

Supplementary Materials

Supplementary Table 1. SNPs used for the LTL instruments in the Mendelian Randomization analyses.

Supplementary Table 2. GWAS summary statistics on outcomes: source and description.

Supplementary Table 3 MR steiger analysis showing the causal direction of leukocyte telomere length (LTL) on Immune-mediated Inflammatory Diseases (IMIDs).

Supplementary Table 1. SNPs used for the LTL instruments in the Mendelian Randomization analyses.

| SNP | effect_allele | other_allele | eaf | beta | se | F | pval |
|-------------|---------------|--------------|-------|--------|-------|----------|-----------|
| rs2977608 | A | C | 0.256 | -0.013 | 0.002 | 30.694 | 3.00E-08 |
| rs66731853 | G | A | 0.683 | 0.018 | 0.002 | 68.115 | 1.50E-16 |
| rs6669563 | G | A | 0.562 | -0.018 | 0.002 | 81.115 | 2.10E-19 |
| rs4660456 | A | G | 0.770 | -0.014 | 0.002 | 35.307 | 2.80E-09 |
| rs41269079 | T | A | 0.811 | -0.015 | 0.003 | 36.294 | 1.70E-09 |
| rs139795227 | A | C | 0.986 | -0.060 | 0.009 | 47.112 | 6.70E-12 |
| rs145114957 | C | G | 0.957 | -0.027 | 0.005 | 29.860 | 4.60E-08 |
| rs4498805 | G | T | 0.453 | -0.015 | 0.002 | 56.489 | 5.70E-14 |
| rs17464525 | G | A | 0.819 | 0.032 | 0.003 | 156.506 | 6.60E-36 |
| rs11579626 | A | C | 0.915 | -0.027 | 0.004 | 54.916 | 1.30E-13 |
| rs6587577 | A | G | 0.174 | 0.018 | 0.003 | 47.752 | 4.80E-12 |
| rs6659669 | C | T | 0.395 | 0.012 | 0.002 | 32.571 | 1.10E-08 |
| rs932002 | C | T | 0.849 | 0.040 | 0.003 | 206.672 | 7.30E-47 |
| rs2555104 | A | C | 0.566 | 0.014 | 0.002 | 47.139 | 6.60E-12 |
| rs56178008 | T | A | 0.563 | -0.014 | 0.002 | 50.904 | 9.70E-13 |
| rs6751209 | T | C | 0.796 | 0.014 | 0.002 | 31.960 | 1.60E-08 |
| rs965109 | C | T | 0.976 | 0.102 | 0.006 | 246.173 | 1.80E-55 |
| rs188918174 | C | T | 0.964 | -0.040 | 0.005 | 54.977 | 1.20E-13 |
| rs12619538 | A | C | 0.859 | -0.017 | 0.003 | 33.865 | 5.90E-09 |
| rs17803849 | C | T | 0.595 | -0.027 | 0.002 | 180.268 | 4.20E-41 |
| rs4535042 | T | G | 0.701 | -0.012 | 0.002 | 30.532 | 3.30E-08 |
| rs869785 | T | C | 0.328 | 0.015 | 0.002 | 47.915 | 4.40E-12 |
| rs2230590 | T | C | 0.489 | 0.016 | 0.002 | 61.927 | 3.60E-15 |
| rs78491606 | A | C | 0.982 | 0.076 | 0.007 | 104.128 | 1.90E-24 |
| rs13062095 | T | C | 0.672 | -0.014 | 0.002 | 41.874 | 9.70E-11 |
| rs6776756 | G | A | 0.402 | 0.017 | 0.002 | 73.300 | 1.10E-17 |
| rs9878436 | C | T | 0.566 | 0.014 | 0.002 | 50.491 | 1.20E-12 |
| rs10936598 | A | C | 0.676 | 0.066 | 0.002 | 935.118 | 1.00E-200 |
| rs76094497 | G | A | 0.948 | -0.028 | 0.005 | 36.430 | 1.60E-09 |
| rs563069803 | G | T | 0.982 | 0.057 | 0.009 | 43.873 | 3.50E-11 |
| rs112394943 | T | C | 0.837 | 0.020 | 0.003 | 49.905 | 1.60E-12 |
| rs2282764 | A | G | 0.858 | 0.022 | 0.003 | 60.039 | 9.30E-15 |
| rs871134 | C | T | 0.431 | 0.018 | 0.002 | 81.551 | 1.70E-19 |
| rs10805346 | T | C | 0.561 | -0.012 | 0.002 | 33.541 | 7.00E-09 |
| rs4695407 | A | G | 0.492 | -0.014 | 0.002 | 50.101 | 1.50E-12 |
| rs10024820 | T | C | 0.611 | 0.014 | 0.002 | 49.366 | 2.10E-12 |
| rs4435700 | C | A | 0.235 | -0.054 | 0.002 | 507.529 | 2.20E-112 |
| rs11746381 | T | C | 0.943 | -0.033 | 0.004 | 58.598 | 1.90E-14 |
| rs11745132 | G | T | 0.992 | -0.071 | 0.012 | 35.284 | 2.80E-09 |
| rs7726159 | C | A | 0.673 | -0.071 | 0.002 | 1105.852 | 1.00E-200 |
| rs61748181 | C | T | 0.971 | 0.059 | 0.006 | 98.800 | 2.80E-23 |
| rs6881568 | C | A | 0.637 | -0.017 | 0.002 | 66.385 | 3.70E-16 |
| rs6873104 | A | T | 0.899 | 0.025 | 0.003 | 53.496 | 2.60E-13 |
| rs55747751 | G | A | 0.923 | 0.021 | 0.004 | 31.815 | 1.70E-08 |
| rs185174247 | G | A | 0.944 | -0.037 | 0.004 | 73.400 | 1.10E-17 |
| rs80324517 | G | A | 0.952 | -0.040 | 0.005 | 72.313 | 1.80E-17 |
| rs7772289 | G | T | 0.497 | -0.018 | 0.002 | 76.990 | 1.70E-18 |
| rs2763979 | C | T | 0.640 | 0.028 | 0.002 | 178.107 | 1.30E-40 |
| rs112817717 | G | C | 0.524 | -0.014 | 0.002 | 41.206 | 1.40E-10 |
| rs141127771 | G | A | 0.741 | 0.016 | 0.003 | 35.618 | 2.40E-09 |
| rs9398196 | A | G | 0.480 | 0.014 | 0.002 | 50.942 | 9.50E-13 |
| rs61405042 | C | T | 0.971 | 0.050 | 0.006 | 69.282 | 8.50E-17 |
| rs13230646 | T | C | 0.751 | 0.017 | 0.002 | 55.603 | 8.90E-14 |
| rs11769630 | T | A | 0.928 | 0.026 | 0.004 | 43.476 | 4.30E-11 |
| rs38664 | T | C | 0.403 | 0.012 | 0.002 | 35.197 | 3.00E-09 |
| rs2056726 | G | A | 0.786 | 0.023 | 0.002 | 87.635 | 7.90E-21 |
| rs7790856 | C | T | 0.711 | 0.044 | 0.002 | 393.042 | 1.80E-87 |
| rs565783711 | C | T | 0.982 | -0.057 | 0.008 | 49.655 | 1.80E-12 |
| rs6969930 | T | C | 0.387 | 0.020 | 0.002 | 100.112 | 1.40E-23 |
| rs117407747 | C | T | 0.972 | -0.045 | 0.006 | 54.246 | 1.80E-13 |
| rs1985369 | A | G | 0.132 | 0.031 | 0.003 | 107.403 | 3.60E-25 |

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|-------------|---|---|-------|--------|-------|---------|-----------|
| rs2306646 | G | C | 0.441 | 0.021 | 0.002 | 107.587 | 3.30E-25 |
| rs762679 | T | A | 0.143 | -0.031 | 0.003 | 118.373 | 1.40E-27 |
| rs10808899 | G | C | 0.111 | 0.030 | 0.003 | 89.464 | 3.10E-21 |
| rs10112752 | G | A | 0.570 | 0.029 | 0.002 | 201.565 | 9.50E-46 |
| rs1023767 | G | A | 0.762 | 0.018 | 0.002 | 61.246 | 5.00E-15 |
| rs4742448 | C | G | 0.531 | -0.015 | 0.002 | 56.239 | 6.40E-14 |
| rs11557154 | C | T | 0.870 | 0.034 | 0.003 | 132.559 | 1.10E-30 |
| rs4743037 | C | T | 0.769 | -0.015 | 0.002 | 38.624 | 5.10E-10 |
| rs10905255 | G | T | 0.421 | 0.018 | 0.002 | 80.738 | 2.60E-19 |
| rs7906139 | G | A | 0.870 | 0.019 | 0.003 | 39.214 | 3.80E-10 |
| rs12412214 | G | A | 0.720 | 0.025 | 0.002 | 121.218 | 3.40E-28 |
| rs11190270 | G | A | 0.798 | 0.014 | 0.003 | 29.790 | 4.80E-08 |
| rs9419958 | T | C | 0.139 | 0.081 | 0.003 | 760.033 | 2.60E-167 |
| rs805664 | A | T | 0.013 | 0.087 | 0.009 | 86.197 | 1.60E-20 |
| rs77231040 | G | C | 0.994 | -0.099 | 0.013 | 53.982 | 2.00E-13 |
| rs939916 | G | A | 0.330 | -0.024 | 0.002 | 124.475 | 6.60E-29 |
| rs1609812 | G | A | 0.160 | -0.047 | 0.003 | 290.464 | 3.90E-65 |
| rs10840270 | C | G | 0.344 | -0.014 | 0.002 | 45.815 | 1.30E-11 |
| rs2293579 | G | A | 0.614 | 0.013 | 0.002 | 39.504 | 3.30E-10 |
| rs611646 | T | A | 0.591 | 0.037 | 0.002 | 327.412 | 3.50E-73 |
| rs11212631 | T | C | 0.801 | 0.019 | 0.003 | 56.861 | 4.70E-14 |
| rs6590343 | A | G | 0.484 | -0.012 | 0.002 | 36.522 | 1.50E-09 |
| rs10845387 | G | A | 0.647 | 0.014 | 0.002 | 45.480 | 1.50E-11 |
| rs12369950 | T | C | 0.859 | 0.018 | 0.003 | 37.751 | 8.00E-10 |
| rs79755767 | G | A | 0.904 | -0.028 | 0.003 | 65.895 | 4.80E-16 |
| rs17445108 | G | A | 0.873 | 0.017 | 0.003 | 31.498 | 2.00E-08 |
| rs1907702 | G | A | 0.233 | -0.015 | 0.002 | 38.340 | 5.90E-10 |
| rs10774624 | G | A | 0.467 | -0.015 | 0.002 | 53.243 | 2.90E-13 |
| rs76666449 | T | C | 0.899 | -0.030 | 0.003 | 78.458 | 8.20E-19 |
| rs10773176 | A | G | 0.259 | 0.017 | 0.002 | 56.650 | 5.20E-14 |
| rs28577594 | G | C | 0.290 | -0.019 | 0.002 | 70.168 | 5.40E-17 |
| rs1332941 | A | G | 0.180 | -0.026 | 0.003 | 88.210 | 5.90E-21 |
| rs670180 | T | A | 0.431 | 0.012 | 0.002 | 32.521 | 1.20E-08 |
| rs9600019 | C | T | 0.664 | -0.013 | 0.002 | 35.594 | 2.40E-09 |
| rs3093888 | G | A | 0.949 | 0.029 | 0.005 | 41.004 | 1.50E-10 |
| rs73581419 | C | T | 0.893 | -0.023 | 0.003 | 50.273 | 1.30E-12 |
| rs113525195 | C | A | 0.710 | 0.012 | 0.002 | 30.645 | 3.10E-08 |
| rs45604339 | C | T | 0.658 | 0.020 | 0.002 | 93.394 | 4.30E-22 |
| rs137901416 | G | A | 0.900 | -0.046 | 0.003 | 189.238 | 4.70E-43 |
| rs8006485 | G | T | 0.547 | -0.019 | 0.002 | 91.418 | 1.20E-21 |
| rs1957937 | A | T | 0.840 | -0.021 | 0.003 | 58.659 | 1.90E-14 |
| rs11629678 | G | A | 0.671 | -0.022 | 0.002 | 104.991 | 1.20E-24 |
| rs181647350 | T | C | 0.761 | 0.034 | 0.002 | 201.990 | 7.70E-46 |
| rs1980240 | A | C | 0.595 | -0.013 | 0.002 | 40.312 | 2.20E-10 |
| rs5742915 | T | C | 0.554 | -0.019 | 0.002 | 90.846 | 1.60E-21 |
| rs113490934 | T | C | 0.938 | 0.035 | 0.004 | 71.229 | 3.20E-17 |
| rs12932179 | A | G | 0.439 | 0.014 | 0.002 | 45.160 | 1.80E-11 |
| rs182059586 | T | C | 0.975 | 0.057 | 0.007 | 70.373 | 4.90E-17 |
| rs450962 | A | G | 0.716 | -0.014 | 0.002 | 33.870 | 5.90E-09 |
| rs1105407 | C | G | 0.833 | -0.016 | 0.003 | 34.099 | 5.20E-09 |
| rs76219171 | G | A | 0.942 | -0.036 | 0.004 | 69.466 | 7.80E-17 |
| rs528301822 | A | T | 0.711 | -0.024 | 0.002 | 118.080 | 1.70E-27 |
| rs62050964 | G | A | 0.662 | 0.019 | 0.002 | 77.106 | 1.60E-18 |
| rs11866592 | G | A | 0.858 | -0.035 | 0.003 | 146.073 | 1.30E-33 |
| rs2303262 | C | T | 0.223 | 0.047 | 0.002 | 382.932 | 2.90E-85 |
| rs11117354 | T | C | 0.303 | -0.023 | 0.002 | 112.098 | 3.40E-26 |
| rs12925933 | A | C | 0.338 | 0.015 | 0.002 | 47.033 | 7.00E-12 |
| rs59409453 | A | G | 0.269 | -0.020 | 0.002 | 77.118 | 1.60E-18 |
| rs12451892 | T | C | 0.619 | 0.012 | 0.002 | 31.307 | 2.20E-08 |
| rs4724 | G | A | 0.883 | 0.055 | 0.003 | 307.006 | 9.80E-69 |
| rs75664430 | C | G | 0.752 | 0.024 | 0.002 | 102.883 | 3.60E-24 |
| rs111527438 | T | C | 0.649 | -0.013 | 0.002 | 35.090 | 3.10E-09 |

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|----|-------------|---|---|-------|--------|-------|---------|-----------|
| | rs12941945 | A | G | 0.832 | 0.026 | 0.003 | 94.099 | 3.00E-22 |
| | rs7209057 | G | A | 0.439 | -0.012 | 0.002 | 33.943 | 5.70E-09 |
| | rs6501181 | T | A | 0.463 | -0.013 | 0.002 | 42.685 | 6.40E-11 |
| | rs144204502 | C | T | 0.987 | 0.101 | 0.009 | 121.249 | 3.40E-28 |
| | rs3891167 | A | G | 0.747 | 0.043 | 0.002 | 315.777 | 1.20E-70 |
| | rs150150565 | C | T | 0.979 | -0.064 | 0.007 | 74.269 | 6.80E-18 |
| | rs116863223 | G | A | 0.988 | 0.082 | 0.009 | 76.164 | 2.60E-18 |
| | rs139669835 | C | T | 0.991 | 0.061 | 0.011 | 33.812 | 6.10E-09 |
| | rs16978028 | A | T | 0.856 | 0.030 | 0.003 | 110.345 | 8.20E-26 |
| | rs2276182 | C | G | 0.597 | -0.023 | 0.002 | 130.728 | 2.80E-30 |
| | rs1879100 | C | T | 0.138 | 0.019 | 0.003 | 42.234 | 8.10E-11 |
| | rs11085072 | C | T | 0.763 | 0.013 | 0.002 | 31.005 | 2.60E-08 |
| | rs8105767 | A | G | 0.705 | -0.033 | 0.002 | 222.565 | 2.50E-50 |
| | rs4530278 | G | T | 0.402 | -0.014 | 0.002 | 45.540 | 1.50E-11 |
| | rs429358 | T | C | 0.846 | -0.017 | 0.003 | 39.205 | 3.80E-10 |
| | rs8102497 | G | A | 0.568 | 0.015 | 0.002 | 54.709 | 1.40E-13 |
| | rs6054257 | G | A | 0.206 | 0.014 | 0.002 | 32.711 | 1.10E-08 |
| | rs1291143 | A | C | 0.151 | -0.049 | 0.003 | 310.393 | 1.80E-69 |
| | rs188546415 | G | A | 0.984 | 0.054 | 0.009 | 36.807 | 1.30E-09 |
| | rs3865523 | G | T | 0.188 | 0.055 | 0.003 | 420.626 | 1.80E-93 |
| | rs552374163 | C | T | 0.992 | 0.072 | 0.012 | 36.398 | 1.60E-09 |
| | rs35640778 | G | A | 0.979 | 0.209 | 0.007 | 886.250 | 9.60E-195 |
| | rs61736615 | G | A | 0.963 | 0.037 | 0.005 | 47.866 | 4.60E-12 |
| | rs115610405 | C | A | 0.981 | 0.110 | 0.007 | 223.197 | 1.80E-50 |
| | rs139228302 | G | A | 0.975 | 0.047 | 0.007 | 52.733 | 3.80E-13 |
| | rs151255005 | C | A | 0.987 | -0.054 | 0.009 | 37.936 | 7.30E-10 |
| | rs28502153 | C | A | 0.622 | 0.022 | 0.002 | 109.637 | 1.20E-25 |
| | rs6007020 | T | C | 0.632 | -0.014 | 0.002 | 47.778 | 4.80E-12 |
| | rs131795 | A | T | 0.208 | 0.025 | 0.002 | 101.438 | 7.40E-24 |
| 29 | rs1003322 | C | A | 0.786 | -0.014 | 0.002 | 32.782 | 1.00E-08 |

30 eaf, effect allele frequency; SNP, single-nucleotide polymorphisms.

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42 **Supplementary Table 2.** GWAS summary statistics on outcomes: source and description.

| Outcomes | Population | Cases | Controls | phenocode | PMID/ consortium |
|--|------------|-------|----------|---|------------------|
| systemic lupus erythematosus | European | 835 | 300162 | M13_SLE | FinnGen |
| Ulcerative colitis (all Crohn cases excluded) | European | 3407 | 303191 | K11_UC_NOCD | FinnGen |
| Crohn disease (all Ulcerative Colitis excluded) | European | 1021 | 301234 | K11_CD_NOUC | FinnGen |
| Crohn disease (small intestine) | European | 1501 | 296008 | CHRONSMALL | FinnGen |
| Crohn disease (large intestine) | European | 1220 | 296008 | CHRONLARGE | FinnGen |
| type 1 diabetes | European | 8671 | 255466 | E4_DM1 | FinnGen |
| Primary sclerosing cholangitis | European | 1231 | 273442 | K11_CHOLANGI | FinnGen |
| inflammatory bowel disease | European | 8704 | 300450 | K11_IBD | FinnGen |
| atopic dermatitis (strict definition) | European | 7895 | 300873 | ATOPIC_STRICT | FinnGen |
| childhood asthma (age<16) | European | 4549 | 175182 | ASTHMA_CHILD | FinnGen |
| ankylosing spondylitis | European | 2252 | 227388 | M13_ANKYLOSPON | FinnGen |
| psoriasis | European | 6995 | 299128 | L12_PSORIASIS | FinnGen |
| sicca syndrome | European | 1981 | 300162 | M13_SJOGREN | FinnGen |
| rheumatoid arthritis | European | 9855 | 202617 | M13_RHEUMA | FinnGen |
| hypothyroidism | European | 33422 | 227415 | E4_HYTHY_AI_STRICT | FinnGen |
| hyperthyroidism | European | 1421 | 231654 | AUTOIMMUNE_HYPERTHYROIDISM | FinnGen |
| sarcoidosis | European | 3103 | 304494 | D3_SARCOIDOSIS | FinnGen |
| idiopathic pulmonary fibrosis | European | 1514 | 306063 | IPF | FinnGen |
| SLE (James Benthams) | European | 5201 | 9066 | No phenocode. diagnostic criteria: Standard American College of Rheumatology classification criteria | 26502338 |

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51 **Supplementary Table 3** MR steiger analysis showing the causal direction of leukocyte telomere
52 length (LTL) on Immune-mediated Inflammatory Diseases (IMIDs).

| Exposure | Outcomes | Correct causal direction | r2 exposure | r2 outcome | Steiger P-value |
|--|-------------------------------|--------------------------|-----------------------|-----------------------|------------------------|
| leukocyte telomere length (LTL) | ankylosing spondylitis | TRUE | 2.86×10^{-2} | 4.75×10^{-4} | <0.0001 |
| | psoriasis | TRUE | 2.67×10^{-2} | 3.83×10^{-4} | <0.0001 |
| | sicca syndrome | TRUE | 2.84×10^{-2} | 2.71×10^{-4} | <0.0001 |
| | rheumatoid arthritis | TRUE | 2.55×10^{-2} | 5.15×10^{-4} | <0.0001 |
| | hypothyroidism | TRUE | 2.61×10^{-2} | 3.96×10^{-4} | <0.0001 |
| | hyperthyroidism | TRUE | 2.67×10^{-2} | 3.67×10^{-4} | <0.0001 |
| | sarcoidosis | TRUE | 2.70×10^{-2} | 2.87×10^{-4} | <0.0001 |
| | idiopathic pulmonary fibrosis | TRUE | 2.28×10^{-2} | 2.98×10^{-4} | <0.0001 |
| | SLE (James Bentham) | TRUE | 1.90×10^{-2} | 5.93×10^{-3} | 3.70×10^{-13} |

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