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Variants in *CPT1A*, *FADS1*, and *FADS2* are associated with higher levels of estimated plasma and erythrocyte delta-5 desaturases in Alaskan Eskimos

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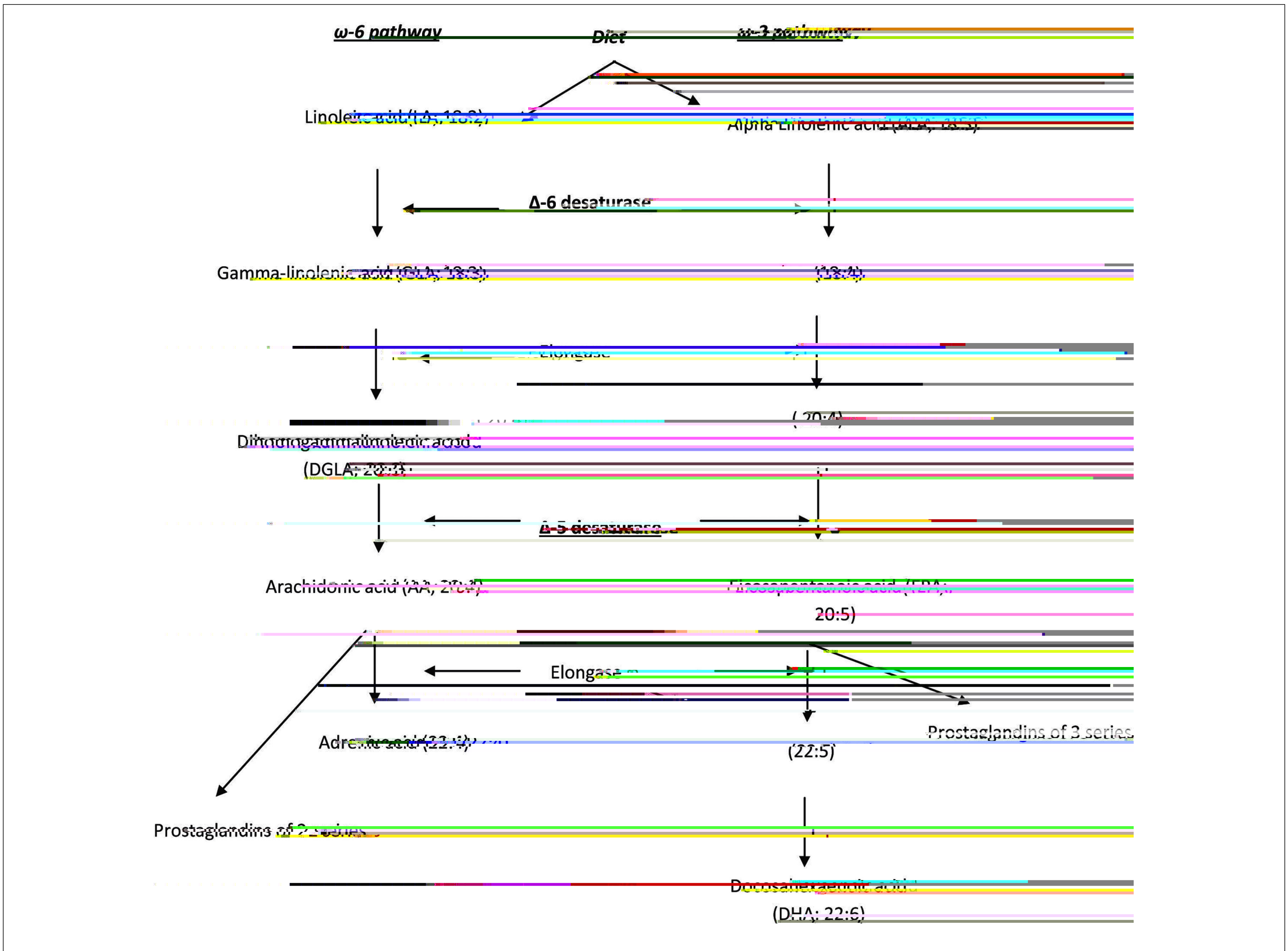
The delta-5 and delta-6 desaturases (D5D and D6D), encoded by fatty acid desaturase 1 (*FADS1*) and 2 (*FADS2*) genes, respectively, are rate-limiting enzymes in the metabolism of ω-3 and ω-6 fatty acids. The objective of this study was to identify genes influencing variation in estimated D5D and D6D activities in plasma and erythrocytes in Alaskan Eskimos ($n = 761$) participating in the genetics of coronary artery disease in Alaska Natives (GOCADAN) study. Desaturase activity was estimated by product: precursor ratios of polyunsaturated fatty acids. We found evidence of linkage for estimated erythrocyte D5D (eD5D) on chromosome 11q12-q13 (logarithm of odds score = 3.5). The confidence interval contains candidate genes *FADS1*, *FADS2*, 7-dehydrocholesterol reductase (*DHCR7*), and carnitine palmitoyl transferase 1A, liver (*CPT1A*). Measured genotype analysis found association between *CPT1A*, *FADS1*, and *FADS2* single-nucleotide polymorphisms (SNPs) and estimated eD5D activity (p-values between 10^{-28} and 10^{-5}). A Bayesian quantitative trait nucleotide analysis showed that rs3019594 in *CPT1A*



1 | [illegible]

[illegible] 2 ([illegible] ., 200). [illegible] fi [illegible] 2 [illegible] ([illegible] ., 2006 [illegible] ., 200 [illegible] ., 200 [illegible] ., 200 , 2010 [illegible] ., 200 [illegible] ., 2010 [illegible] ., 2010 [illegible] ., 2010 [illegible] ., 2011). [illegible] *FAD1* [illegible] *FAD2* [illegible] ([illegible] ., 200). [illegible] 11, 12- 13.1. [illegible] 2 [illegible] ([illegible] ., 2006

[illegible]

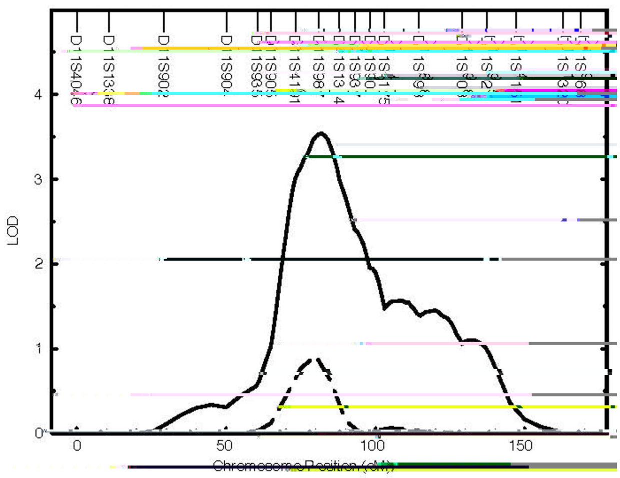
) 2 2 5 (**Table 5**). 0.5 2 2 6).

CONDITIONAL LINKAGE

2 0. , 2 2 5 fi 2 3.5 1.5 *CP 1A* 1. *FAD 1* *FAD 2* (**Figure 4**).

EXAMINATION OF CIS-REGULATED FADS1, FADS2, AND CPT1A TRANSCRIPTS IN MEXICAN AMERICANS

) 2 2 . (2007), 2 2)

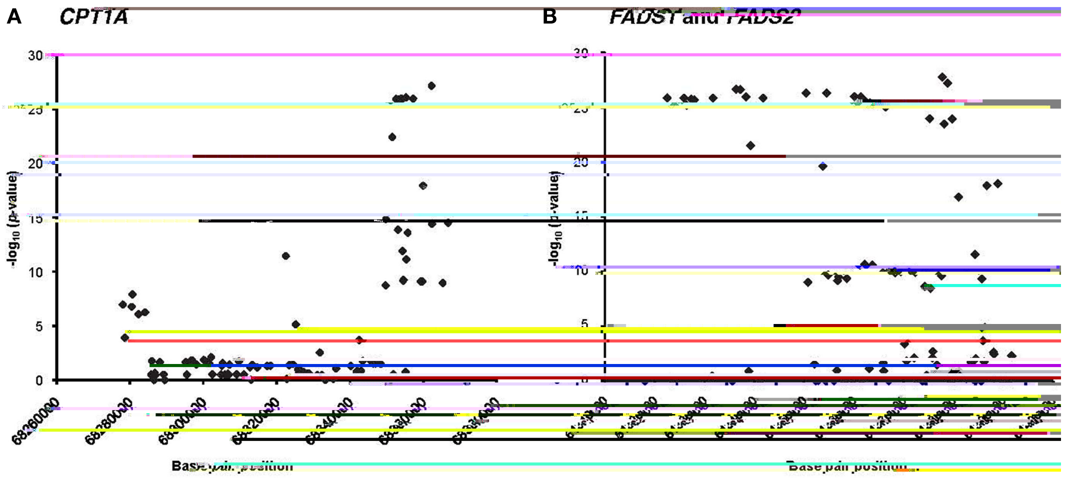


2 | 5 11. The QTL for plasma and erythrocyte D5D estimate on chromosome 11. Solid line, erythrocyte D5D (LOD = 3.5 at 82 cM); dashed line, plasma D5D (LOD = 0.9 at 81 cM).

) fi *is* - , *FAD 1*, *FAD 2*, *CP 1A*) 2 2 (*is*) , *p*-) 10^{-75} 10^{-7}. 2) , 2 , , , 2- 2 2 2 1, (**Table 6**).

DISCUSSION

2 fi 2 *FAD 1*, *FAD 2*, *CP 1A*) - 2 2 5 , 2) 2 (20 4 ω-6) (20 5 ω-3). 2 2 2 5 6)) 2 fi fl) 2.) ,))) (., 200 ., 2010). 2)) - 2 2 5 6) 2) 2 fi 11, 12-, 13 2 2 5 , *FAD 1*, *FAD 2*, *CP 1A*, *DHC 7*. 2 , 2 - 2 2 2 5 6 . 2 2 2 2 .



3 | 1A A 1 A 2 5 . (A) *CPT1A* and ( ) *FADS1* and *FADS2*.

| 2| 5 .

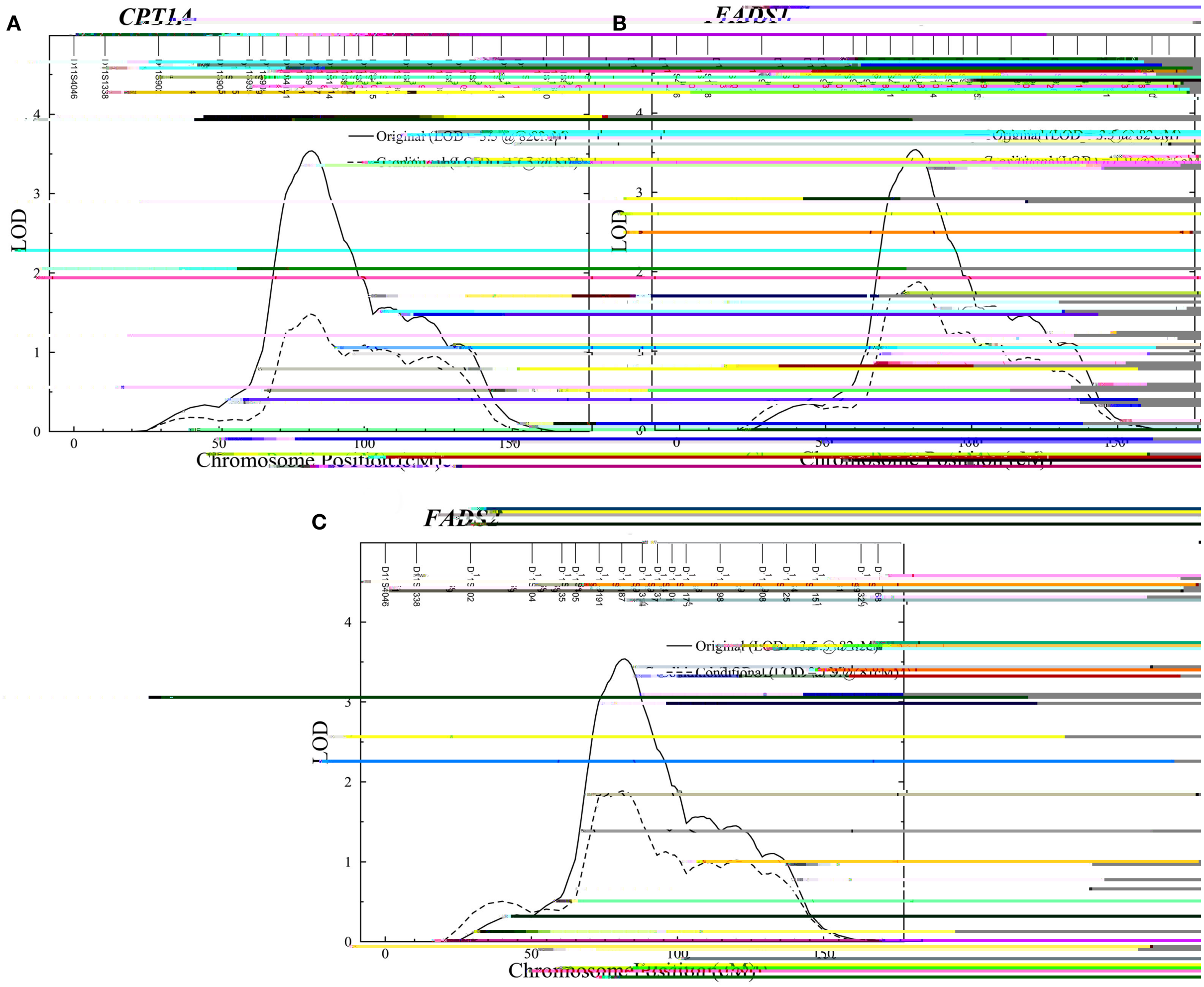


FIGURE 4 | [illegible] **11.** Linkage analysis conditional on the most significant[illegible] associated SNP in **(A)** *CPT1A*, **(B)** *FADS1*, and **(C)** *FADS2*. Solid line, [illegible] D5D; dashed line, [illegible] D5D conditional on SNP[illegible].

[illegible] (… et al., 2001). [illegible] (200…) [illegible] 47 [illegible] *CPT1A* [illegible] *CPT1A* [illegible] *CPT1B* [illegible] (… et al., 2007). [illegible] *CPT1A* [illegible] (… et al., 2005). [illegible]

l 6 | l - l *cis-* l x A .

A (*p*-v l)*

[illegible]