**Finding PCSK9 SNPs affecting LDL-C levels**

Given the biochemistry direct measurements of LDL-C (Low-Density Lipoprotein Cholesterol) concentration, and the SNP genotype data, we can perform association studies to identify relevant genes, and their genetic variants.

PCSK9 (proprotein convertase subtilisin/kexin type 9) is a fat-control drug target, well studied with Caucasian populations. The protein causes LDL-C receptors on the surface of liver to degrade. Less active receptor removing LDL-C from bloodstream leads to higher LDL-C concentration and increased risk of cardiovascular events. Drugs blocking PCSK9 have been developed to reduce LDL-C concentration in blood.

Given some Caucasian PCSK9 variants identified as associated with LDL-C are absent from or present at low frequencies in Chinese, we seek to identify additional PCSK9 variants associated with LDL-C levels in Chinese populations.

The original genotype data is the stage3 set from /kuser/shared/data/GWASphase12 on nc2. Only autosome SNPs are used, leaving 636670 variants and 32205 people in the set.

The direct LDL-C measurements are from LDL-c\_biochem\_data.xlsx in K:\kadoorie\Groups\Genetics\PROJECTS\PCSK9.

1. PCA

A LD (Linkage Disequilibrium) - free subset of 120201 SNPs was used for pairwise identity-by-descent (IBD) estimates for all pairs of subjects with plink. Pairs of subjects with IBD values higher than 0.05 were considered as related. In the network of related subjects, the most connected subject would be removed. Then the connection degrees were updated. The process iterated till no subjects were related to each other. 6990 subjects were ejected during this process. Principle component analysis (PCA) was performed using plink on the rest and projected to the removed subjects. Eigensoft produced very similar results.

1. Sample stratification and linear regression

Given GWAS\_SNPdata\_samples.xlsx from K:\kadoorie\Groups\Genetics\Data Archive\Project Sample Lists\Lists\, we grouped the subjects into 6 strata.

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| --- | --- | --- | --- | --- |
| **stratum** | **Ascertainment** | **size** | **lambda\_raw** | **lambda\_RINT** |
| stratum\_1 | ICH | 4762 | 1.007485 | 1.019263 |
| stratum\_2 | IS | 5210 | 1.008424 | 1.010303 |
| stratum\_3 | SAH | 167 | 0.9920914 | 0.9990672 |
| stratum\_4 | MI/IHD | 1265 | 0.9907005 | 0.998135 |
| stratum\_5 | Control | 6687 | 1.024951 | 1.026377 |
| stratum\_6 | Control/resurvey 2 | 4177 | 1.019736 | 1.02971 |

We have direct measurements of LDL-C concentration for the first 5 strata. For the 6th we have only indirect measures.

We performed genome-wide linear regression of the genetic variants against the direct LDL-C measurements with covariates including the region code, sex, age and the 10 leading principal components using plink. On the smallest stratum (SAH), only sex, age and the 2 leading components were employed as covariates.

For each stratum, direct LDL-C values were regressed against region, sex and age. We rank inverse-normal transformed (RINT) the residuals to obtained phenotype sets with the standard normal distribution. In the linear regression of these RINT LDL-C values, we used only the 10 leading components as covariates (2 leading components only for the stratum 3).

The inflation factors (Lambda) of the GWAS are acceptable, range between 0.99 and 1.03.

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| --- |
| Stratum 1, raw LDL-C |
| Stratum 2, raw LDL-C |
| Stratum 3, raw LDL-C |

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| Stratum 4, raw LDL-C |
| Stratum 5, raw LDL-C |
| Stratum 6, raw LDL-C (indirect) |

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| Stratum 1, RINT LDL-C |
| Stratum 2, RINT LDL-C |
| Stratum 3, RINT LDL-C |

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| Stratum 4, RINT LDL-C |
| Stratum 5, RINT LDL-C |
| Stratum 6, RINT LDL-C |

1. Meta analysis

We used Metal for meta-analysis. The beta and standard errors estimated in the linear regression of the first five strata were combined using the inverse-variance-weighted fixed-effects scheme.

Then the stratum 6 linear regression results were included with the meta-analysis result of the first round.

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The meta-analysis results:

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNP** | **CHR** | **BP** | **MAF** | **A1** | **A2** | **Beta** | **SE\_Beta** | **Q** | **direction** | **P** |
| AX-83389438 | 1 | 55509585 | 1.36E-02 | T | C | -3.86E-01 | 0.0302 | 0.938 | ----- | 1.45E-37 |
| AX-11576926 | 1 | 55630151 | 0.1165 | T | C | 0.0535 | 0.011 | 0.6708 | +++++ | 1.06E-06 |
| AX-39912161 | 1 | 55513061 | 1.95E-01 | T | C | -4.01E-02 | 0.0088 | 0.7789 | ----- | 4.82E-06 |
| AX-31642001 | 1 | 55517883 | 0.2873 | C | G | -0.035 | 0.0077 | 0.2967 | ----- | 5.61E-06 |
| AX-31642169 | 1 | 55521242 | 0.2477 | T | G | -0.036 | 0.0081 | 0.8867 | ----- | 8.52E-06 |
| AX-31641677 | 1 | 55509939 | 0.06613 | T | C | 0.0539 | 0.0141 | 0.8634 | ++-++ | 0.0001352 |
| AX-11541856 | 1 | 55529187 | 0.06007 | A | G | -0.0525 | 0.0145 | 0.4883 | ----- | 0.0002852 |
| AX-39912159 | 1 | 55512995 | 0.07861 | A | G | -0.0465 | 0.013 | 0.8858 | --+-- | 0.0003583 |
| AX-11629248 | 1 | 55719166 | 0.2107 | T | G | 0.0293 | 0.0086 | 0.7209 | +++++ | 0.0006577 |
| AX-31641243 | 1 | 55498982 | 0.1261 | A | G | -0.0354 | 0.0106 | 0.1539 | ----- | 0.000828 |
| AX-51209582 | 1 | 55498949 | 0.3514 | T | C | 0.0237 | 0.0073 | 0.8529 | +++++ | 0.0012 |

1. RINT measurements
2. Conditional analysis

To find the independently-associated SNPs, we iteratively performed the linear regression and the meta-analysis. After each iteration, the SNP with the lowest P value found in the previous meta-analysis was to be added to the list of SNP hits. The linear regression would then be performed conditioned on the genotypes of these SNPs. We stopped when no additional SNP hits with P value less than 10-4 can be found or conditioned upon.

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| The original meta-analysis of direct LDL-C. The vertical lines are 10-4 and 0.05 accordingly. |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | SNP | CHR | BP | MAF | a1 | a2 | meta\_beta | meta\_se | meta\_q | meta\_dir | meta\_p | | AX-83389438 | 1 | 55509585 | 1.36E-02 | T | C | -3.86E-01 | 0.0302 | 0.938 | ----- | 1.45E-37 | | AX-11576926 | 1 | 55630151 | 0.1165 | T | C | 0.0535 | 0.011 | 0.6708 | +++++ | 1.06E-06 | | AX-39912161 | 1 | 55513061 | 1.95E-01 | T | C | -4.01E-02 | 0.0088 | 0.7789 | ----- | 4.82E-06 | | AX-31642001 | 1 | 55517883 | 0.2873 | C | G | -0.035 | 0.0077 | 0.2967 | ----- | 5.61E-06 | | AX-31642169 | 1 | 55521242 | 0.2477 | T | G | -0.036 | 0.0081 | 0.8867 | ----- | 8.52E-06 | | AX-31641677 | 1 | 55509939 | 0.06613 | T | C | 0.0539 | 0.0141 | 0.8634 | ++-++ | 0.0001352 | | AX-11541856 | 1 | 55529187 | 0.06007 | A | G | -0.0525 | 0.0145 | 0.4883 | ----- | 0.0002852 | | AX-39912159 | 1 | 55512995 | 0.07861 | A | G | -0.0465 | 0.013 | 0.8858 | --+-- | 0.0003583 | | AX-11629248 | 1 | 55719166 | 0.2107 | T | G | 0.0293 | 0.0086 | 0.7209 | +++++ | 0.0006577 | | AX-31641243 | 1 | 55498982 | 0.1261 | A | G | -0.0354 | 0.0106 | 0.1539 | ----- | 0.000828 | |

After the initial round, the linear regression would be performed condition on the top SNP AX-83389438.

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| Direct LDL-C, conditioned on AX-83389438 |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | SNP | CHR | BP | MAF | a1 | a2 | meta\_beta | meta\_se | meta\_q | meta\_dir | meta\_p | | AX-31642001 | 1 | 55517883 | 0.2873 | C | G | -0.0425 | 0.0077 | 0.2819 | ----- | 3.41E-08 | | AX-11576926 | 1 | 55630151 | 0.1165 | T | C | 0.0587 | 0.0109 | 0.7909 | +++++ | 7.84E-08 | | AX-39912161 | 1 | 55513061 | 0.1947 | T | C | -0.0466 | 0.0087 | 0.8085 | ----- | 1.01E-07 | | AX-31642169 | 1 | 55521242 | 0.2477 | T | G | -0.0428 | 0.0081 | 0.9458 | ----- | 1.19E-07 | | AX-51209582 | 1 | 55498949 | 0.3514 | T | C | 0.031 | 0.0073 | 0.8995 | +++++ | 2.19E-05 | | AX-31641677 | 1 | 55509939 | 0.06613 | T | C | 0.0588 | 0.0141 | 0.8474 | ++-++ | 2.96E-05 | | AX-11629248 | 1 | 55719166 | 0.2107 | T | G | 0.0344 | 0.0086 | 0.8304 | +++++ | 5.90E-05 | | AX-39912159 | 1 | 55512995 | 0.07861 | A | G | -0.0519 | 0.013 | 0.9019 | --+-- | 6.30E-05 | | AX-31641243 | 1 | 55498982 | 0.1261 | A | G | -0.0407 | 0.0106 | 0.199 | ----- | 0.0001156 | |

The top SNP hit AX-31642001 was added to the list of SNPs to be conditioned upon.

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| Direct LDL-C, conditioned on AX-83389438 and AX-31642001 |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | SNP | CHR | BP | MAF | a1 | a2 | meta\_beta | meta\_se | meta\_q | meta\_dir | meta\_p | | AX-11541856 | 1 | 55529187 | 0.06007 | A | G | -0.0674 | 0.0148 | 0.5517 | ----- | 5.07E-06 | | AX-39912161 | 1 | 55513061 | 0.1947 | T | C | -0.0327 | 0.0096 | 0.6193 | ----- | 0.0006279 | | AX-11576926 | 1 | 55630151 | 0.1165 | T | C | 0.0396 | 0.0121 | 0.7732 | +++++ | 0.001094 | | AX-39912661 | 1 | 55529828 | 0.1115 | T | C | -0.0363 | 0.0117 | 0.1707 | ----- | 0.001845 | | AX-12930867 | 1 | 55486064 | 0.4125 | A | G | -0.0214 | 0.0071 | 0.08162 | +-++- | 0.002652 | | AX-64101281 | 1 | 55837600 | 0.01583 | T | C | 0.0833 | 0.0282 | 0.4171 | +++++ | 0.00313 | | AX-39911557 | 1 | 55484810 | 0.4638 | T | C | -0.0197 | 0.0071 | 0.06822 | +-+-- | 0.005147 | | AX-50958112 | 1 | 55496556 | 0.4706 | T | C | 0.019 | 0.0071 | 0.04406 | -+-++ | 0.007468 | | AX-51209582 | 1 | 55498949 | 0.3514 | T | C | 0.0205 | 0.0077 | 0.8707 | +++++ | 0.00773 | | AX-11532730 | 1 | 55541174 | 0.106 | A | G | 0.0317 | 0.0119 | 0.4849 | +++++ | 0.007954 | |

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| Direct LDL-C, conditioned on AX-83389438, AX-31642001 and AX-11541856 |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | SNP | CHR | BP | MAF | a1 | a2 | meta\_beta | meta\_se | meta\_q | meta\_dir | meta\_p | | AX-31642169 | 1 | 55521242 | 0.2477 | T | G | -0.047 | 0.0126 | 0.31 | ----- | 0.0001938 | | AX-12930867 | 1 | 55486064 | 0.4125 | A | G | -0.0217 | 0.0071 | 0.09975 | +-++- | 0.002412 | | AX-39912161 | 1 | 55513061 | 0.1947 | T | C | -0.0282 | 0.0096 | 0.5948 | ----- | 0.003415 | | AX-51209582 | 1 | 55498949 | 0.3514 | T | C | 0.0222 | 0.0077 | 0.855 | +++++ | 0.00387 | | AX-39911557 | 1 | 55484810 | 0.4638 | T | C | -0.0197 | 0.0071 | 0.07759 | +-+-- | 0.005333 | | AX-11447635 | 1 | 55766150 | 0.1156 | T | C | -0.0308 | 0.0113 | 0.619 | --+-- | 0.006578 | | AX-50958112 | 1 | 55496556 | 0.4706 | T | C | 0.0187 | 0.0071 | 0.05692 | -+-++ | 0.00862 | | AX-39912909 | 1 | 55541050 | 0.04024 | T | C | 0.0449 | 0.0174 | 0.7185 | ++-++ | 0.009886 | |

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| RINT direct LDL-C, original meta-analysis |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | SNP | CHR | BP | MAF | a1 | a2 | meta\_beta | meta\_se | meta\_q | meta\_dir | meta\_p | | AX-83389438 | 1 | 55509585 | 0.01357 | T | C | -0.621 | 0.0455 | 0.6727 | ----- | 1.91E-42 | | AX-11576926 | 1 | 55630151 | 0.1165 | T | C | 0.0811 | 0.0166 | 0.7462 | +++++ | 9.82E-07 | | AX-39912161 | 1 | 55513061 | 0.1947 | T | C | -0.0638 | 0.0132 | 0.9448 | ----- | 1.44E-06 | | AX-31642001 | 1 | 55517883 | 0.2873 | C | G | -0.0507 | 0.0116 | 0.3767 | ----- | 1.34E-05 | | AX-31642169 | 1 | 55521242 | 0.2477 | T | G | -0.053 | 0.0122 | 0.9855 | ----- | 1.48E-05 | | AX-31641677 | 1 | 55509939 | 0.06613 | T | C | 0.0881 | 0.0213 | 0.9513 | ++-++ | 3.66E-05 | | AX-11541856 | 1 | 55529187 | 0.06007 | A | G | -0.0855 | 0.0219 | 0.412 | ----- | 9.14E-05 | | AX-39912159 | 1 | 55512995 | 0.07861 | A | G | -0.0749 | 0.0197 | 0.9052 | --+-- | 0.0001397 | |

The same process was applied on RINT LDL-C measurements.

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| RINT direct LDL-C, conditioned on AX-83389438 |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | SNP | CHR | BP | MAF | a1 | a2 | meta\_beta | meta\_se | meta\_q | meta\_dir | meta\_p | | AX-39912161 | 1 | 55513061 | 0.1947 | T | C | -0.0742 | 0.0132 | 0.9572 | ----- | 1.91E-08 | | AX-11576926 | 1 | 55630151 | 0.1165 | T | C | 0.0892 | 0.0165 | 0.8511 | +++++ | 6.49E-08 | | AX-31642001 | 1 | 55517883 | 0.2873 | C | G | -0.0626 | 0.0116 | 0.3141 | ----- | 7.25E-08 | | AX-31642169 | 1 | 55521242 | 0.2477 | T | G | -0.0636 | 0.0122 | 0.9856 | ----- | 1.81E-07 | | AX-31641677 | 1 | 55509939 | 0.06613 | T | C | 0.0957 | 0.0212 | 0.9184 | ++-++ | 6.54E-06 | | AX-51209582 | 1 | 55498949 | 0.3514 | T | C | 0.0492 | 0.011 | 0.9208 | +++++ | 8.20E-06 | | AX-39912159 | 1 | 55512995 | 0.07861 | A | G | -0.0835 | 0.0196 | 0.9109 | --+-- | 1.98E-05 | | AX-11629248 | 1 | 55719166 | 0.2107 | T | G | 0.0546 | 0.0129 | 0.8881 | +++++ | 2.43E-05 | | AX-31641243 | 1 | 55498982 | 0.1261 | A | G | -0.0637 | 0.0159 | 0.299 | ----- | 6.40E-05 | | AX-11541856 | 1 | 55529187 | 0.06007 | A | G | -0.0762 | 0.0218 | 0.4945 | ----- | 0.0004647 | |

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| RINT direct LDL-C, conditioned on AX-83389438 and AX-39912161 |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | SNP | CHR | BP | MAF | a1 | a2 | meta\_beta | meta\_se | meta\_q | meta\_dir | meta\_p | | AX-11576926 | 1 | 55630151 | 0.1165 | T | C | 0.0723 | 0.0169 | 0.8426 | +++++ | 1.93E-05 | | AX-11541856 | 1 | 55529187 | 0.06007 | A | G | -0.0762 | 0.0217 | 0.4009 | ----- | 0.0004606 | | AX-31642001 | 1 | 55517883 | 0.2873 | C | G | -0.0432 | 0.0127 | 0.1764 | -++-- | 0.0006774 | | AX-11629248 | 1 | 55719166 | 0.2107 | T | G | 0.0429 | 0.0131 | 0.866 | +++++ | 0.001108 | | AX-31642169 | 1 | 55521242 | 0.2477 | T | G | -0.0432 | 0.0133 | 0.956 | --+-- | 0.001169 | | AX-64101281 | 1 | 55837600 | 0.01583 | T | C | 0.131 | 0.0423 | 0.2685 | +++++ | 0.00197 | | AX-12930867 | 1 | 55486064 | 0.4125 | A | G | -0.031 | 0.0107 | 0.1735 | --++- | 0.003827 | |

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| RINT direct LDL-C, conditioned on AX-83389438, AX-39912161 and AX-11576926 |
| |  |  |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | | SNP | CHR | BP | MAF | a1 | a2 | meta\_beta | meta\_se | meta\_q | meta\_dir | meta\_p | | AX-64101281 | 1 | 55837600 | 0.01583 | T | C | 0.1295 | 0.0424 | 0.3135 | +++++ | 0.002235 | | AX-11541856 | 1 | 55529187 | 0.06007 | A | G | -0.0659 | 0.0219 | 0.3565 | ----- | 0.002579 | | AX-12930867 | 1 | 55486064 | 0.4125 | A | G | -0.0306 | 0.0107 | 0.1651 | --++- | 0.004382 | | AX-31639191 | 1 | 55447704 | 0.06497 | T | G | -0.0552 | 0.0214 | 0.315 | --+-- | 0.009942 | | AX-39911557 | 1 | 55484810 | 0.4638 | T | C | -0.0267 | 0.0107 | 0.1962 | +-++- | 0.01233 | |

SNPs selected using the two sets of LDL-C measurements:

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| SNP | rs\_id | BP | MAF | Function | raw\_beta | raw\_P | RINT\_beta | RINT\_P | direction | org\_raw\_p |
| AX-83389438 | rs151193009 | 55509585 | 0.0136 | R93→C | -0.3864 | 1.45E-37 | -0.6210 | 1.91E-42 | ----- | 1.45E-37 |
| AX-11576926 | rs6663252 | 55630151 | 0.1165 | intron |  |  | 0.0723 | 1.93E-05 | +++++ | 1.06E-06 |
| AX-39912161 | rs10888897 | 55513061 | 0.1947 | intron |  |  | -0.0742 | 1.91E-08 | ----- | 4.82E-06 |
| AX-31642001 | rs624612 | 55517883 | 0.2873 | intron | -0.0425 | 3.41E-08 |  |  | ----- | 5.61E-06 |
| AX-31642169 | rs471705 | 55521242 | 0.2477 | intron | -0.0470 | 1.94E-04 |  |  | ----- | 8.52E-06 |
| AX-31641677 | rs4275490 | 55509939 | 0.0661 |  |  |  |  |  | ++-++ | 1.35E-04 |
| AX-11541856 | rs505151 | 55529187 | 0.0601 | G670→E | -0.0674 | 5.07E-06 |  |  | ----- | 2.85E-04 |
| AX-39912159 | rs2495478 | 55512995 | 0.0786 |  |  |  |  |  | --+-- | 3.58E-04 |

1. Some side notes

The leading SNP hit AX-83389438 (rs151193009) was found only in the CHB, CHS, JPT and KHV cohorts in the 1000 Genomes Project (phase 3) data set, with the MAF ranges between 1-2%.

Two SNPs in this region are also available in the SNP 384 panel.

AX-11150762 (rs11206510)

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| META | CHR | BP | MAF | a1 | a2 | meta\_beta | meta\_se | meta\_q | meta\_dir | meta\_p |
| raw\_dir\_ldl\_meta\_0 | 1 | 55496039 | 0.0564 | T | C | 0.0308 | 0.0151 | 0.4555 | +++-+ | 0.04063 |
| raw\_dir\_ldl\_meta\_1 | 1 | 55496039 | 0.0564 | T | C | 0.0351 | 0.015 | 0.4839 | +++-+ | 0.01933 |
| raw\_dir\_ldl\_meta\_2 | 1 | 55496039 | 0.0564 | T | C | 0.0287 | 0.0151 | 0.4496 | +++-+ | 0.05688 |
| raw\_dir\_ldl\_meta\_3 | 1 | 55496039 | 0.0564 | T | C | 0.0245 | 0.0151 | 0.4445 | +++-+ | 0.1048 |
| Rint\_dir\_ldl\_meta\_0 | 1 | 55496039 | 0.0564 | T | C | 0.0444 | 0.0228 | 0.5506 | +++-+ | 0.05113 |
| rint\_dir \_ldl\_meta\_1 | 1 | 55496039 | 0.0564 | T | C | 0.0514 | 0.0227 | 0.5647 | +++-+ | 0.02332 |
| rint\_dir \_ldl\_meta\_2 | 1 | 55496039 | 0.0564 | T | C | 0.0132 | 0.0238 | 0.5117 | +-+-+ | 0.579 |
| rint\_dir \_ldl\_meta\_3 | 1 | 55496039 | 0.0564 | T | C | 0.0166 | 0.0238 | 0.5042 | +-+-+ | 0.4857 |

AX-39911995 (rs2479409)

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| META | CHR | BP | MAF | a1 | a2 | meta\_beta | meta\_se | meta\_q | meta\_dir | meta\_p |
| raw\_dir\_ldl\_meta\_0 | 1 | 55504650 | 0.3181 | A | G | -0.0073 | 0.0075 | 0.5959 | ---+- | 0.3301 |
| raw\_dir\_ldl\_meta\_1 | 1 | 55504650 | 0.3181 | A | G | -0.0156 | 0.0075 | 0.5641 | ---+- | 0.0378 |
| raw\_dir\_ldl\_meta\_2 | 1 | 55504650 | 0.3181 | A | G | -0.0124 | 0.0076 | 0.5271 | ---+- | 0.1011 |
| raw\_dir\_ldl\_meta\_3 | 1 | 55504650 | 0.3181 | A | G | -0.0148 | 0.0076 | 0.4978 | ---+- | 0.05061 |
| rint\_dir \_ldl\_meta\_0 | 1 | 55504650 | 0.3181 | A | G | -0.0117 | 0.0114 | 0.7847 | ---+- | 0.3039 |
| rint\_dir \_ldl\_meta\_1 | 1 | 55504650 | 0.3181 | A | G | -0.0249 | 0.0113 | 0.7438 | ---+- | 0.02813 |
| rint\_dir \_ldl\_meta\_2 | 1 | 55504650 | 0.3181 | A | G | -0.0096 | 0.0117 | 0.7401 | ---+- | 0.4134 |
| rint\_dir \_ldl\_meta\_3 | 1 | 55504650 | 0.3181 | A | G | -0.0118 | 0.0117 | 0.7811 | --++- | 0.3156 |