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Supplemental Data

Integrative DNA, RNA, and Protein Evidence

Connects *TREML4* to Coronary Artery Calcification

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Supplemental Figures

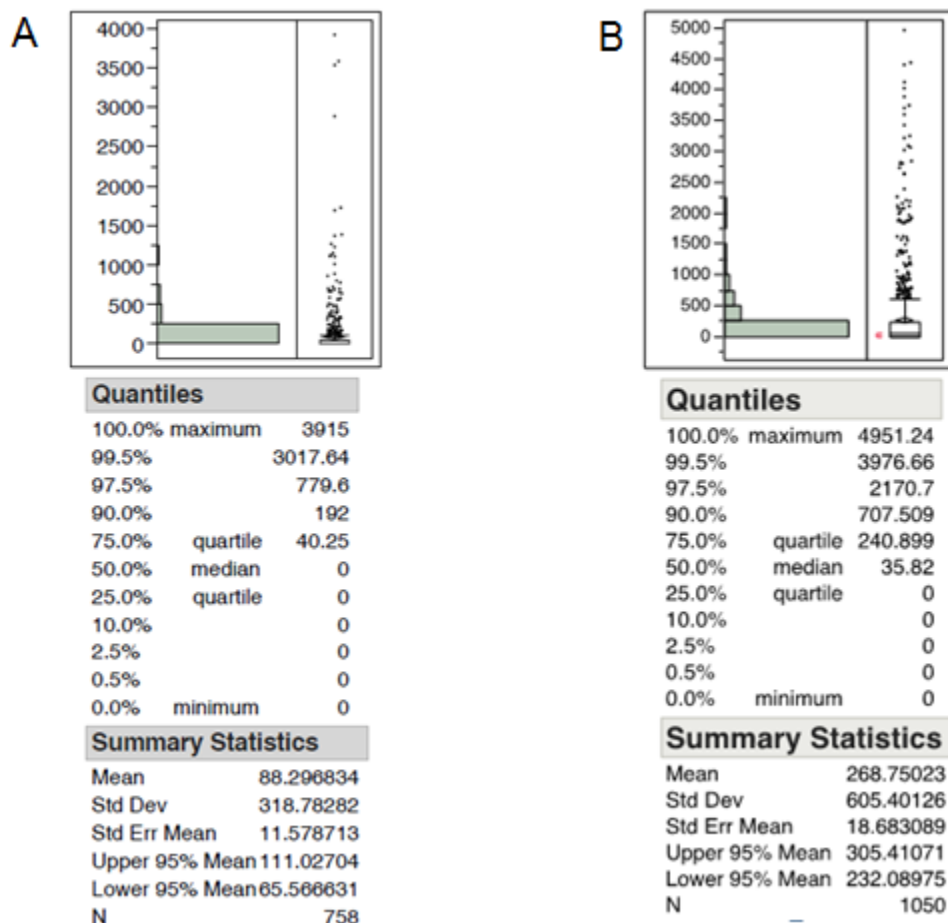


Figure S1: Distribution of CAC scores in (A) ClinSeq[®] and (B) the Framingham Heart Study

Appendix S1

Calculation of CAC relative risk conferred by the *rs2803496* C allele

For relative risk calculations, for each CAC score threshold x , we the following four values were tabulated:

- The number of individuals with $CAC \geq x$ and having the C allele (i.e. CC or CT, the non-TT genotypes)
- The number of individuals with $CAC = 0$ and having the C allele (i.e. CC or CT, the non-TT genotypes)
- The number of individuals with $CAC \geq x$ and without the C allele (i.e. with the TT genotype).
- The number of individuals with $CAC = 0$ and without the C allele (i.e. with the TT genotype).

These values are provided in Supplemental Table 7. Note that b and d are constant across all values of x .

E.g., at a CAC threshold of 400, the 2x2 table would look like this:

	CAC \geq x	CAC=0
Non TT	a	b
TT	c	d

And from our data:

	CAC \geq 400	CAC=0
Non TT	18	87
TT	30	345

The relative risk (RR) of having CAC \geq 400 in the non-TT group (versus the TT group) was then calculated using the standard formula:

$$RR = (a/(a+b))/(c/(c+d))$$

$$\text{Hence, at CAC}\geq 400, RR = (18/(18+87)) / (30/(30+345)) = .1714 / .08 = 2.14$$

95% confidence intervals for the RR value at each CAC threshold were derived in the following manner:

1. First, we derived the natural log of the RR: $\ln(RR)$
2. The sampling distribution of the RR is approximately normally distributed on the natural log scale.
3. The confidence coefficient is 1.96 for a 95% confidence interval from the standard normal distribution.
4. The standard error (SE) of $\ln(RR)$ is $\text{Sqrt}(b/(a(a+b))+d/(c(c+d)))$
5. Combining points 3 and 4 above, the upper and lower 95% confidence interval limits (UCL and LCL, respectively) on the natural log scale are: $\ln(RR) \pm 1.96 * SE \ln(RR)$
6. Next, we used the exponential function to find the upper and lower 95% confidence limits back to the original scale (e.g., at CAC=400, 95% UCL = 3.69 and LCL = 1.24, respectively)
7. If the 95% confidence interval does not contain the value 1 then the association is statistically significant at alpha of 0.05.

To generate Figure 2, the RR values were plotted as an X-Y scatter plot including the lower 95% confidence interval at each threshold.