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Heritability and association with distinct genetic loci of erythropoietin levels in the general population

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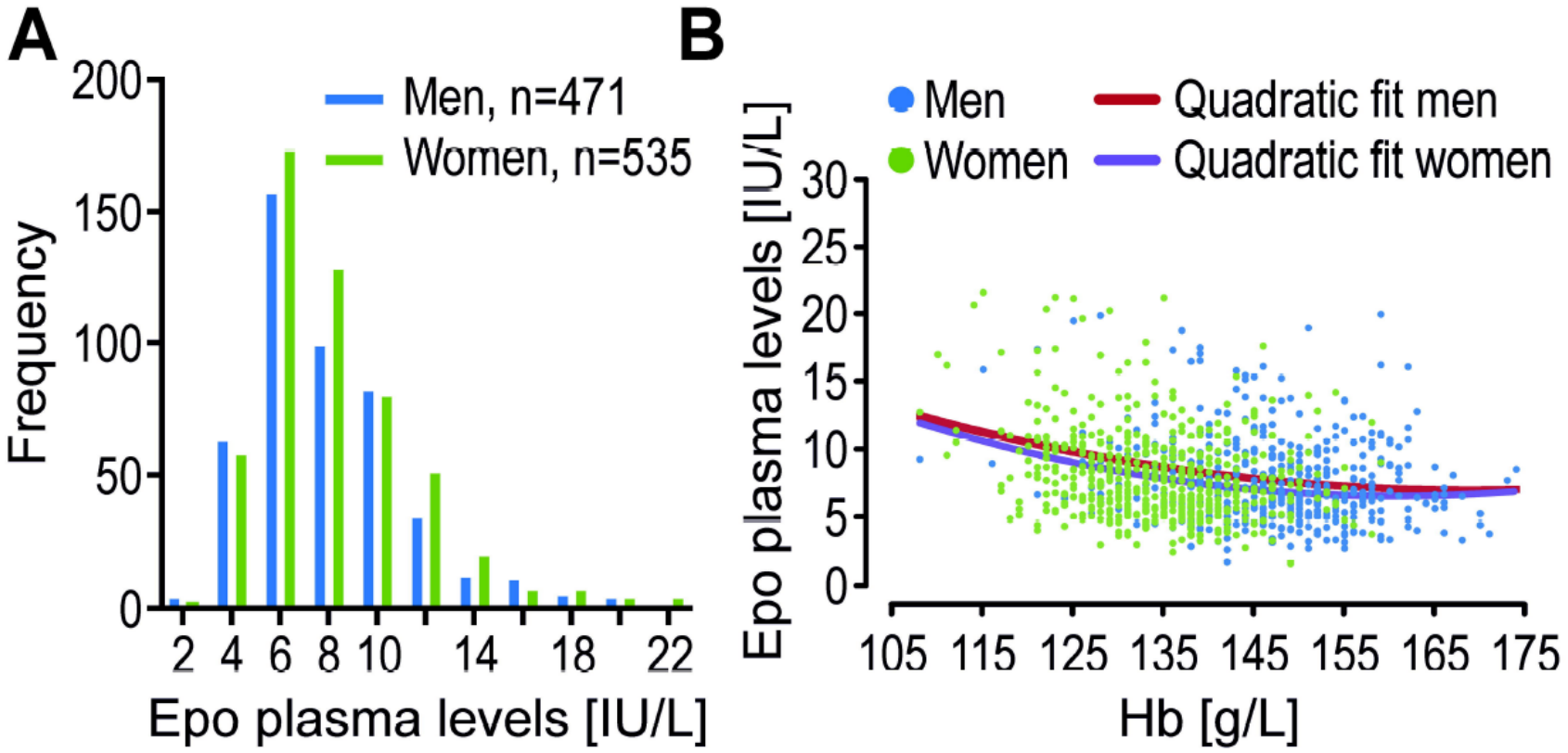
Heritability of plasma Epo levels in the SKIPOGH cohort

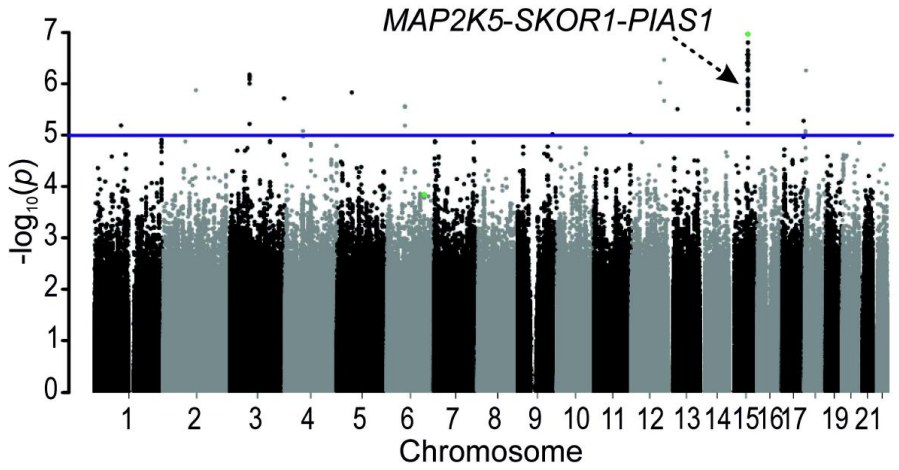
Variance components	Adjustment	Heritability ± SD	p-Value
P* - M - S	Age, sex, center	0.40 ± 0.07	<0.001
P* - M	Age, sex, center	0.41 ± 0.07	<0.001
P* - S	Age, sex, center	0.39 ± 0.07	<0.001
P*	Age, sex, center	0.40 ± 0.06	<0.001
P* - M - S	Fully adjusted	0.51 ± 0.08	<0.001
P* - M	Fully adjusted	0.52 ± 0.07	<0.001
P* - S	Fully adjusted	0.48 ± 0.07	<0.001
P*	Fully adjusted	0.49 ± 0.06	<0.001

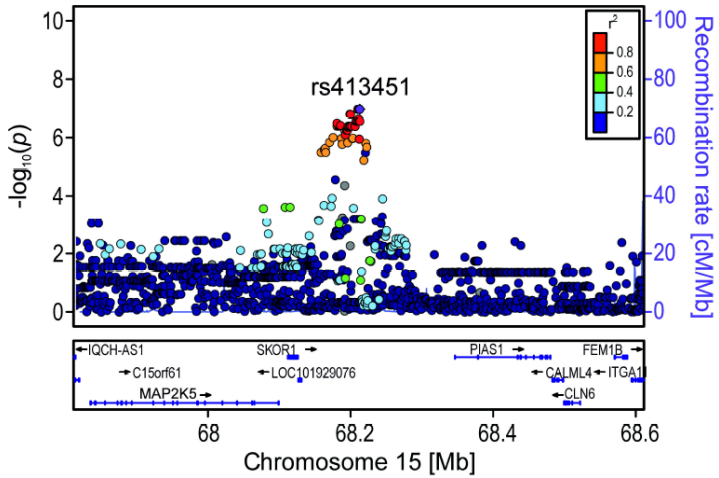
Shown is the heritability of ln(Epo) ± SD. Narrow sense heritability was estimated from family data using the ASSOC program in the Statistical Analysis in Genetic Epidemiology software package (Case Western Reserve University). P, polygenic; M, marital; S, sibling. Fully adjusted: age, sex, center, current smoker (yes/no), hemoglobin level, eGFR (ckd-epi formula). *Only the polygenic component of the variance was significantly different from 0 in all models.

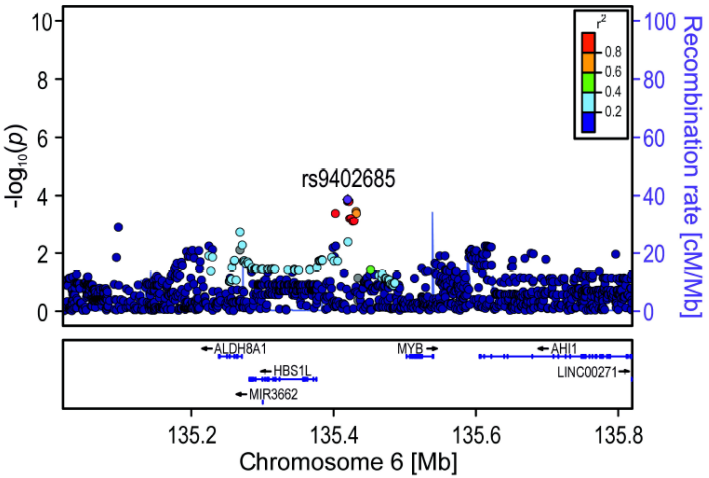
A) Histogram distribution of the Epo measurements
B) Correlation between Epo and Hemoglobin levels



A Genome-Wide association study in the SKIPOGH cohort revealed a new EPO locus (MAP2K5-SKOR1-PIAS1)) and replicated the previously identified locus HBS1L-MYB







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A candidate gene approach also identified OS9 as implicated in EPO levels' variations. The two associations newly identified in this study require replication, and the functional implication of all three loci in Epo regulation needs to be further investigated.

Regarding the idiopathic nature of the majority of erythrocytosis cases, we suggest that especially in patients with high Epo levels, indicative of secondary erythrocytosis, these loci should be considered for further investigation.

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