

## Online Supporting Material

Supplemental Table 1. Candidate genes for magnesium homeostasis in human.

Gene Symbol / Protein Name	Gene Name	Location	Biological Function
<i>CLDN16</i>	Paracellin-1 or claudin-16	Cell membrane	Paracellular calcium and magnesium fluxes in the nephron
<i>CLDN19</i>	Claudin-19	Cell membrane	Renal calcium and magnesium reabsorption
<i>SLC41A1</i>	Solute Carrier Family 41 Member 1	Cell membrane	Relatively nonselective cellular magnesium and other divalent cation transport
<i>SLC41A2</i>	Solute Carrier Family 41 Member 2	Cell membrane	Cellular magnesium and other divalent cation transport
<i>SLC12A3</i>	Solute Carrier Family 12 Member 3	Cell membrane	Renal sodium, chloride, and magnesium reabsorption
<i>CNNM1</i>	Cyclin M1	Cell membrane	Cellular divalent cation transport
<i>CNNM2</i>	Cyclin M2	Cell membrane	Cellular divalent cation transport
<i>NIPA1</i>	Non-imprinted in Prader- Willi/Angelman syndrome 1	Cell membrane	Cellular magnesium transport

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<i>NIPA2</i>	Non-imprinted in Prader-Willi/Angelman syndrome 2	Cell membrane	Cellular magnesium transport
<i>ZDHHC17</i>	Zinc finger, DHHC-type containing 17	Cell membrane	Cellular magnesium transport
<i>MRS2</i>	Mitochondrial RNA Splicing 2	Mitochondria	Mitochondrial magnesium homeostasis
<i>MMGT1</i>	Membrane magnesium transporter 1	Golgi system	Regulation of magnesium dependent enzymes
<i>FXVD2</i>	FXVD domain containing ion transport regulator 2	Cellular member in the nephron	Renal sodium and magnesium handling

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Supplemental Table 2. Odds Ratios and 95% confidence intervals<sup>1</sup> for top 10 associations (ranked by nominal p-values among African Americans) between ion channels related genes and diabetes risk in the WHI-SHARe cohort (n=10,572).

Locus	SNP	Major/Minor Allele	Minor Allele Frequency (AA/HA) <sup>2</sup>		African Americans (n=7,287)		Hispanic American (n=3,285)	
			Cases	Controls	OR (95% CI)	P-value (FDR adjusted p-value)	OR (95% CI)	P-value
<i>CNNM1</i>	rs6584273	G/A	0.20/0.05	0.22/0.05	0.81 (0.72,0.90)	<0.001 (0.01)***	1.03 (0.74,1.44)	0.84
<i>CLDN16</i>	rs4438632	G/A	0.04/0.25	0.03/0.22	1.41 (1.10,1.75)	0.002 (0.06)*	1.03 (0.85,1.26)	0.74
<i>ABCC8</i>	rs7947462	G/A	0.07/0.23	0.09/0.24	0.78 (0.67,0.92)	0.003 (0.19)*	0.89 (0.73,1.08)	0.22
<i>CLDN16</i>	rs1593313	T/C	0.06/0.32	0.05/0.29	1.32 (1.10,1.59)	0.003 (0.06)*	1.05 (0.86,1.28)	0.63
<i>TRPM7</i>	rs2011064	C/G	0.19/0.46	0.17/0.45	1.19 (1.10,1.34)	0.005 (0.17)*	1.09 (0.89,1.35)	0.41

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<i>SLC12A3</i>	rs9921780	A/G	0.50/0.39	0.48/0.40	1.21 (1.10,1.38)	0.005 (0.14)*	1.06 (0.87,1.29)	0.55
<i>TRPM6</i>	rs7046143	T/C	0.30/0.24	0.27/0.22	1.17 (1.00,1.31)	0.01 (0.26)*	1.03 (0.85,1.25)	0.77
<i>CNNM1</i>	rs41444048	G/C	0.17/0.02	0.19/0.02	0.85 (0.75,0.96)	0.01 (0.20)*	1.00 (0.63,1.61)	0.98
<i>ABCC8</i>	rs7111475	G/A	0.11/0.03	0.13/0.03	0.84 (0.73,0.96)	0.01 (0.30)*	1.01 (0.69,1.48)	0.95
<i>TRPM7</i>	rs3109894	C/T	0.30/0.47	0.28/0.46	1.16 (1.00,1.30)	0.01 (0.17)*	1.08 (0.87,1.33)	0.49

<sup>1</sup>Odds Ratios (OR) and 95% confidence interval (CIs) were computed using dominant model with multivariate logistic regression models.

Adjusted for age, region, and three principal components of global ancestry.

<sup>2</sup>AA: African American; HA: Hispanic American.

\*Nominal p-values  $\leq 0.05$ .

\*\* False discovery rate (FDR) adjusted p-values  $\leq 0.05$ .

\*\*\* FDR adjusted p-values  $\leq 0.01$ .

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Supplemental Table 3. Odds Ratios and 95% confidence intervals<sup>1</sup> for top 10 associations (ranked by nominal p-values among Hispanic Americans) between ion channels related genes and diabetes risk in the WHI-SHARe cohort (n=10,572).

Locus	SNP	Major/Minor Allele	Minor Allele Frequency (AA/HA) <sup>2</sup>		African Americans (n=7,287)		Hispanic Americans (n=3,285)	
			Cases	Controls	OR (95% CI)	P-value	OR (95% CI)	P-value (FDR adjusted p-value)
<i>SLC41A2</i>	rs10861279	T/G	0.08/0.03	0.07/0.07	1.10 (0.93,1.29)	0.27	0.49 (0.34,0.72)	<0.001 (0.01)***
<i>MRS2</i>	rs7738943	G/C	0.13/0.08	0.12/0.06	1.04 (0.91,1.18)	0.58	1.57 (1.20,2.05)	0.001 (0.02)**
<i>MRS2</i>	rs1056285	G/A	0.14/0.08	0.14/0.06	1.04 (0.92,1.19)	0.53	1.54 (1.20,2.00)	0.001 (0.02)**
<i>NIPAI</i>	rs7174119	G/A	0.22/0.30	0.22/0.27	1.02 (0.91,1.14)	0.73	1.35 (1.10,1.64)	0.002 (0.05)**
<i>NIPAI</i>	rs6606830	C/T	0.21/0.29	0.22/0.27	1.03 (0.92,1.15)	0.66	1.31 (1.10,1.59)	0.01 (0.07)*

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<i>SLC41A2</i>	rs11112211	G/C	0.09/0.05	0.08/0.07	1.05 (0.91,1.22)	0.51	0.65 (0.47,0.89)	0.01 (0.13)*
<i>SLC41A2</i>	rs10861285	G/T	0.05/0.04	0.05/0.07	0.97 (0.81,1.17)	0.78	0.64 (0.46,0.89)	0.01 (0.13)*
<i>SLC41A2</i>	rs10861284	C/T	0.06/0.04	0.06/0.07	1.00 (0.84,1.20)	0.99	0.65 (0.47,0.90)	0.01 (0.13)*
<i>FXYD2</i>	rs479991	T/C	0.27/0.19	0.28/0.23	1.01 (0.90,1.13)	0.84	0.77 (0.64,0.94)	0.01 (0.08)*
<i>SLC41A2</i>	rs11112216	C/T	0.06/0.04	0.06/0.07	0.97 (0.81,1.16)	0.72	0.65 (0.47,0.90)	0.01 (0.13)*

<sup>1</sup>Odds Ratios (OR) and 95% confidence interval (CIs) were computed using dominant model with multivariate logistic regression models.

Adjusted for age, region, and three principal components of global ancestry.

<sup>2</sup>AA: African American; HA: Hispanic American.

\*Nominal p-values  $\leq 0.05$ .

\*\* False discovery rate (FDR) adjusted p-values  $\leq 0.05$ .

\*\*\* FDR adjusted p-values  $\leq 0.01$ .

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Supplemental Table 4. Odds Ratios and 95% confidence intervals<sup>1</sup> for significant associations (FDR q-values  $\leq 0.05$ ) between ion channels related genes and diabetes risk stratified by total Mg intake in the WHI-SHARe cohort.

Locus	SNP	African Americans				Hispanic Americans			
		Low ( $\leq 0.164$ g/day) (n=2,154)		High ( $\geq 0.291$ g/day) (n=2,120)		Low ( $\leq 0.185$ g/day) (n=1,015)		High ( $\geq 0.313$ g/day) (n=954)	
		OR (95% CI)	p-value	OR (95% CI)	P-value	OR (95% CI)	P-value (FDR adjusted p-value)	OR (95% CI)	P-value (FDR adjusted p-value)
<i>CLDN19</i>	rs11590362	1.24 (0.79,1.93)	0.34	1.25 (0.81,1.91)	0.31	2.01 (1.20,3.37)	0.01 (0.04)**	1.41 (0.80,2.48)	0.24
<i>SLC12A3</i>	rs6499858	0.996 (0.81,1.23)	0.97	1.03 (0.82,1.28)	0.82	0.88 (0.64,1.21)	0.44	0.52 (0.36,0.75)	<0.001 (0.01)***
<i>SLC12A3</i>	rs8049280	1.15 (0.91,1.46)	0.25	1.02 (0.80,1.30)	0.88	1.02 (0.74,1.41)	0.89	0.48 (0.32,0.73)	<0.001 (0.01)***

<sup>1</sup>Odds Ratios (OR) and 95% confidence interval (CIs) were computed using dominant model with multivariate logistic regression models.

Adjusted for age, region, and three principal components of global ancestry. Mg: magnesium.

\*Nominal p-values  $\leq 0.05$ .

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\*\* False discovery rate (FDR) adjusted p-values  $\leq 0.05$ .

\*\*\* FDR adjusted p-values  $\leq 0.01$ .