

## Supplementary Material

**Table S1.** Haplotype Association Analyses in Family Samples with SNPs in the *POMC* Region

Haplotypes	Haplotype Freq <sup>c</sup> (in AAs)	AA-AD <i>P</i> -haplo <sup>a</sup>	AA-CD <i>P</i> -haplo <sup>a</sup>	AA-OD <i>P</i> -haplo <sup>a</sup>	Haplotype Freq <sup>c</sup> (in EAs)	EA-AD <i>P</i> -haplo <sup>a</sup>	EA-CD <i>P</i> -haplo <sup>a</sup>	EA-OD <i>P</i> -haplo <sup>a</sup>
C-G-A-T-T	0.37	0.892 (55)	0.242 (48)	0.822 (29)	0.61	0.497 (49)	0.836 (38)	0.787
G-T-A-C-T	0.24	0.985 (51)	0.519 (36)	0.101 (20)				
C-T-A-C-T	0.12	0.891 (19)	0.407 (18)	0.434 (7)				
C-G-A-C-T	0.07	0.172 (14)	0.375 (12)	0.384 (6)				
C-G-A-C-C	0.07	0.413 (20)	0.139 (19)	0.694 (10)	0.17	0.621 (28)	0.121 (22)	0.976
C-G-A-T-C					0.13	0.894 (22)	0.063 (18)	0.323
<i>P</i> -global <sup>b</sup>	0.644	0.343	0.537			0.863	0.109	0.735

Abbreviations: AA (or EA)-AD, African American (AA) or European American (EA) families with siblings affected with alcohol dependence (AD); AA (or EA)-CD, AA (or EA) families with siblings affected with cocaine dependence (CD); AA (or EA)-OD, AA (or EA) families with siblings affected with opioid dependence (OD).

<sup>a,b</sup> *P* values for individual haplotypes (*P*-haplo) and global *P* values (*P*-global) were obtained by the haplotype-based association test (HBAT) (numbers in parentheses are numbers of informative families).

<sup>c</sup> Rare haplotypes (frequency < 5%) are not listed.

**Table S2.** Haplotype Association Analyses in Case-control Samples with SNPs in the *POMC* Region

<i>POMC</i> Haplotypes (SNP1-5)	AA-Con Freq <sup>c</sup>	AA-AD Freq <sup>c</sup>	AA-AD vs. AA-Con <i>P</i> -haplo <sup>a</sup>	AA-CD Freq <sup>c</sup>	AA-CD vs. AA-Con <i>P</i> -haplo <sup>a</sup>	AA-OD Freq <sup>c</sup>	AA-OD vs. AA-Con <i>P</i> -haplo <sup>a</sup>
C-G-A-T-T	0.36	0.34	0.308	0.34	0.402	0.42	0.925
G-T-A-C-T	0.29	0.27	0.284	0.26	0.343	0.26	0.806
C-T-A-C-T	0.12	0.11	0.242	0.11	0.283	0.09	0.492
G-T-A-T-T	0.06	0.06	0.425	0.06	0.508		
C-G-A-C-C	0.05	0.08	0.879	0.10	0.811	0.11	0.590
<i>P</i> -global <sup>b</sup>			0.791		0.395		0.112
<i>POMC</i> Haplotypes (SNP1-5)	EA-Con Freq <sup>c</sup>	EA-AD Freq <sup>c</sup>	EA-AD vs. EA-Con <i>P</i> -haplo <sup>a</sup>	EA-CD Freq <sup>c</sup>	EA-CD vs. EA-Con <i>P</i> -haplo <sup>a</sup>	EA-OD Freq <sup>c</sup>	EA-OD vs. EA-Con <i>P</i> -haplo <sup>a</sup>
C-G-A-T-T	0.65	0.58	0.098	0.56	<b>0.028</b>	0.57	0.202
C-G-A-C-C	0.15	0.19	0.326	0.19	0.058	0.18	0.383
C-G-A-T-C	0.11	0.13	0.367	0.15	0.071	0.16	0.623
<i>P</i> -global <sup>b</sup>			<b>0.031</b>		<b>0.001</b>		0.056

Abbreviations: AA (or EA)-Con, African American (AA) or European American (EA) controls; AA (or EA)-AD, AA (or EA) cases with alcohol dependence (AD); AA (or EA)-CD, AA (or EA) cases with cocaine dependence (CD); AA (or EA)-OD, AA (or EA) cases with opioid dependence (OD).

<sup>a,b</sup> *P* values for individual haplotypes (*P*-haplo) and global *P* values (*P*-global) were obtained by haplotype trend regression analyses.

<sup>c</sup> Rare haplotypes (frequency < 5%) are not listed.

Note: statistically significant *P*-values are in bold.

## Abbreviations

AA:	African American
ACTH:	Adrenocorticotropin
AD:	Alcohol Dependence
AIMs:	Ancestry Informative Markers
ASP:	Affected Sibling Pair
Beta ( $\beta$ ):	Regression Coefficient
CD:	Cocaine Dependence
CLIP	Corticotrophin Like Intermediate Lobe Peptide
Con:	Controls
DSM-III-R:	Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised
DSM-IV:	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
EA:	European American
FBAT:	Family-based Association Test
HBAT:	Haplotype-based Association Test
HWE:	Hardy Weinberg Equilibrium
IRB:	Institutional Review Board
LD:	Linkage Disequilibrium
LPH:	Lipotropin
MSH:	Melanocyte-stimulating Hormone
OD:	Opioid Dependence
OR:	Odds Ratio
POMC:	Pro-opiomelanocortin
SSADDA:	Semi-Structured Assessment for Drug Dependence and Alcoholism
SCID-III-R:	Structured Clinical Interview for DSM-III-R
SCID-IV:	Structured Clinical Interview for DSM-IV
SNP:	Single Nucleotide Polymorphism
SP:	Signal Peptide