



THE UNIVERSITY *of* EDINBURGH

Edinburgh Research Explorer

Exome Sequencing to Detect Rare Variants Associated With General Cognitive Ability

Citation for published version:

Luciano, M, Svinti MacLeod, V, Campbell, A, Marioni, RE, Hayward, C, Wright, AF, Taylor, MS, Porteous, DJ, Thomson, P, Prendergast, JGD, Hastie, ND, Farrington, SM, Scotland, G, Dunlop, MG & Deary, IJ 2015, 'Exome Sequencing to Detect Rare Variants Associated With General Cognitive Ability: A Pilot Study' Twin Research and Human Genetics, vol. 18, no. 2, pp. 117-125. DOI: 10.1017/thg.2015.10

Digital Object Identifier (DOI):

[10.1017/thg.2015.10](https://doi.org/10.1017/thg.2015.10)

Link:

[Link to publication record in Edinburgh Research Explorer](#)

Document Version:

Peer reviewed version

Published In:

Twin Research and Human Genetics

Publisher Rights Statement:

© Luciano, M., Svinti, V., Campbell, A., Marioni, R. E., Hayward, C., Wright, A. F., ... Deary, I. J. (2015). Exome Sequencing to Detect Rare Variants Associated With General Cognitive Ability: A Pilot Study. Twin Research and Human Genetics, 1-9. 10.1017/thg.2015.10

General rights

Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.



Exome Sequencing to Detect Rare Variants Associated With General Cognitive Ability: A Pilot Study

Michelle Luciano, Victoria Svinti, Archie Campbell, Riccardo E Marioni, Caroline Hayward, Alan F. Wright, Martin Taylor, David J Porteous, Pippa Thomson, James Prendergast, Nick Hastie, Susan Farrington, Generation Scotland, Malcolm Dunlop, Ian J Deary

Supplementary Table S1

Results From Gene Set Analysis for Significant Variants With Frequency <0.01

	Obesity controls			Depression controls		
	Gene	Number of variants	<i>p</i> -value	Gene	Number of variants	<i>p</i> -value
All variants				<i>RP11-414H17.5</i>	2	1.34 ⁻⁶
				<i>RP11-118B18.1</i>	2	1.97 ⁻⁶
				<i>MESP2/SNORD113-9</i>	2	5.51 ⁻⁶
Nonsynonymous	<i>SYNGAP1</i>	3	4.0⁻⁶	<i>SYNGAP1</i>	2	1.23⁻⁶
				<i>HOXD1/ HOXD-AS1</i>	2	8.82 ⁻⁷
				<i>CECR6</i>	2	6.22 ⁻⁷
				<i>AC022201.5</i>	2	1.04 ⁻⁵
				<i>CYP26C1</i>	2	6.99 ⁻⁶
				<i>ZNF703</i>	2	5.75 ⁻⁷
				<i>NFKBIL1</i>	3	2.77 ⁻⁵
Synonymous				<i>C9orf66</i>	2	1.92 ⁻⁸
				<i>FAM110C</i>	2	3.91 ⁻⁶
				<i>ID4/ RP1-167F1.2</i>	2	9.91 ⁻⁶
				<i>TBC1</i>	2	3.44 ⁻⁶

Note: Significant genes containing a single variant are not shown. Bold indicates common results across case-control subgroup analyses.

Supplementary Table S2

Results From Gene Set Analysis for Significant Variants With Frequency <0.05

	Obesity controls			Depression controls		
	Gene	Number of variants	<i>p</i> -value	Gene	Number of variants	<i>p</i> -value
All variants	<i>RP11-673E1.4/ GYPB</i>	14	2.74^{-12}	<i>RP11-673E1.4/GYPB</i>	11	9.94^{-7}
	<i>/GYPA</i>	/ 9	5.76^{-12}	<i>/GYPA</i>	/ 7	8.05^{-7}
Nonsynonymous				<i>RP11-414H17.5</i>	2	1.16^{-6}
				<i>RP11-118B18.1</i>	2	1.08^{-6}
	<i>RP11-673E1.4/ GYPB</i>	6	4.35^{-12}	<i>RP11-673E1.4/ GYPB</i>	5	2.85^{-7}
	<i>/GYPA</i>	/ 2	5.17^{-12}	<i>/GYPA</i>	/ 2	2.4^{-7}
				<i>CECR6</i>	2	4.41^{-8}
				<i>FAM136A/AC022201.5</i>	2	4.62^{-6}
				<i>ZNF703</i>	2	7.40^{-7}
Synonymous				<i>SOX17</i>	2	2.61^{-7}
				<i>FAM110C</i>	2	4.16^{-6}
				<i>ID4/RP1-167F1.2</i>	2	9.35^{-6}

Note: Significant genes containing a single variant are not shown. Bold indicates common results across case-control subgroup analyses.

Supplementary Table S3

Significant Gene Ontology Pathways Enriched in the Varying Analyses Comprising the Depression Controls

	Gene ontology	<i>p</i> -value	FDR <i>p</i> -value	Enrichment values*	Genes in pathway
Synonymous					
SNVs<.01					
Molecular Function GO:0008376	acetylgalactosaminyl transferase activity	1.23E-5	.03	5.63 (6764,18,667,10)	<i>GALNT6</i> — udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 6 (galnac-t6) <i>GALNT12</i> — udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 12 (galnac-t12) <i>GALNT10</i> — udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 10 (galnac-t10) <i>B4GALNT3</i> — beta-1,4-n-acetyl-galactosaminyl transferase 3 <i>GALNT18</i> — udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 18 <i>GALNT3</i> — udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 3 (galnac-t3) <i>GALNT2</i> — udp-n-acetyl-alpha-d-galactosamine:polypeptide n-acetylgalactosaminyltransferase 2 (galnac-t2) <i>CHPF</i> — chondroitin polymerizing factor <i>B3GALNT2</i> — beta-1,3-n-acetylgalactosaminyltransferase 2 <i>B4GALNT4</i> — beta-1,4-n-acetyl-galactosaminyl transferase 4

Note: *p*-value, FDR corrected *p*-value, enrichment values, and prominent genes in each pathway are listed.

SNV: Single nucleotide variants* Enrichment is defined as (b/n)/(B/N) [*N*: Total number of genes; *B*: Total number of genes associated with a specific GO term, *n*: Number of genes in the 'target set', *b*: Number of genes in the 'target set' associated with a specific GO term].