

Meta genome-wide association study of ME/CFS highlights 42 26 risk loci

Martin Broberg

Institute for Molecular Medicine Finland (FIMM),

University of Helsinki

Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS):

› Symptoms:

- Consistent fatigue
- Post-exertional malaise
- Sleep problems
- Brain fog



› Affects more than 60 million people world-wide.

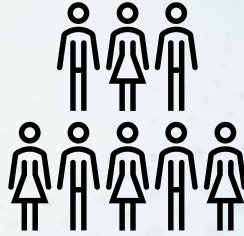
- Unknown cause
- Sex-biased towards females
- Rare full recovery
- Connection with post viral infections

Genome-Wide association Study (GWAS):

Question



Cohort



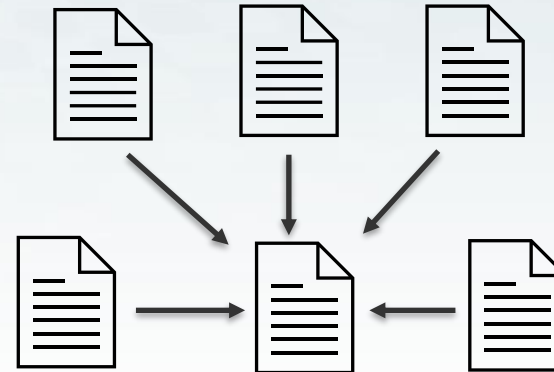
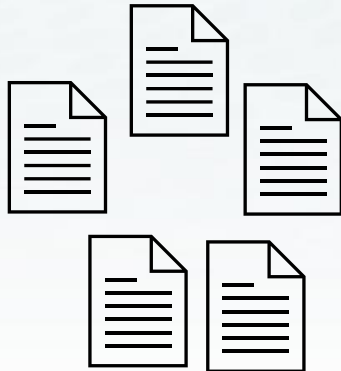
Genotype



Associate

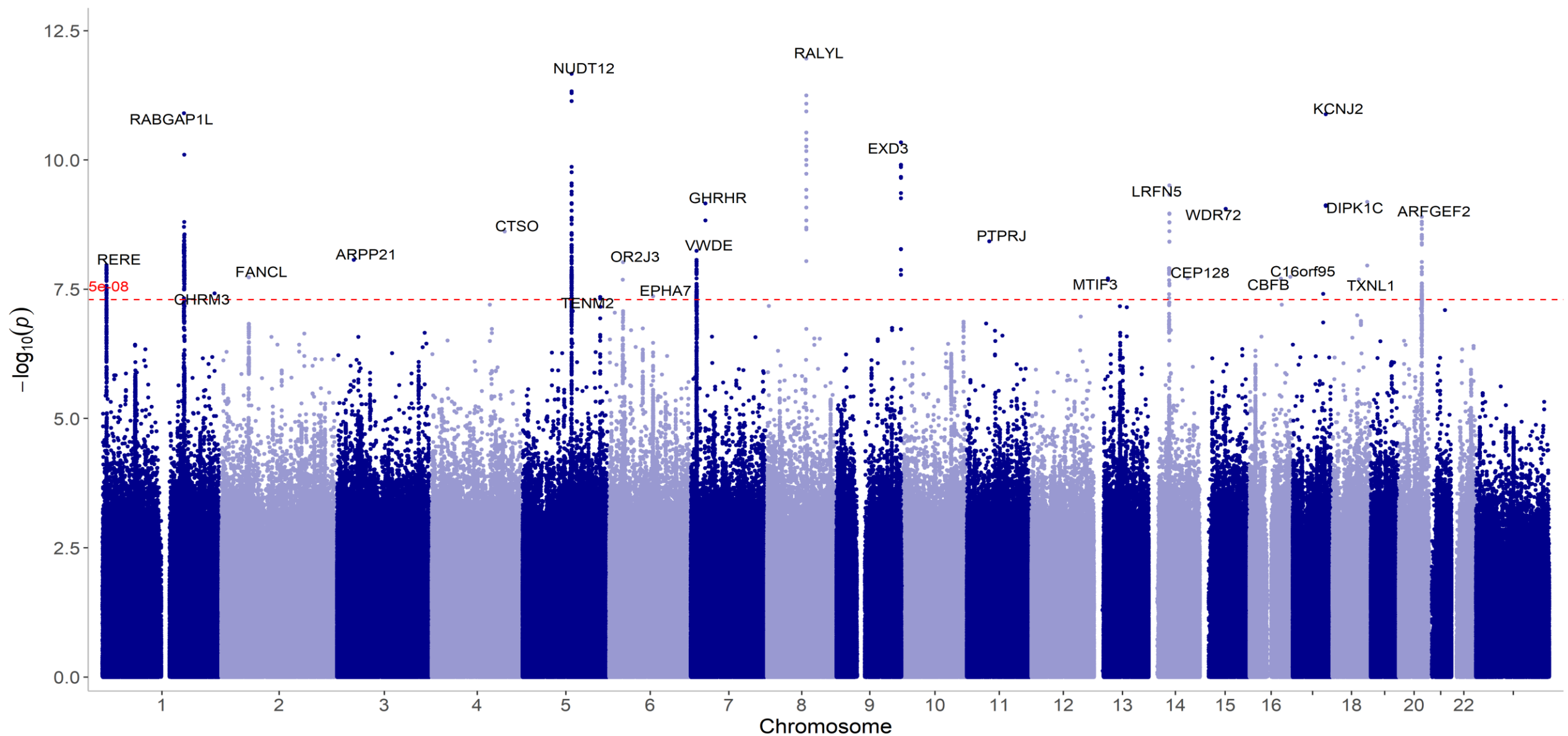


Meta Analysis:



Cohort	Cases	Controls	Total N	Ancestry
Million Veteran Program	648	119584	120232	AFR
Million Veteran Program	3891	439202	443093	EUR
FinnGen	745	499441	500186	EUR
UK Biobank	12096	142376	154472	EUR
Decode Iceland	340	343742	344082	EUR
DecodeME	15579	259909	275488	EUR
Estonian Biobank	2561	205391	207952	EUR
All Of US	722	81852	82574	AFR
All Of US	336	78013	78349	AMR
All Of US	3813	228528	232341	EUR
MoBa	1240	127897	129137	EUR
Michigan Genomics Initiative	3926	57247	61173	EUR
Lifelines	899	18048	18947	EUR
Mass General Brigham	114	50941	51055	EUR
Genes and Health	5021	41396	46417	EAS
Geisinger MyCode rule1	183	2696	2879	AFR
Geisinger MyCode rule1	114	1184	1298	AMR
Geisinger MyCode rule1	11	255	266	EAS
Geisinger MyCode rule1	8273	68622	76895	EUR
Geisinger MyCode rule1	30	266	296	SAS
Total	60542	2766590	2827132	Mixed

Cases = 60,542
Controls = 2,766,590



RABGAP1L

- GTPase activating protein
- Immunity
- Intracellular membrane trafficking

AC099520.1 (NUDT12)

- lincRNA
- Highlighted in neurodevelopmental genetics

LRFN5

- lincRNA
- Highlighted in neurodevelopmental genetics

ARFGEF2

- Intracellular membrane trafficking
- Neurodevelopment during embryonic stage

Initial findings from the DecodeME genome-wide association study of myalgic encephalomyelitis/chronic fatigue syndrome

Genetics Delivery Team,  Thibaud Boutin,  Andrew D. Bretherick, Joshua J. Dibble, Esther Ewaoluwabemiga, Emma Northwood, Gemma L. Samms, Veronique Vitart, Project and Cohort Delivery Team, Øyvind Almeland, Tom Baker, Malgorzata Clyde, Anne Connolly, Diana Garcia,  Shona M. Kerr, Claire Tripp,  Jareth C. Wolfe, Patient and Public Involvement, Jackie Goold, Gemma Hoyes, Sian Leary, Simon J. McGrath, Julie Milton, Anna Redshaw, Jim M. Wilson, Marketing and Communications Team, Helen Baxter, Danielle Boobyer, Claire Dransfield, Daphne Lamirel, Isabel Lewis, Nina Muirhead, Ella Ponting, Charles Shepherd, Alice Turner, University of Edinburgh Team, Sumy V. Baby, Sjoerd Beentjes, John Ireland,  Ava Khamseh, Ewan McDowall, David Perry, Joshua Slaughter, Genetic Epidemiology of ME/CFS Consortium, Erik Abner, Cindy G. Boer, Estonian Biobank Research Team, Sarah Finer, Genes & Health Research Team, Hele Haapaniemi, Hanna M. Ollila, Beth Pollack, Judith Rosmalen, Erika Romppanen, Sirine Saafi, Richa Saxena,  Nasa Sinnott-Armstrong, Anniina Tervi, Lea Urpa, Jesse Valliere,  David A. van Heel, Management Team, Sonya Chowdhury, Andy Devereux-Cooke,  Chris P. Ponting

doi: <https://doi.org/10.1101/2025.08.06.25333109>

Other significantly associating loci

RERE

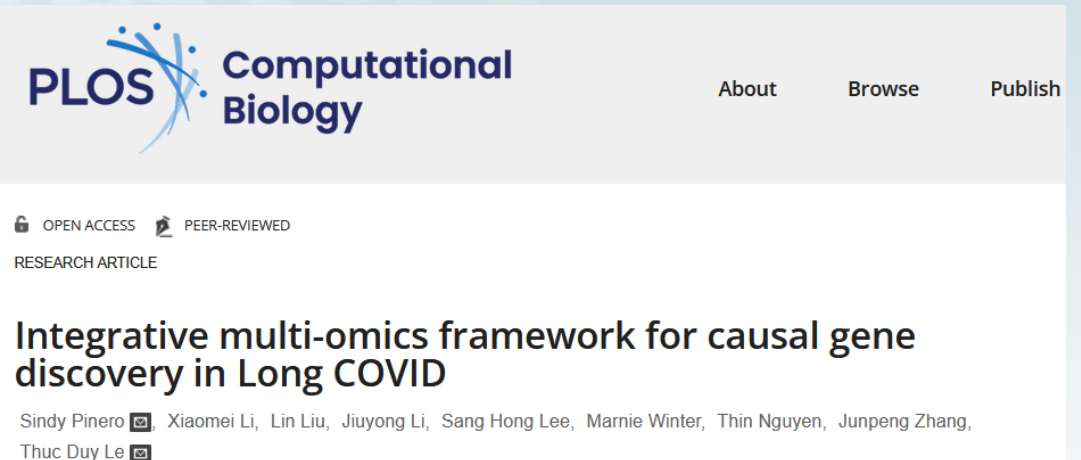
- Nuclear receptor co-regulator
- Embryonic development

GHRHR

- Growth hormone releasing hormone receptor
- Involved with growth, immune defence maturation and regulation

VWDE

- Secreted protein active in ECM
- Recently found associated to long covid



Conclusions/Take-away:

- › **ME/CFS is a global disease similar to chronic post-infection diseases such as long-Covid**
- › **This is the largest multi-ancestral GWAS of ME/CFS, consisting of over 2.8 million individuals**
- › **26 genome-wide significant loci associated with ME/CFS**
 - 4 previously described loci, 22 novel loci
 - Loci involved with neurodevelopment and immunity

Next steps:

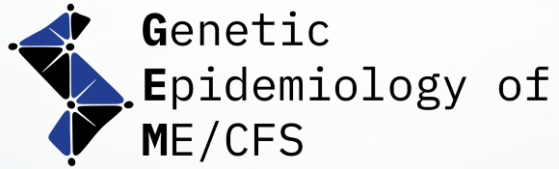
› Post GWAS analyses:

- Genetic correlations
- Gene-based associations
- Experimental verification of genetics

› Sex/ancestry-stratified GWAS and associations

› Increasing the cohort pool

Acknowledgements



ME/CFS Lines
ME/ CVS-onderzoeksconsortium en biobank



Dr. Hanna M. Ollila

hanna.m.ollila@helsinki.fi



Dr. Nasa Sinnot-Armstrong

nasa@fredhutch.org



Dr. Cindy G. Boer

c.boer@erasmusmc.nl

GEM

Dr. Erik Abner

Dr. Martin Broberg

Dr. Elizabeth Corfield

Dr. Joshua Dibble

Dr. Vilma Lammi

Hele Haapaniemi

Dr. Alexandra Havdahl

Pr. dr. Chris Ponting

Dr. Anniina Tervi

Dr. Lea Urpa

Jesse Valliere

ME/CFS Lines

Theo Kuiphof

Pr. dr. Joyce van Meurs

Justien Ramakers

Pr. dr. ir. Marcel Reinders

Pr. dr. Judith Rosmalen

Funders



Thank you for your attention