=rs4938572_Non-risk (C)  <b>Blue</b>=rs7117261_Non-risk (T)</p>

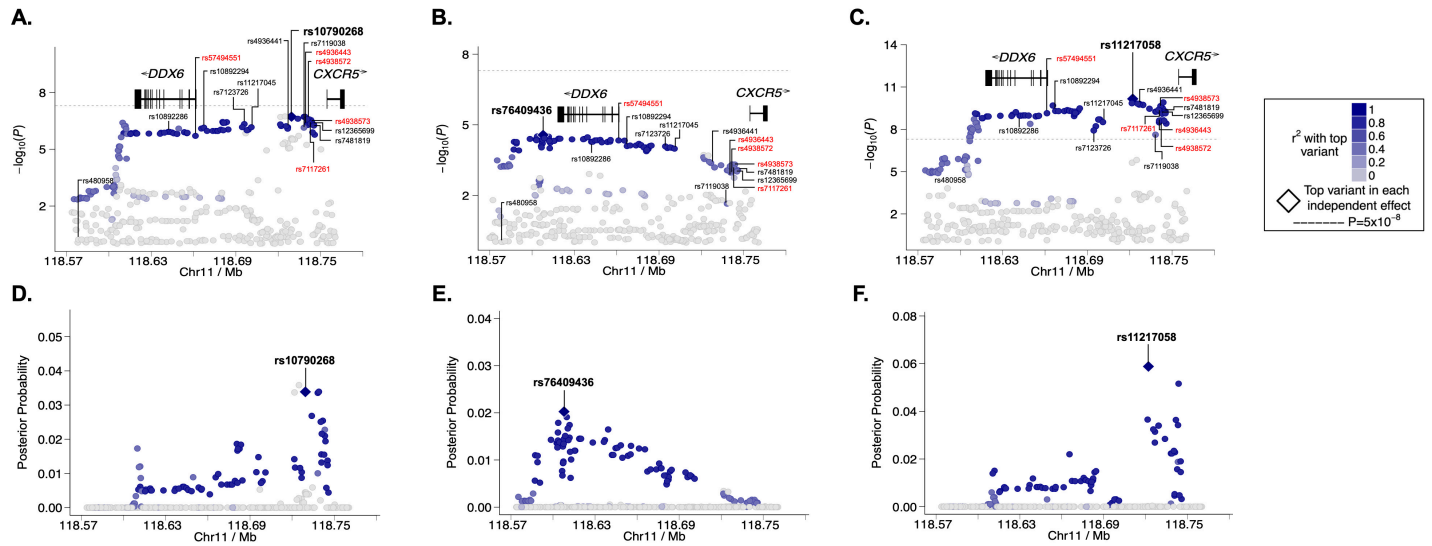
**Supplementary Table 4 Continued**

<b>All Risk</b>	<p>TCTGAGAGGTACCCATGGCTCCAGGTCACACAGCCCAAAGCCTTGGCCTGTTTTGTA  CGTGGACGGGGCAAAGAGAACACCCTCGCCGCTTCTCTCTGCCTTTAGCAGGGCTGT  AGGAAACCCCCACCAGAGACCTCCAGCTTGGAGAGGAAAGAGTGGAACAGCCCTCT  GGAAGCAAGTTACCCACAGGTTTAGTTTTGCCTGGAGAGAAACAGGC<b>T</b>GGAGAGAGAC  TGCGGCCTCCCTAGGGTCTTCTGACGGCAAATTCCTCCAGCTCAGTGGCTGCTGGG<b>T</b>  AGCAGCACAGCCGTTTTCTCTCAAGGGCACACCCACACACCCGCGTCACTGTGCACT  AGCCTCAGATGACAGACAAGCCTTTCACAAGACTTTTTGTGGCACTGTTTCATTTCTGAG  ACCTTCTCTATGATGAGCTCAAACCTGCTTACCTCAGAGAAGAAACTGCGTGCACAGAA  AGCTGCTGAGGCCAGCTTGGGGCCCCTTCTTTCCTGTCCCTGGGCACTTCCC<b>C</b>GGCT  GCTCTCTTTCCTCACTGCCAGCCCAAGGAGTCCCCTCTGCAGCTGACCCGGGTTCA  GCCTCCAGAACAGCGAGTTCCACAGCCCTGAAGCCTGGCCATCGTCCCTTTTCTGGA  CACTGGACTGGTTCATAGGGCTCAGTGCCCTGCGGCTTTCCTCCCCACCACAGGC  CTGGGAGGGGCAAGAAGCAAGCTTACCAGTT</p> <p><b>Red</b>=rs4936443_Risk (T)  <b>Green</b>=rs4938572_Risk (T)  <b>Blue</b>=rs7117261_Risk (C)</p>
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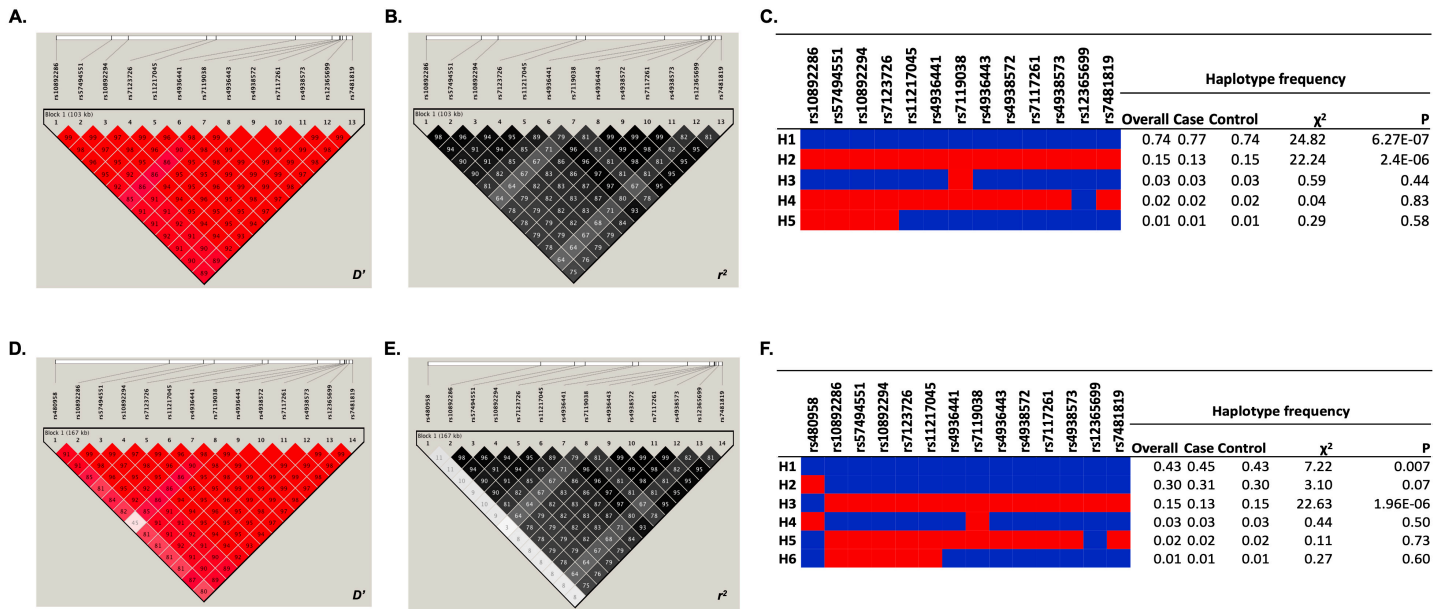
**Supplemental Table 5: 3C-qPCR Primers**

<b>Primer Name</b>	<b>Primer Sequence</b>
rs57494551 Anchor	CTCCACTCAAGATGGCGAAA
1-rs57494551 3C Short Range Primer Control	ACTGAAGAAAGTAGGGGCGG
2-rs57494551	GACACAGGAAACCTGAGGGA
3-rs57494551	GTGCATTCATGATTGTTGCC
4-rs57494551	TTGGTGAGCTGTGATTGAGC
5-rs57494551	AGTCCCTTCCAGAGGGTTTT
6-rs57494551	TTGGTTACAGATTACACCTTGT
7-rs57494551	TCCTTCCTGATCAATGTCCC
8-rs57494551	TGAAGGTAACAGTGGCCCTT
9-rs57494551	AGGTGCATGTTGCTGTCAAG
10-rs57494551	CAAGGCTCTGGGAGAGAGG
11-rs57494551	CAAGGCTCTGGGAGAGAGG
12-rs57494551	TTAGCGTGGGATACAAAGCC
13-rs57494551	TTCTGTATTCCAATTTCCCC
14-rs57494551	TTCTCCACTCACCCCAAAC
15-rs57494551	GAGGTGCTGGAGTATCTGGG
rs4938572 Anchor	TGTAATGGGGTGTGGGTCC
1-rs4938572 3C Short Range Primer Control	TCCTTCCTGATCAATGTCCC
2-rs4938572	TGACTTTGTGATCCAGCTGC
3-rs4938572	CTCCACTCAAGATGGCGAAA
4-rs4938572	CAAGGCTCTGGGAGAGAGG
5-rs4938572	TTTCCCTTCAAGAGAGCCAG
6-rs4938572	GCATAGAAAGGTGCTTTGGG
7-rs4938572	CTCTCCCCACTGAGTCCTCA
8-rs4938572	GAGGTGCTGGAGTATCTGGG
9-rs4938572	AAATCTTCCTTCCCAGCCTG
10-rs4938572	GTCTGAGGGTTCCTGAAGGA
11-rs4938572	CATATCCTGGGCCTTCACTG
12-rs4938572	AGGACAGTCAGAGAGCGTCAG

## SUPPLEMENTAL FIGURES &amp; LEGENDS



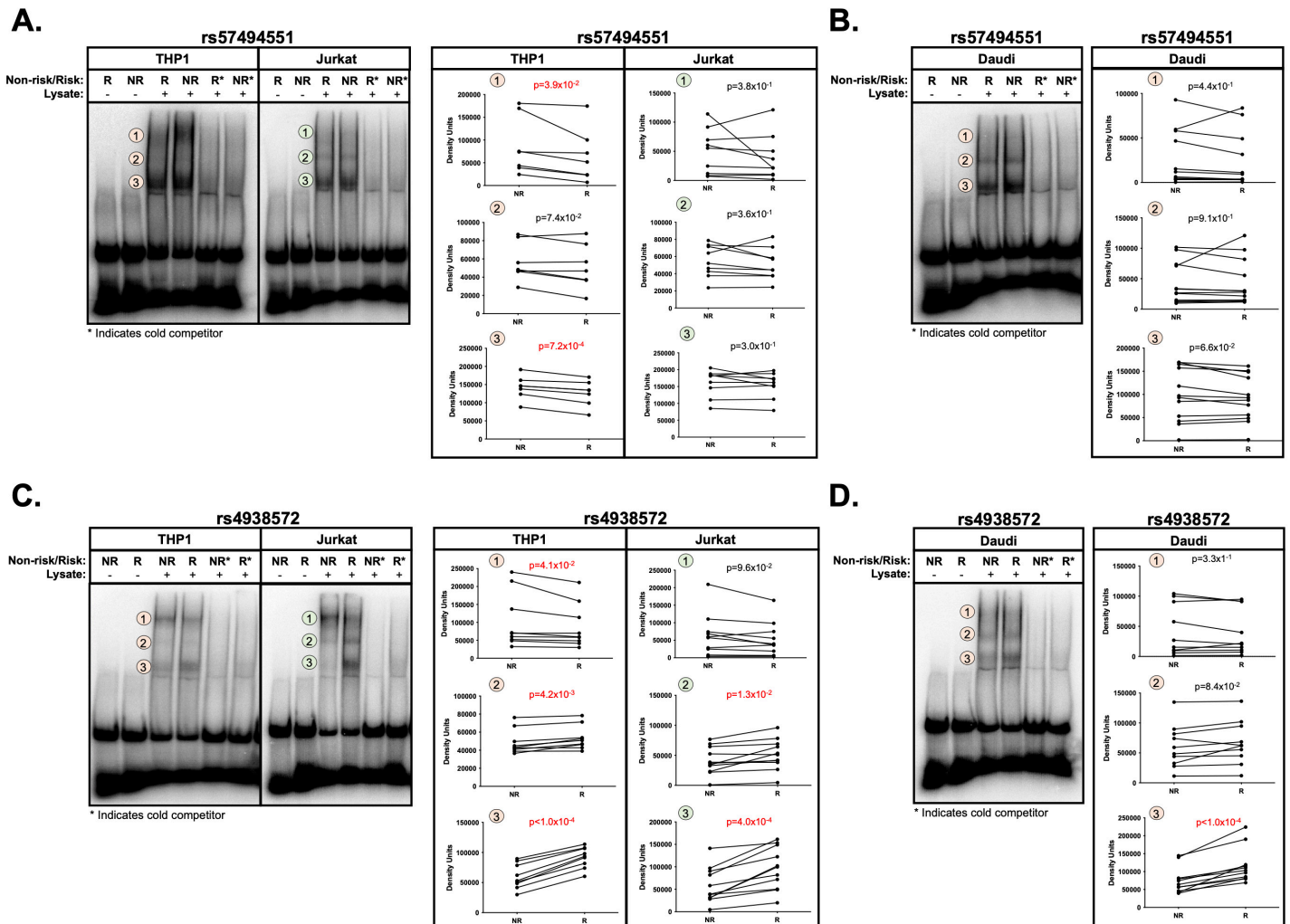
**Supplemental Figure 1. Fine mapping of the *DDX6-CXCR5* region in SjD and SLE ImmunoChip data after imputation. (A-C)** Logistic regression analysis was performed on (A) DS3-SjD (1916 SjD cases; 6194 controls), (B) DS4-SLE (3762 SLE cases; 6194 controls), and (C) DS3+DS4 (merged SjD and SLE) after quality control and imputation, identifying the top SNPs (e.g., index SNPs indicated in bold) of the *DDX6-CXCR5* association. SNPs prioritized for bioinformatic screening in this study are indicated in black; five SNPs prioritized for functional characterized are labeled in red. (D-F) Posterior probability distributions of SNPs in the *DDX6-CXCR5* region of (D) DS3, (E) DS4, and (F) DS3+DS4. SNPs with highest posterior probability are indicated. Pairwise ( $r^2$ ) analysis for DS3-SjD (A, D) was based on the second most significant SNP because the most significant SNP was not in linkage disequilibrium (LD) with the haplotype.



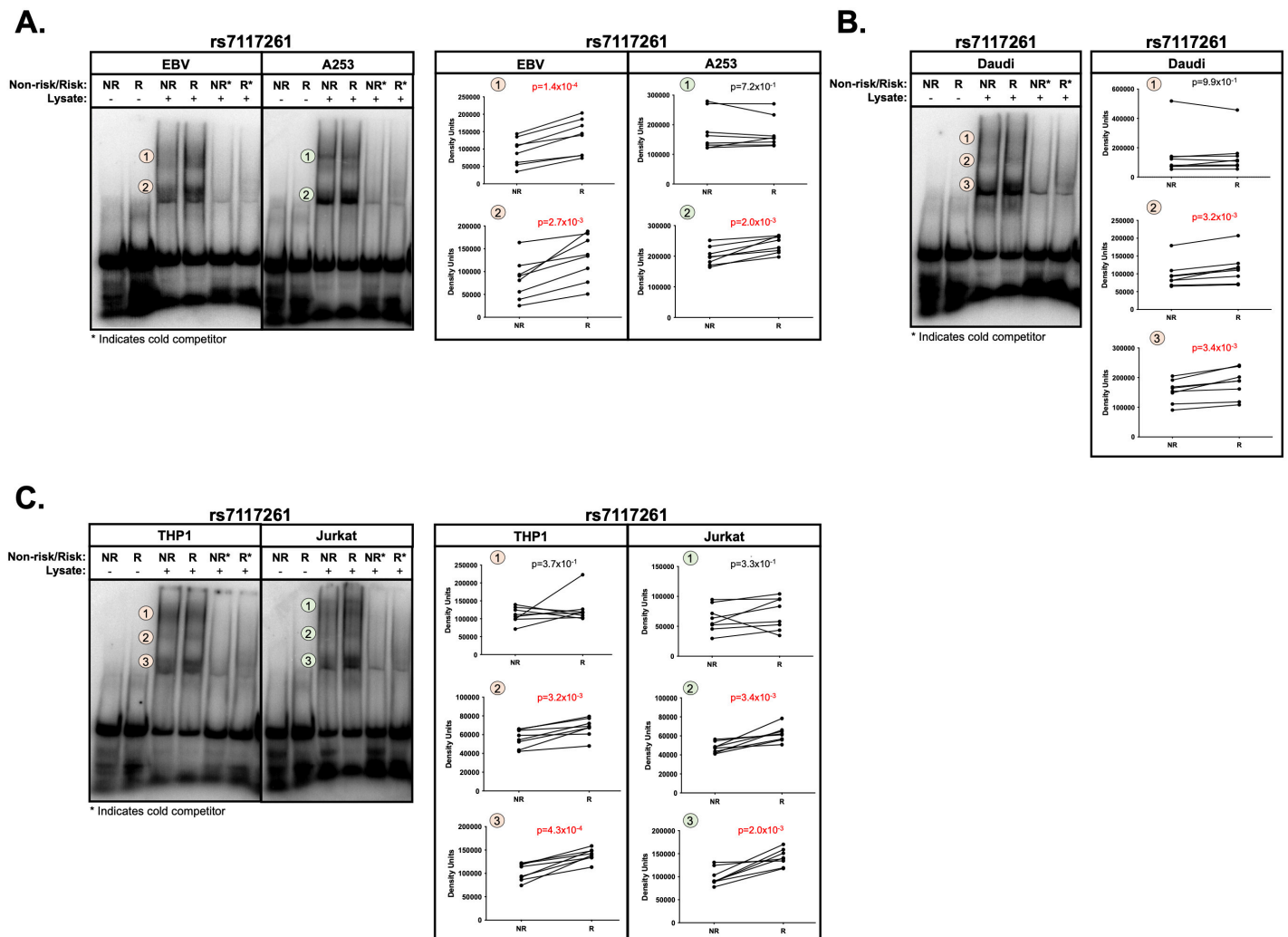
**Supplemental Figure 2. Haplotype frequency of the *DDX6-CXCR5* risk region in SjD. (A,D) Co-inheritance ( $D'$ ) and (B,E) pairwise linkage disequilibrium ( $r^2$ ) were assessed across the *DDX6-CXCR5* risk haplotype of SjD without (A-C) or with (D-F) rs480958. (C,F) Haplotype organization and frequencies of the index SNPs from the meta-analyses, SNPs previously reported as associated with SjD and/or SLE, and SNPs with strong bioinformatic functional evidence are shown.**



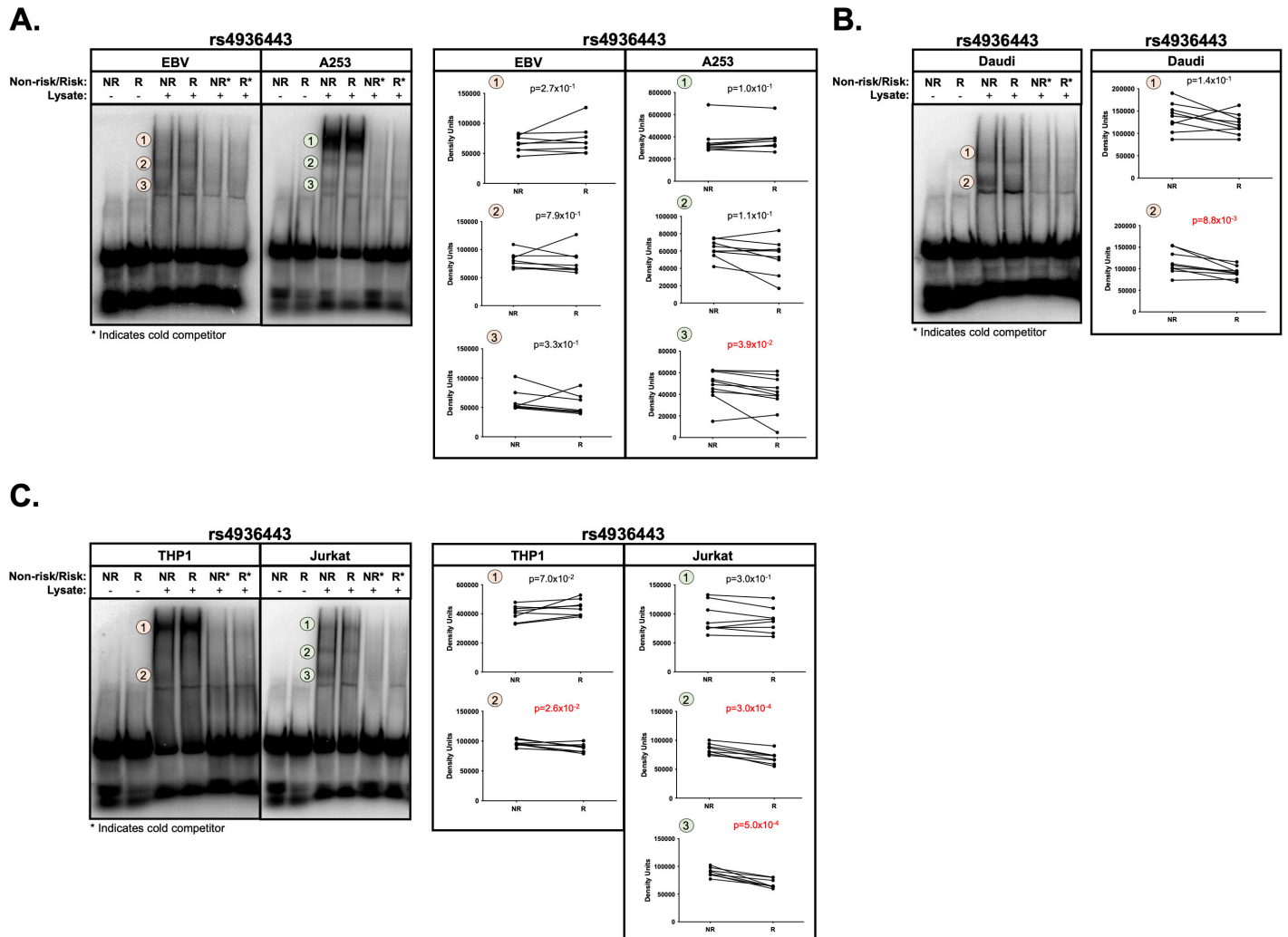




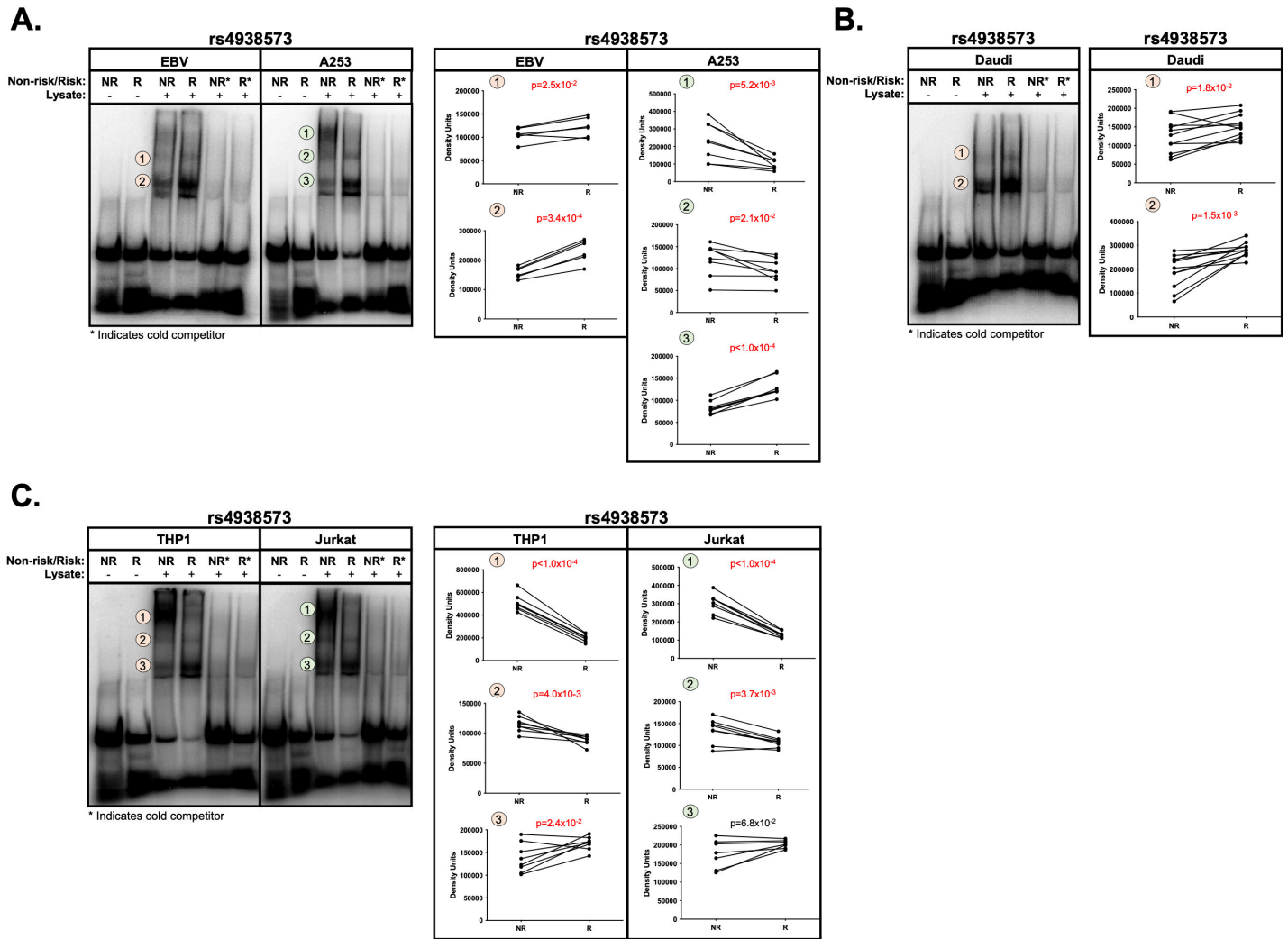
**Supplemental Figure 4. Allele- and cell-type specific differential nuclear protein affinities of SNPs rs57494551 and rs4938572.** (A-B) Radiolabeled electromobility shift assays (EMSA) were performed using oligonucleotides containing the non-risk (NR) or risk (R) allele of rs57494551 and nuclear extracts from (A) THP1 and Jurkat cells or (B) Daudi cells. (C-D) Radiolabeled EMSAs were performed using oligonucleotides containing the NR or R allele of rs4938572 and nuclear extracts from (A) THP1 and Jurkat cells or (B) Daudi cells. For all panels, probes incubated in the absence of nuclear lysate were used as negative control (Lanes 1, 2). Cold competitors were used to assess non-specific binding (Lanes 5, 6). Images are representative of  $n > 6$  biological replicates. Bands indicated by numbered orange or green circles were quantified by densitometry and analyzed using paired t-test; p-values are indicated.



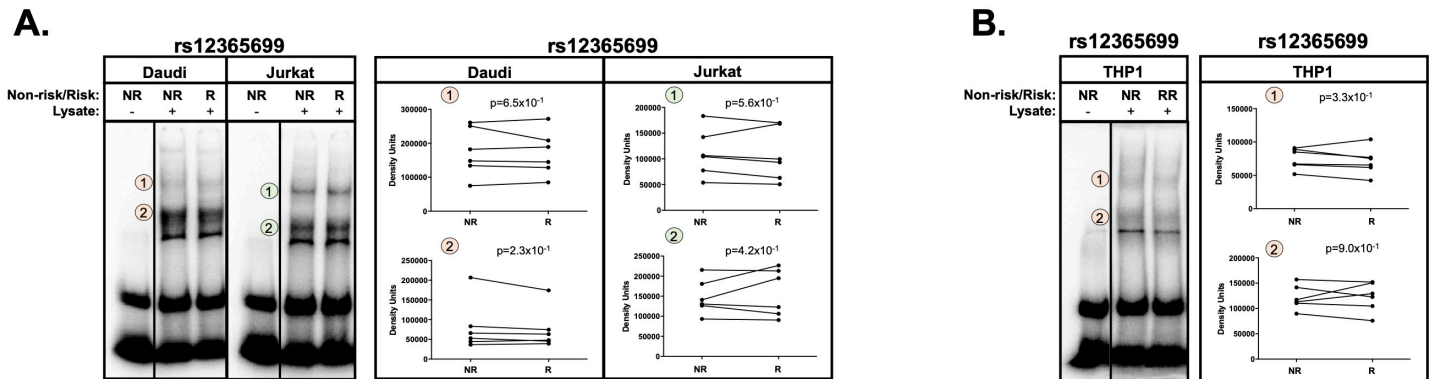
**Supplemental Figure 5. Allele- and cell-type specific differential nuclear protein affinities of SNPs rs7117261.** (A-C) Radiolabeled electromobility shift assays (EMSA) were performed using oligonucleotides containing the non-risk (NR) or risk (R) allele of rs7117261 and nuclear extracts from (A) EBV B and A253 cells, (B) Daudi cells, or (C) THP1 and Jurkat cells. For all panels, probes incubated in the absence of nuclear lysate were used as negative control (Lanes 1, 2). Cold competitors were used to assess non-specific binding (Lanes 5, 6). Images are representative of  $n > 6$  biological replicates. Bands indicated by numbered orange or green circles were quantified by densitometry and analyzed using paired t-test; p-values are indicated.



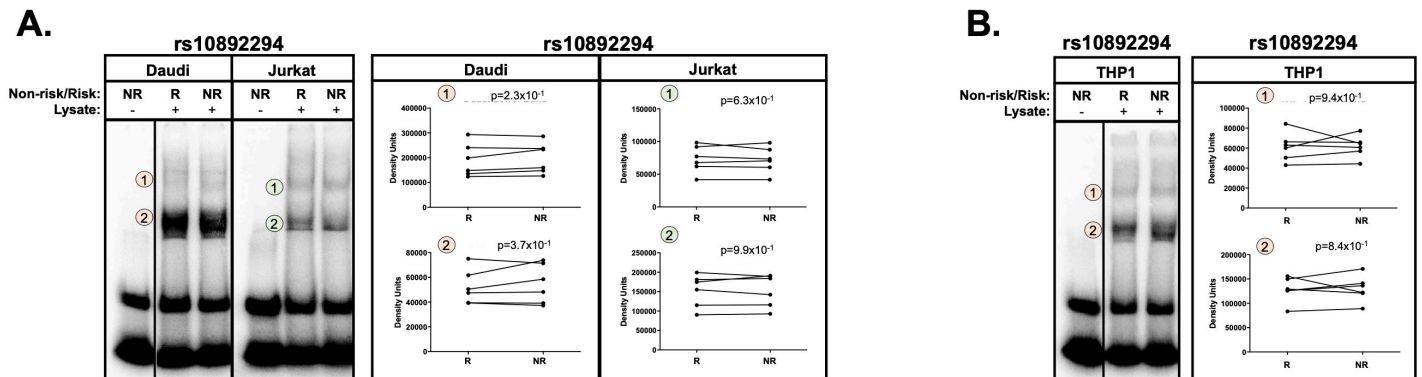
**Supplemental Figure 6. Allele- and cell-type specific differential nuclear protein affinities of SNPs rs4936443.** (A-C) Radiolabeled electromobility shift assays (EMSA) were performed using oligonucleotides containing the non-risk (NR) or risk (R) allele of rs4936443 and nuclear extracts from (A) EBV B and A253 cells, (B) Daudi cells, or (C) THP1 and Jurkat cells. For all panels, probes incubated in the absence of nuclear lysate were used as negative control (Lanes 1, 2). Cold competitors were used to assess non-specific binding (Lanes 5, 6). Images are representative of  $n > 6$  biological replicates. Bands indicated by numbered orange or green circles were quantified by densitometry and analyzed using paired t-test; p-values are indicated.



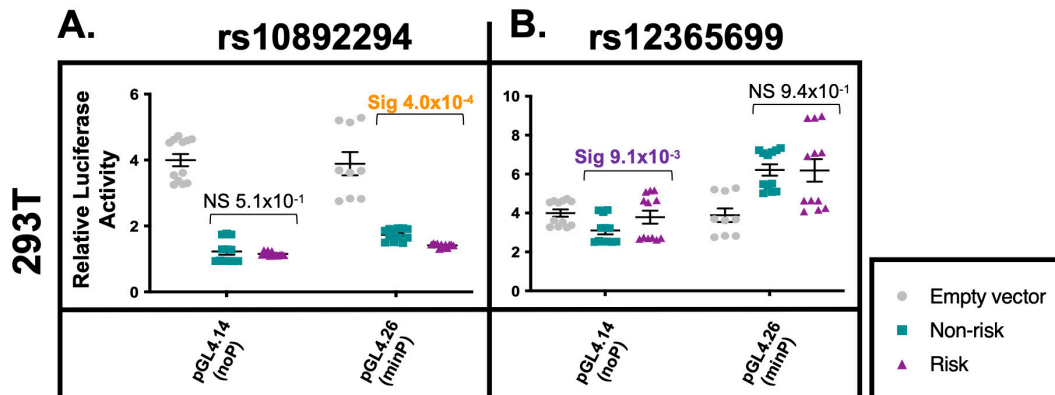
**Supplemental Figure 7. Allele- and cell-type specific differential nuclear protein affinities of SNPs rs4938573.** (A-C) Radiolabeled electromobility shift assays (EMSA) were performed using oligonucleotides containing the non-risk (NR) or risk (R) allele of rs4938573 and nuclear extracts from (A) EBV B and A253 cells, (B) Daudi cells, or (C) THP1 and Jurkat cells. For all panels, probes incubated in the absence of nuclear lysate were used as negative control (Lanes 1, 2). Cold competitors were used to assess non-specific binding (Lanes 5, 6). Images are representative of  $n > 6$  biological replicates. Bands indicated by numbered orange or green circles were quantified by densitometry and analyzed using paired t-test; p-values are indicated.



**Supplemental Figure 8. Allele- and cell-type specific differential nuclear protein affinities of SNPs rs12365699.** (A-B) Radiolabeled electromobility shift assays (EMSA) were performed using oligonucleotides containing the non-risk (NR) or risk (R) allele of rs12365699 and nuclear extracts from (A) Daudi and Jurkat cells or (B) THP 1. For all panels, probes incubated in the absence of nuclear lysate were used as negative control (Lanes 1). Images are representative of  $n > 6$  biological replicates. Bands indicated by numbered orange or green circles were quantified by densitometry and analyzed using paired t-test; p-values are indicated.

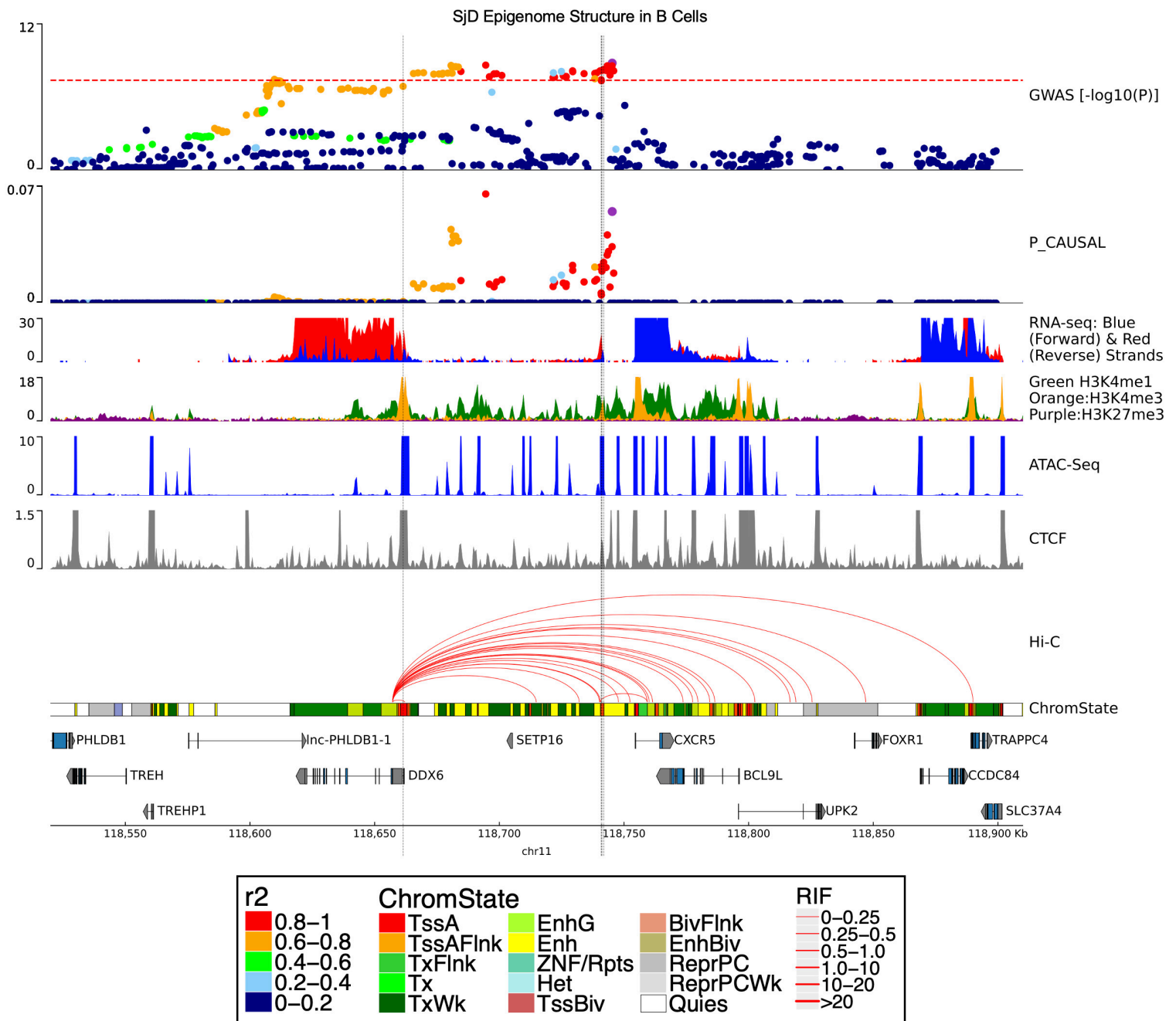


**Supplemental Figure 9. Allele- and cell-type specific differential nuclear protein affinities of SNPs rs10892294.** (A-B) Radiolabeled electromobility shift assays (EMSA) were performed using oligonucleotides containing the non-risk (NR) or risk (R) allele of rs10892294 and nuclear extracts from (A) Daudi and Jurkat cells or (B) THP1 cells. For all panels, probes incubated in the absence of nuclear lysate were used as negative control (Lanes 1). Images are representative of  $n > 6$  biological replicates. Bands indicated by numbered orange or green circles were quantified by densitometry and analyzed using paired t-test; p-values are indicated.

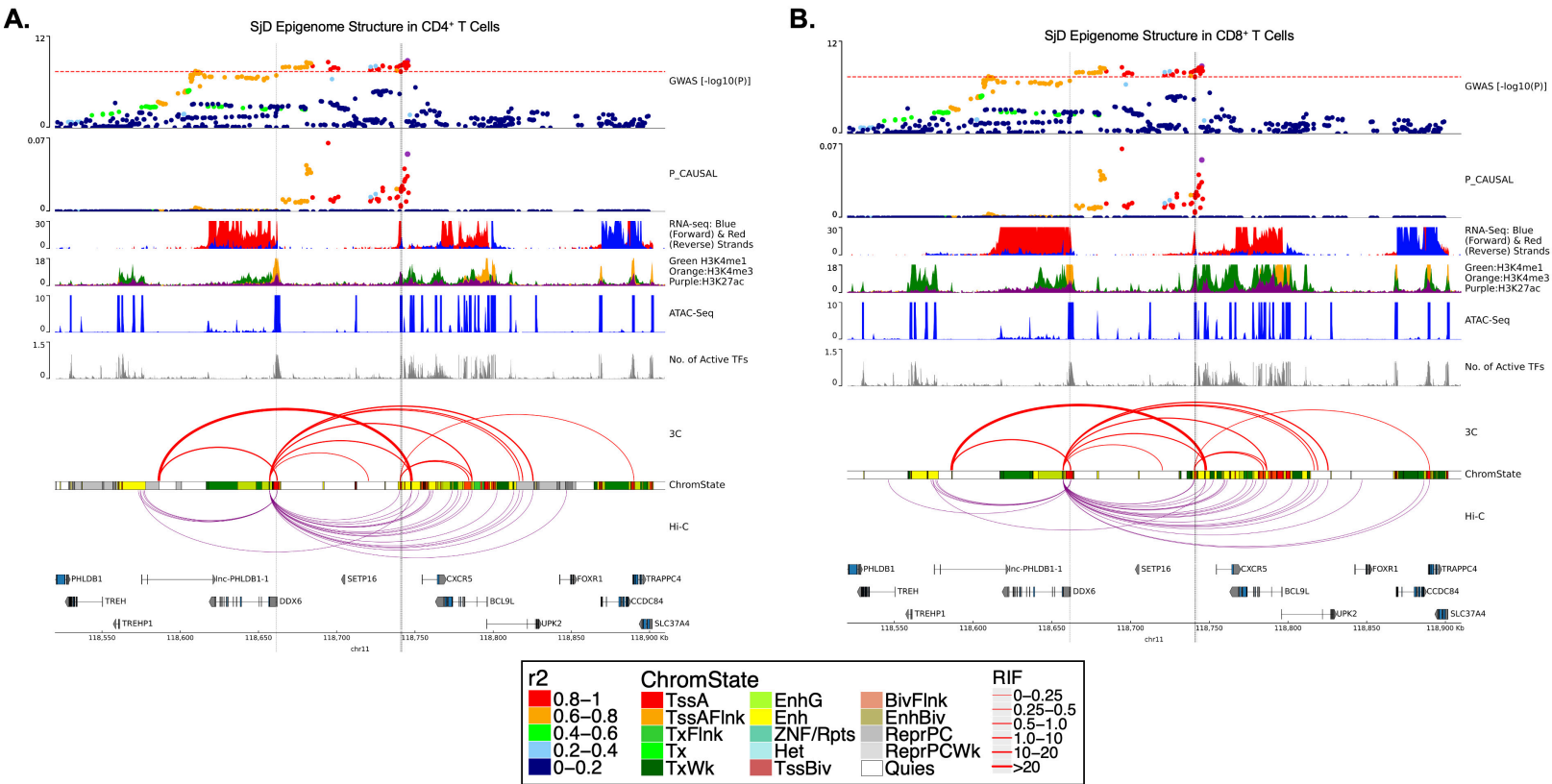


**Supplemental Figure 10. Allele-specific promoter and enhancer activity of rs10892294 and rs12365699 on the *DDX6-CXCR5* region in 293T cells.** gBlocks carrying the non-risk or risk alleles of (A) rs10892294 or (B) rs12365699 were cloned into a promoter-less (pGL4.14; noP) or minimal promoter (pGL4.26; minP) luciferase vector. Plasmids were transfected into 293T cells. Luciferase activity was measured after 24 hours and normalized to the Renilla transfection control and then the vector-only control; reported as Relative Luciferase Activity. Statistical comparisons were performed using a paired t-test; p-values are indicated.

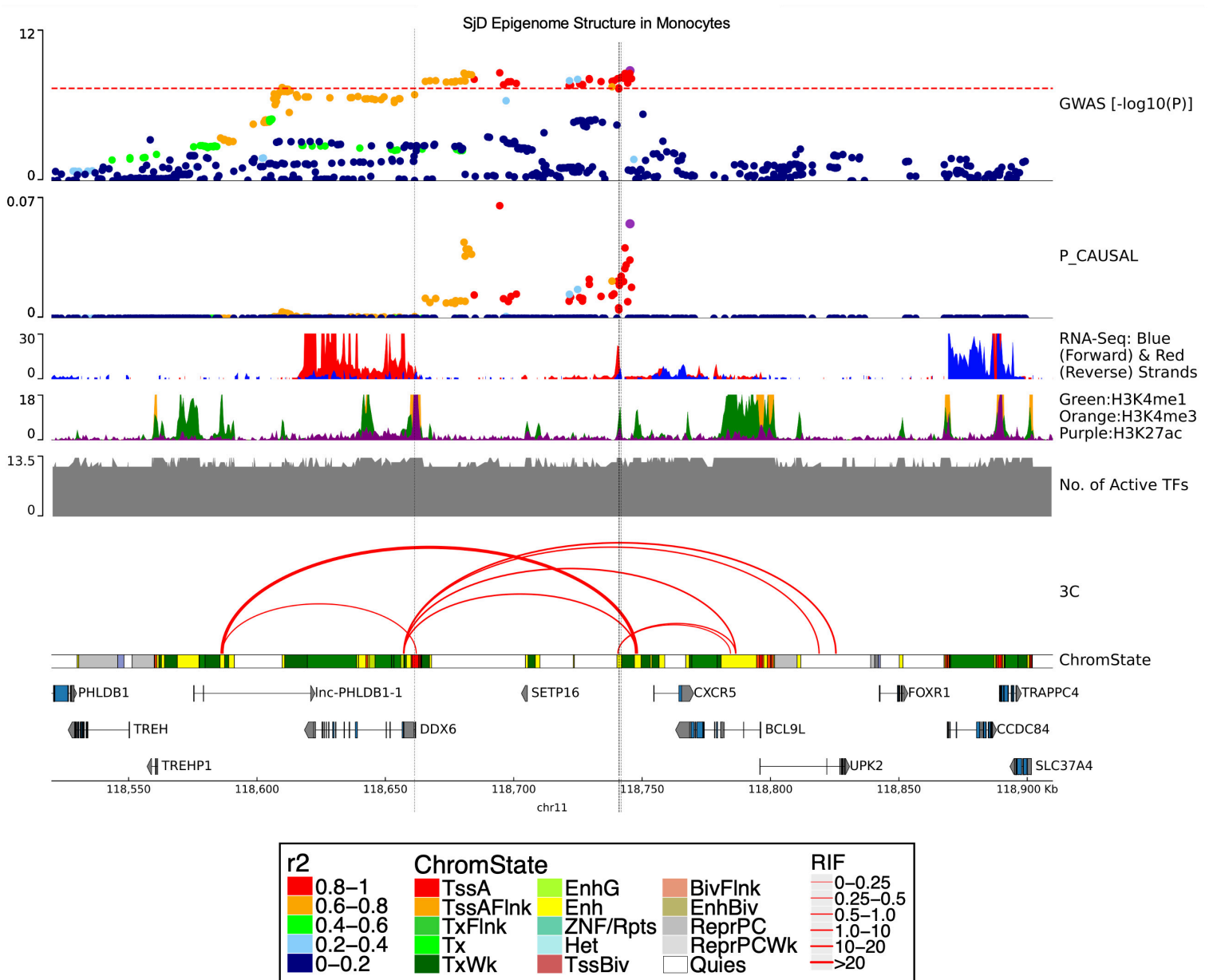




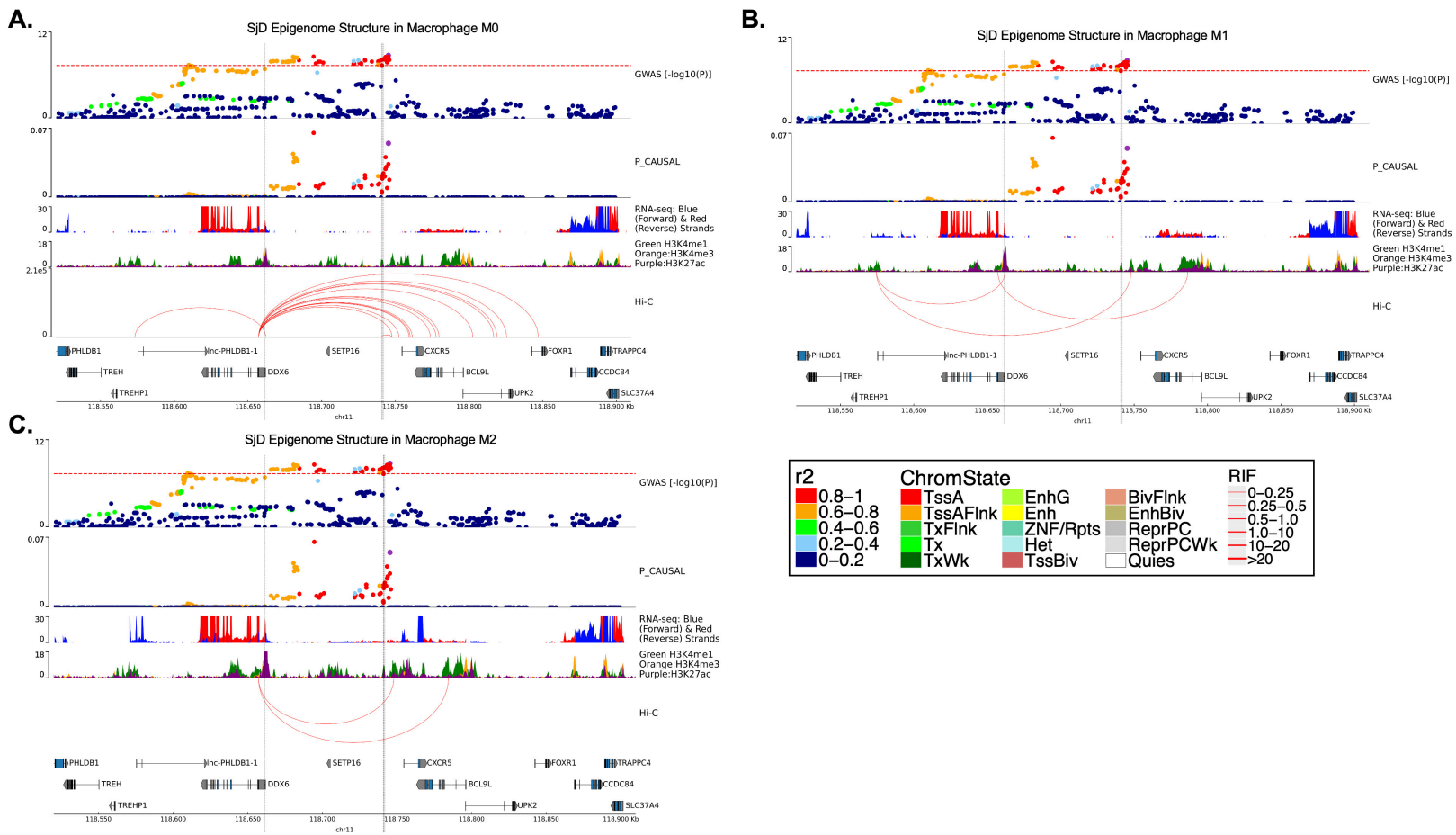
**Supplemental Figure 11. Complex chromatin architecture revealed across the *DDX6-CXCR5* region in human primary B cells.** SjD GWAS association (top panel), publicly available epigenomic enrichment, and promoter-capture Hi-C looping data (red lines) across the *DDX6-CXCR5* region in human primary B cells are shown. Vertical grey lines indicate the locations of rs57494551 or rs4938572, respectively.



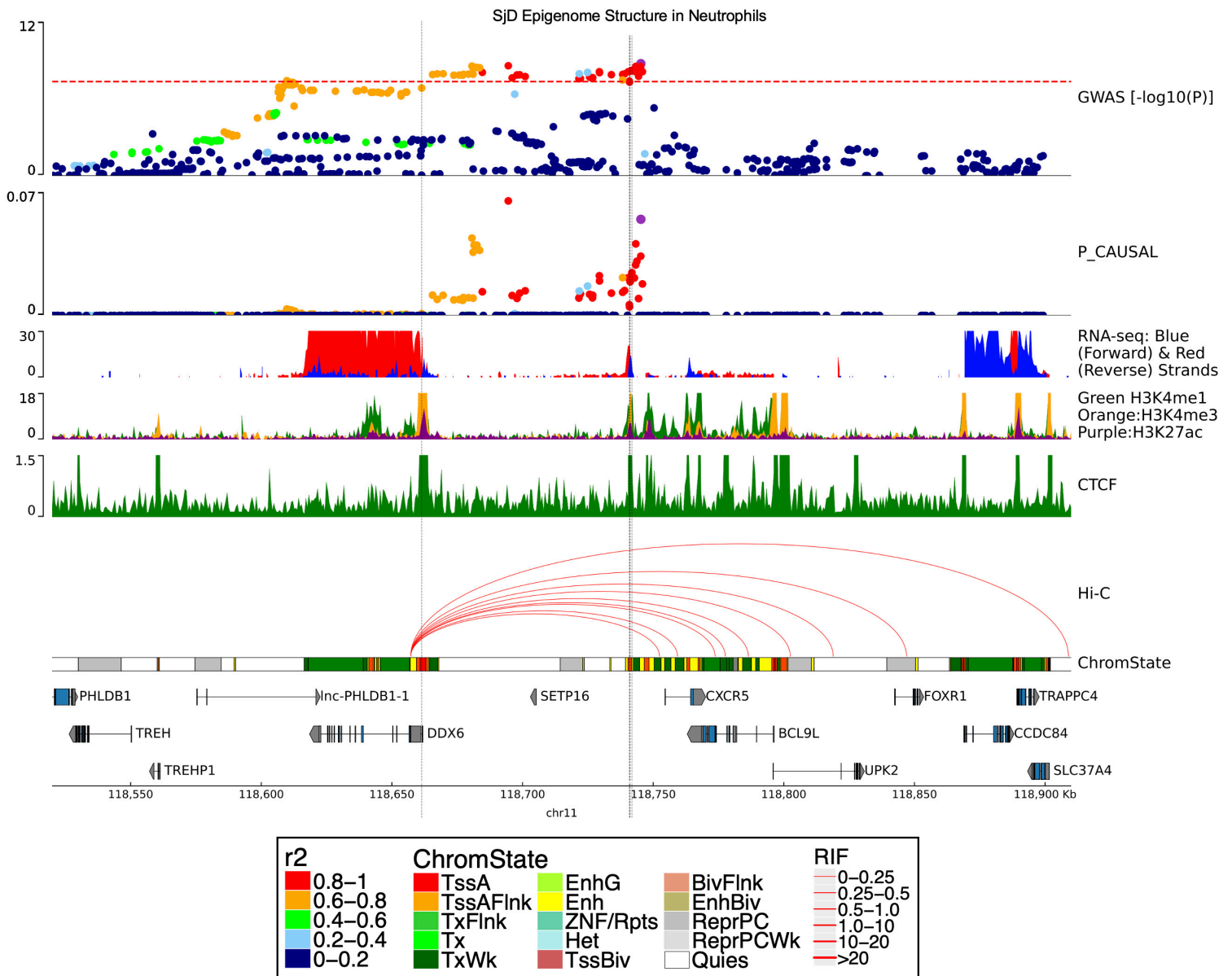
**Supplemental Figure 12. Complex chromatin architecture revealed across the *DDX6*-*CXCR5* region in primary human T cells.** SJD GWAS association (top panel) and publicly available epigenomic enrichment across the *DDX6*-*CXCR5* region in human primary (A) CD4<sup>+</sup> T cells and (B) CD8<sup>+</sup> T cells. Vertical grey lines indicate the locations of rs57494551 or rs4938572, respectively. Promoter-capture Hi-C looping (purple lines) contrasts the summary 3C-qPCR results reported in Figure 6 (red lines); 3C-qPCR line thickness indicates relative interaction frequency (RIF).



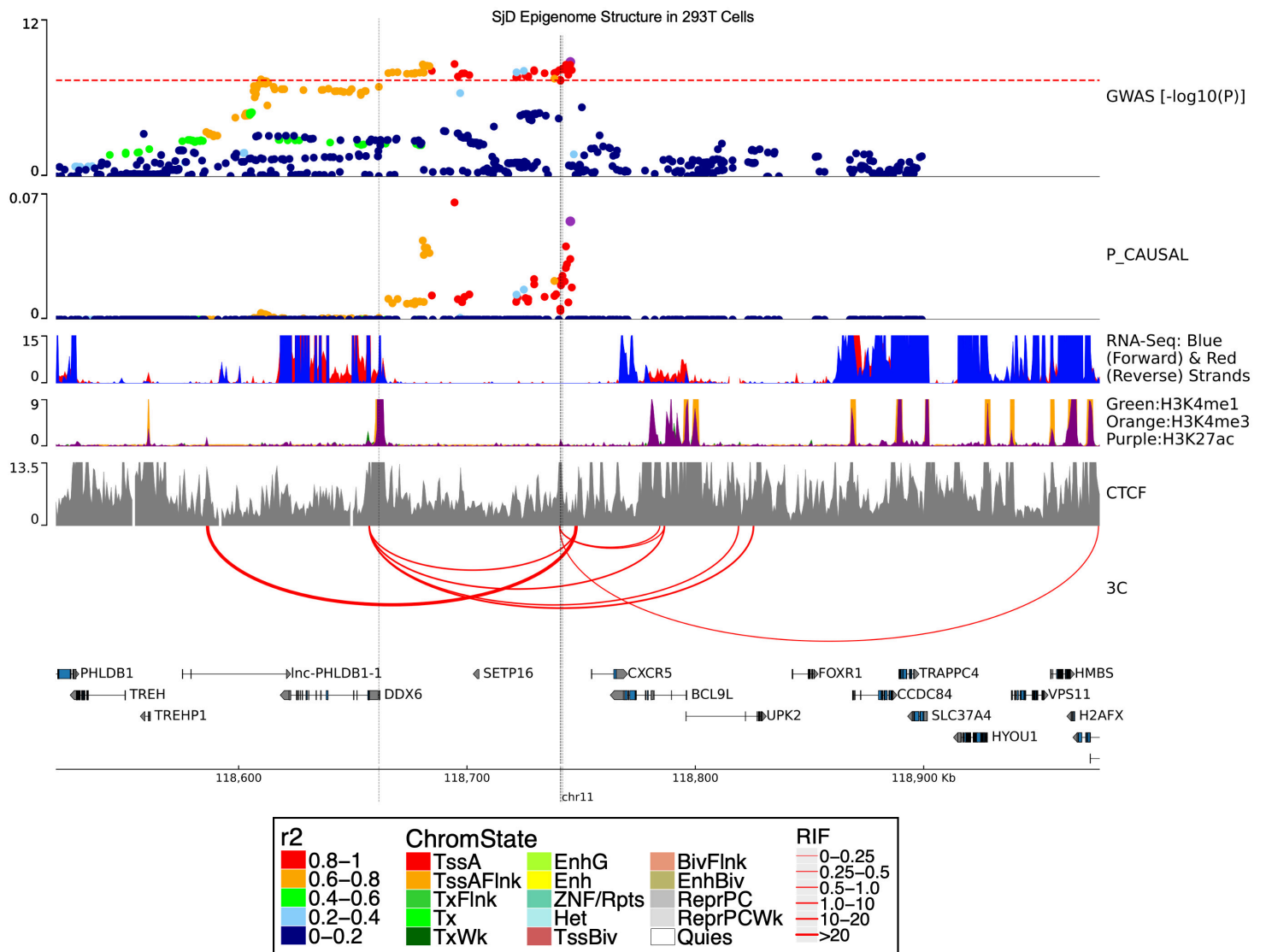
**Supplemental Figure 13. Complex chromatin architecture revealed across the *DDX6-CXCR5* region in human primary monocytes.** SjD GWAS association (top panel) and publicly available epigenomic enrichment across the *DDX6-CXCR5* region in human primary monocytes. Vertical grey lines indicate the locations of rs57494551 or rs4938572, respectively. Summary 3C-qPCR results reported in Figure 6 are also shown (red lines); line thickness indicates relative interaction frequency (RIF).



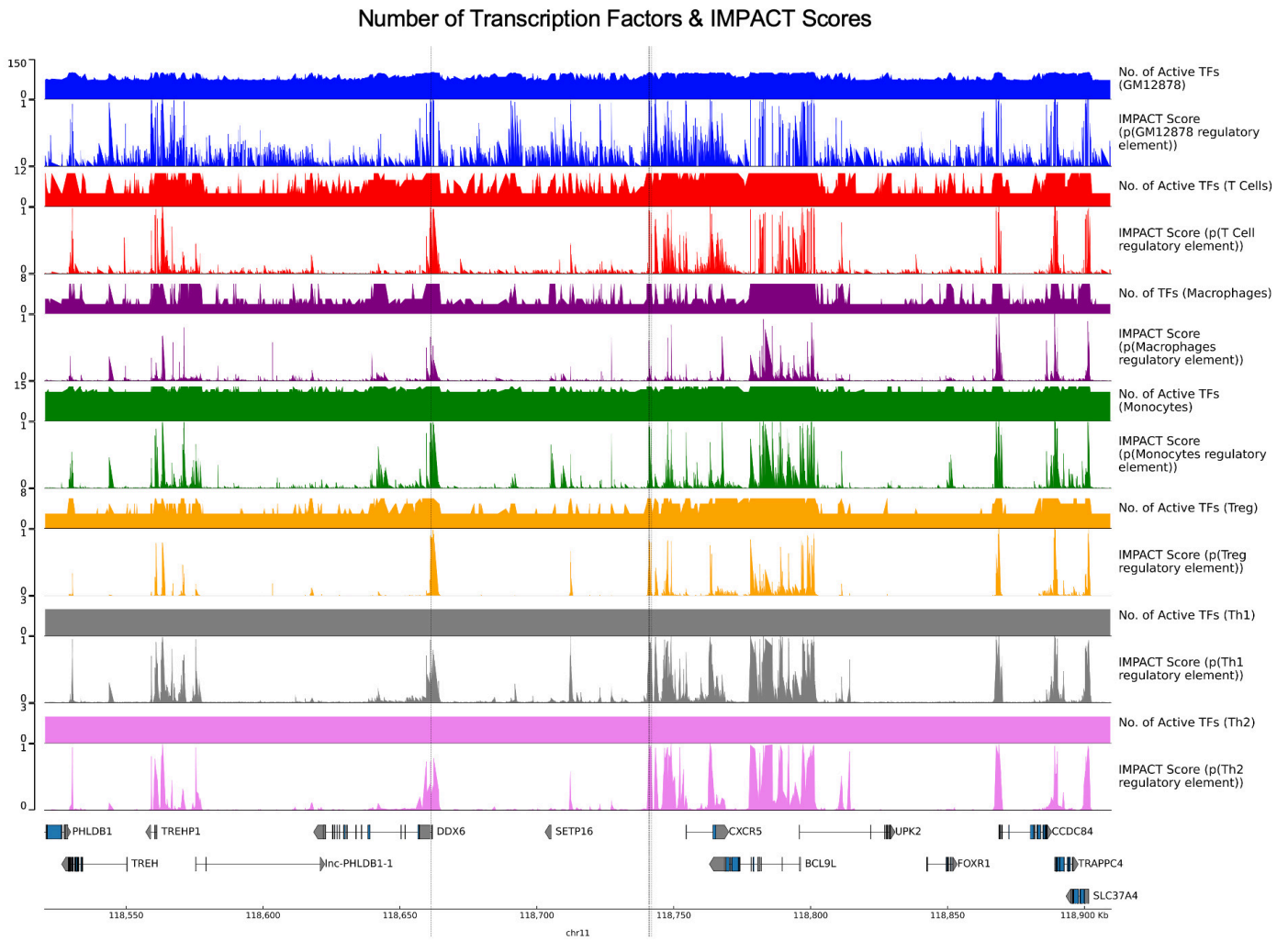
**Supplemental Figure 14. Complex chromatin architecture revealed across the *DDX6-CXCR5* region in human primary macrophages.** SjD GWAS association (top panel), publicly available epigenomic enrichment, and promoter-capture Hi-C looping data (red lines) across the *DDX6-CXCR5* region in human primary (A) M0, (B) M1, and (C) M2 macrophages. Vertical grey lines indicate the locations of rs57494551 or rs4938572, respectively.



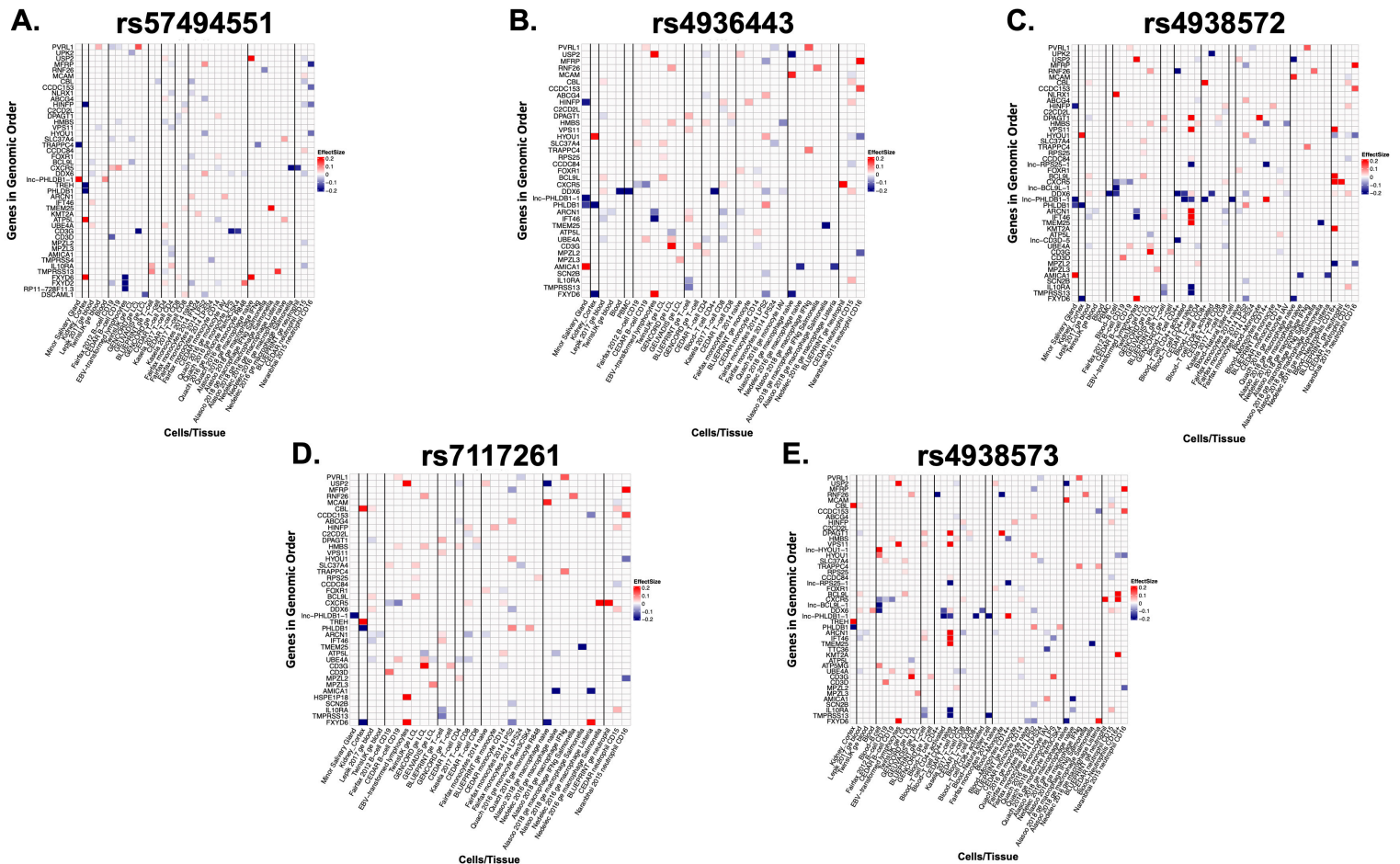
**Supplemental Figure 15. Complex chromatin architecture revealed across the *DDX6-CXCR5* region in human primary neutrophils.** SjD GWAS association (top panel), publicly available epigenomic enrichment, and promoter-capture Hi-C looping data (red lines) across the *DDX6-CXCR5* region in human neutrophils. Vertical grey lines indicate the locations of rs57494551 or rs4938572, respectively.



**Supplemental Figure 16. Complex chromatin architecture revealed across the *DDX6-CXCR5* region in human 293T cells.** SjD GWAS association (top panel) and publicly available epigenomic enrichment across the *DDX6-CXCR5* region in 293T cells. Vertical grey lines indicate the locations of rs57494551 or rs4938572, respectively. Summary 3C-qPCR results reported in Figure 6 are also shown (red lines); line thickness indicates relative interaction frequency (RIF).

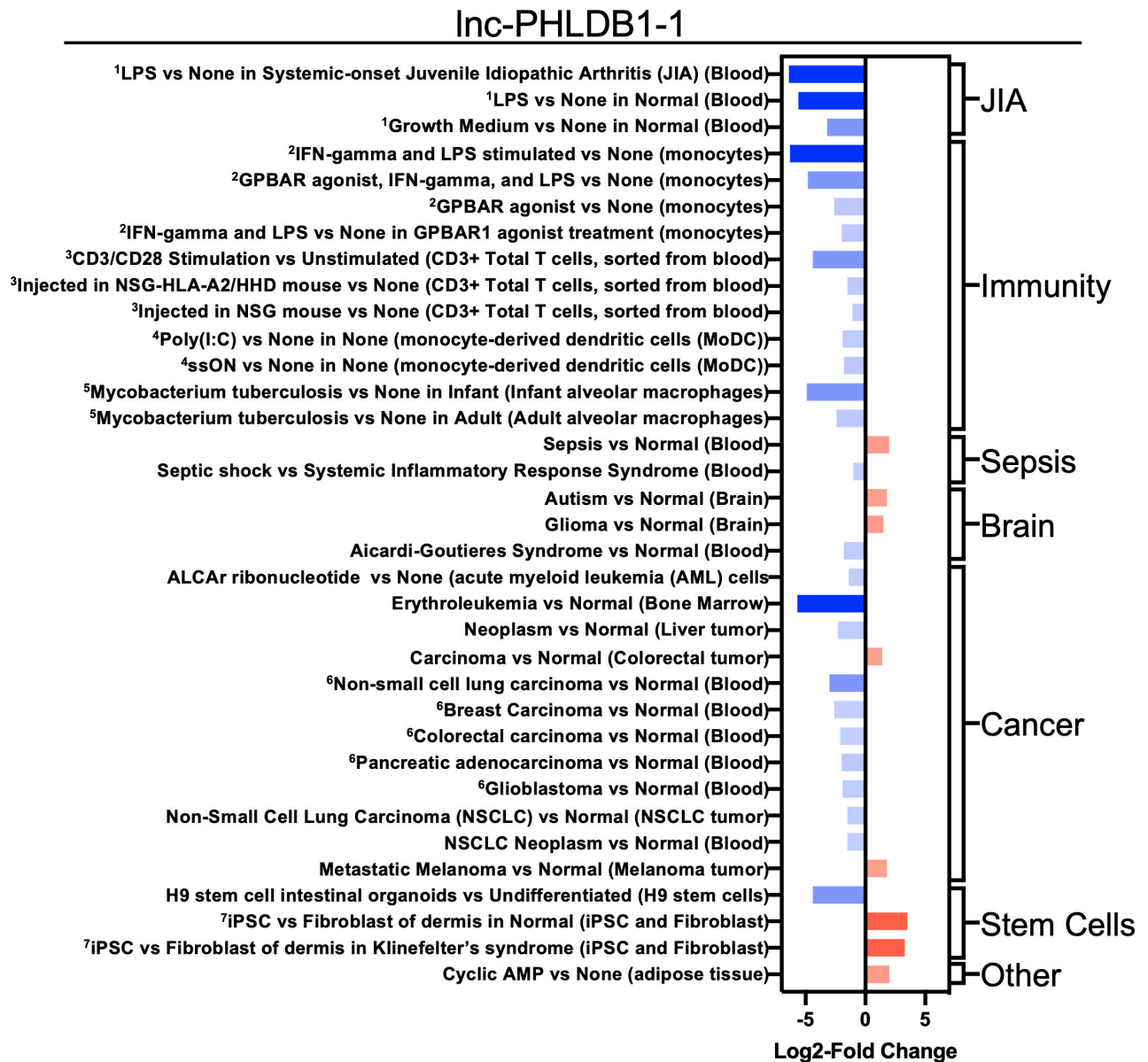


**Supplemental Figure 17. IMPACT regulatory element probabilities and corresponding transcription factor elements in immune cells.** IMPACT uses transcription factor binding sites (TF) to predict the locations of regulatory sites across the genome. Image shows predicted IMPACT regulatory elements for GM12878 B cell line and primary human T cells, macrophages, monocytes, regulatory T cells (Treg), Th1 cells, and Th2 cells. The location of the rs57494551 and rs4938572 are indicates as vertical grey lines.



**Supplemental Figure 18. eQTLs for five prioritized SNPs across blood, salivary and kidney tissue, and immune cells.** eQTL values from GTEx in minor salivary gland, blood, kidney tissue, EBV B cells, and human primary immune cells in genes upstream and downstream of the *DDX6-CXCR5* interval for **(A)** rs57494551, **(B)** rs4936443, **(C)** rs4938572, **(D)** rs7117261, **(E)** rs4938573. Vertical lines separate different cell types. Horizontal lines highlight interesting genes such as *CXCR5*, *DDX6*, *Inc-PHLDB1-1*, *TRAPPC4*, and *IL10RA*.





**Supplemental Figure 19. Expression Atlas results for Inc-PHLDB1-1 (ENSG00000255422).** RNA-seq results from Expression Atlas (<https://www.ebi.ac.uk/gxa/home>) published studies where increases in *Inc-PHLDB1-1* (ENSG00000255422) expression are in red and decreased expression are in blue. Superscripts are used to depict experiments with multiple plotted conditions.