Matters arising

A first update on mapping the human genetic architecture of COVID-19

https://doi.org/10.1038/s41586-022-04826-7

Received: 4 November 2021

Accepted: 29 April 2022

Published online: 3 August 2022

Open access

Check for updates

COVID-19 Host Genetics Initiative*✉

The COVID-19 pandemic continues to pose a major public health threat, especially in countries with low vaccination rates. To better understand the biological underpinnings of SARS-CoV-2 infection and COVID-19 severity, we formed the COVID-19 Host Genetics Initiative[1]. Here we present a genome-wide association study meta-analysis of up to 125,584 cases and over 2.5 million control individuals across 60 studies from 25 countries, adding 11 genome-wide significant loci compared with those previously identified[2]. Genes at new loci, including *SFTPD*, *MUC5B* and *ACE2*, reveal compelling insights regarding disease susceptibility and severity.

Here we present meta-analyses bringing together 60 studies from 25 countries (Fig. 1 and Supplementary Table 1) for three COVID-19-related phenotypes: (1) individuals critically ill with COVID-19 on the basis of requiring respiratory support in hospital or who died as a consequence of the disease (9,376 cases, of which 3,197 are new in this data release, and 1,776,645 control individuals); (2) individuals with moderate or severe COVID-19 defined as those hospitalized due to symptoms associated with the infection (25,027 cases, 11,386 new and 2,836,272 control individuals); and (3) all cases with reported SARS-CoV-2 infection regardless of symptoms (125,584 cases, 76,022 new and 2,575,347 control individuals). Most studies have reported results before the roll out of the COVID-19 vaccination campaign. An overview of the study design is provided in Supplementary Fig. 1. We found a total of 23 genome-wide significant loci ($P < 5 \times 10^{-8}$) of which 20 loci remain significant after correction for multiple testing ($P < 1.67 \times 10^{-8}$) to account for the number of phenotypes examined (Fig. 2, Supplementary Fig. 2 and Supplementary Table 2). We compared the effects of these loci between the previous[2] and current analysis and found that only one locus did not replicate (rs72711165). All of the other loci showed the expected increase in statistical significance (Supplementary Fig. 3).

Across the genome-wide significant loci, we observed clear patterns of association with the different phenotypes under study. We therefore developed a two-class Bayesian model for classifying loci based on the patterns of association across the two better-powered phenotypes (COVID-19 hospitalization and SARS-CoV-2 reported infection). Intuitively, loci that are associated with susceptibility will also be associated with severity as, to develop COVID-19, SARS-CoV-2 infection needs to first occur. By contrast, those genetic effects that solely modify the course of illness should be associated with severity of illness and not show any association with reported infection except through preferential ascertainment of hospitalized cases in a cohort (Supplementary Methods). We identified 16 loci that are substantially more likely (>99% posterior probability) to affect the risk of COVID-19 hospitalization and 7 loci that clearly influence susceptibility to SARS-CoV-2 infection (Supplementary Table 3 and Supplementary Fig. 4).

We observed that several loci had a significant heterogeneous effect across studies (6 out of 23 loci with a *P* value for heterogeneity of $<2.2 \times 10^{-3}$; Supplementary Table 2). Owing to an increased diversity in our study population (Supplementary Fig. 5), we were able to examine whether such heterogeneity was due to effect differences across continental ancestry groups. Only one locus (*FOXP4*) showed a significantly different effect across ancestries (*P* value heterogeneity of $<7 \times 10^{-5}$; Supplementary Table 4 and Supplementary Fig. 6), although even at this locus all of the ancestry groups showed a positive effect estimate. This confirms that factors related to between-study heterogeneity (such as variable definition of COVID-19 severity owing to different thresholds for testing, hospitalization and patient recruitment) rather than differences across ancestries are a more likely explanation for the observed heterogeneity in the effect sizes across studies.

For the 23 genome-wide significant loci, we examined candidate causal genes and performed a phenome-wide association study to better understand their potential biological mechanisms (Supplementary Tables 2, 5 and 6 and Supplementary Fig. 7). Several of these loci with previous and direct connections to lung disease and SARS-CoV-2 infection mechanisms are highlighted here.

Several loci involved in COVID-19 severity implicate lung surfactant biology. A missense variant rs721917:A>G (p.Met31Thr) in *SFTPD* (10q22.3) confers risk for hospitalization (odds ratio (OR) = 1.06, 95% confidence interval (CI) = 1.04–1.08, $P = 1.7 \times 10^{-8}$) and has been previously associated with increased risk of chronic obstructive pulmonary disease[3] (OR = 1.08, $P = 2.0 \times 10^{-8}$) and decreased lung function[4] (FEV1/FVC; $\beta = -0.019$; $P = 2.0 \times 10^{-15}$). *SFTPD* encodes surfactant protein D (SP-D), which participates in innate immune response, protecting the lungs against inhaled microorganisms. The recombinant fragment of SP-D binds to the S1 spike protein of SARS-CoV-2 and potentially inhibits binding to ACE2 receptor and SARS-CoV-2 infection[5]. Another missense variant rs117169628:G>A (p.Pro256Leu) in *SLC22A31* (16q24.3) also confers risk of hospitalization (OR = 1.09, 95% CI = 1.06–1.13, $P = 2.6 \times 10^{-8}$). *SLC22A31* belongs to the family of solute carrier proteins that facilitate transport across membranes[6] and is co-regulated with other surfactant proteins[7].

We found that the variant rs35705950:G>T located in the promoter of *MUC5B* (11p15.5) is protective against hospitalization (OR = 0.83, 95% CI = 0.86–0.93, $P = 6.5 \times 10^{-9}$). This well-studied promoter variant increases the expression of *MUC5B* in lung in GTEx ($P = 6.7 \times 10^{-16}$) and is the strongest known variant associated with an increased risk of

*A list of authors and their affiliations appears at the end of the paper. ✉e-mail: aganna@broadinstitute.org

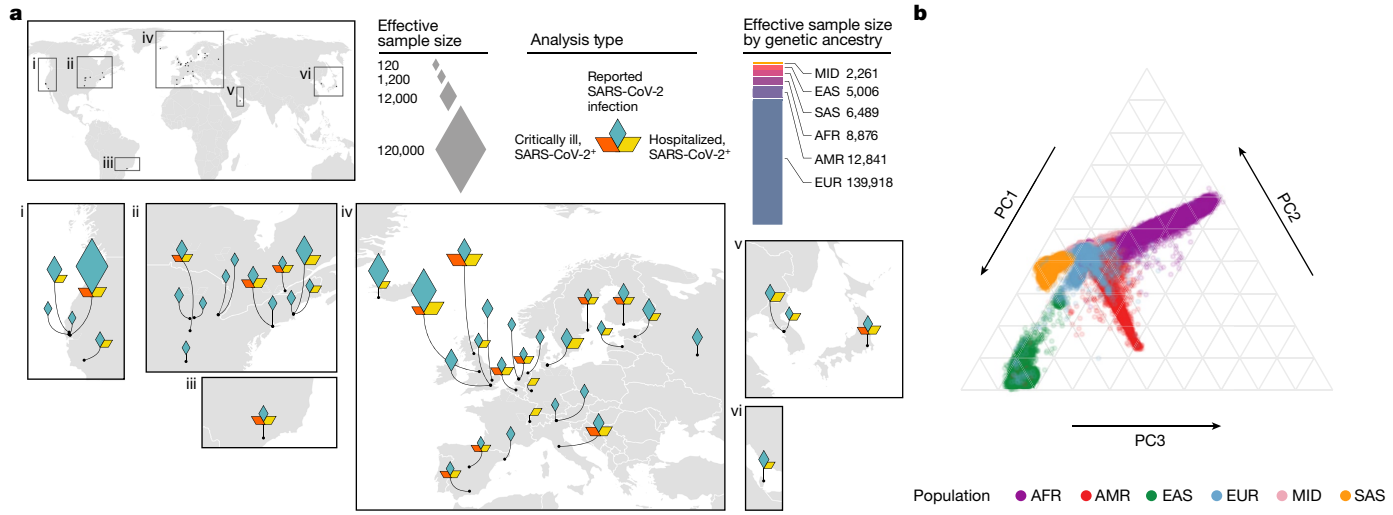

Fig. 1 | Overview of contributing studies in Host Genetics Initiative data freeze 6. a, Geographical overview of the contributing studies to the COVID-19 Host Genetics Initiative and composition by major continental ancestry groups. Ancestry groups are defined as Middle Eastern (MID), south Asian (SAS), east Asian (EAS), African (AFR), admixed American (AMR) and European (EUR). **b**, Principal components analysis highlighting the population structure and the sample ancestry of the individuals participating in the COVID-19 Host Genetics Initiative. This figure is reproduced from the original publication by the COVID-19 Host Genetics Initiative[2] with modifications reflecting the updated analysis from data freeze 6.

developing idiopathic pulmonary fibrosis (IPF)[8,9], but also improves survival in patients with IPF carrying this mutation[10].

Finally, we found that rs190509934:T>C, which is located 69 bp upstream of *ACE2* (Xp22.2), is associated with decreased susceptibility risk (OR = 0.69, 95% CI = 0.63–0.75, $P = 3.6 \times 10^{-18}$). ACE2 is the SARS-CoV-2 receptor and functionally interacts with SLC6A19 and SLC6A20[11], one of which also showed a significant association with susceptibility (rs73062389:G>A at *SLC6A20*; OR = 1.18, 95% CI = 1.16–1.20, $P = 2.5 \times 10^{-74}$). Notably, rs190509934 is ten times more common in south Asian populations (minor allele frequency (MAF) = 0.027) than in European populations (MAF = 0.0024), demonstrating the importance of diversity for variant discovery. Recent results have shown that the

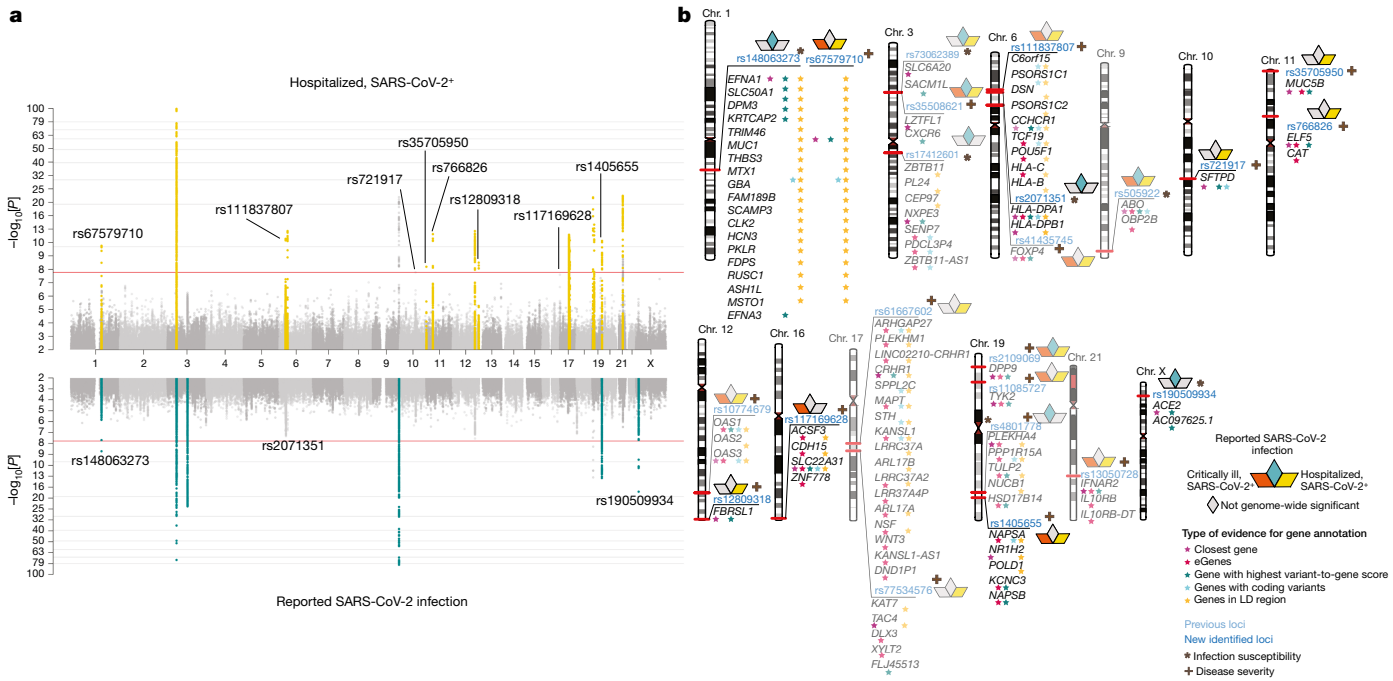

Fig. 2 | Genome-wide association results for COVID-19. a, The results of the genome-wide association study of hospitalized COVID-19 ($n = 25{,}027$ cases and $n = 2{,}836{,}272$ control individuals) (top), and the results of reported SARS-CoV-2 infection ($n = 125{,}584$ cases and $n = 2{,}575{,}347$ control individuals) (bottom). Loci highlighted in yellow (top) represent regions associated with the severity of COVID-19 manifestation. Loci highlighted in green (bottom) are regions associated with SARS-CoV-2-reported infection. Lead variants for the loci identified in this data release are annotated with their respective rs ID. Horizontal lines denote genome-wide significant thresholds. **b**, The results of gene prioritization using different evidence measures of gene annotation. Genes in regions of linkage disequilibrium (LD), genes with coding variants and eGenes (fine-mapped *cis*-eQTL variant PIP > 0.1 in GTEx Lung) are annotated if in linkage disequilibrium with a COVID-19 lead variant ($r^2 > 0.6$). V2G denotes the highest gene prioritized by OpenTargetGenetics' V2G score. The asterisk (*) indicates SARS-CoV-2 reported infection and the plus symbol (+) indicates COVID-19 severity. The transparent loci were reported in the previous freeze (data release 5), and loci in bright blue were identified in the current freeze (data release 6). This figure is reproduced from the original publication by the COVID-19 Host Genetics Initiative[2] with modifications reflecting the updated analysis from data freeze 6.

rs190509934:T>C variant lowers *ACE2* expression, which in turn confers protection against SARS-CoV-2 infection[12].

We applied Mendelian randomization to infer potential causal relationships between COVID-19-related phenotypes and their genetically correlated traits (Supplementary Methods; Supplementary Tables 7–9 and Supplementary Fig. 8). A causal association was observed between genetic liability to type 2 diabetes and SARS-CoV-2 reported infection (OR = 1.02, 95% CI = 1.01–1.03, $P = 1.6 \times 10^{-3}$), and COVID-19 hospitalization (OR = 1.06, 95% CI = 1.03–1.1, $P = 1.4 \times 10^{-4}$). Multivariable Mendelian randomization was used to estimate the direct effect of liability to type 2 diabetes on COVID-19-related phenotypes that was not mediated through body mass index. This analysis indicated that the observed causal association of liability to type 2 diabetes on COVID-19 phenotypes is mediated by body mass index (Supplementary Table 10).

We have substantially expanded the genetic analysis of SARS-CoV-2 infection and COVID-19 severity by doubling the case size, identifying 11 loci. We developed an approach to systematically assign the 23 discovered loci to either disease susceptibility (7 loci) or disease severity (16 loci). Although distinguishing between the two phenotypes is challenging because progression to a severe form of the disease requires susceptibility to infection in the first place, it is now evident that the genetic mechanisms involved in these two aspects of the disease can be differentiated. Among the new loci associated with disease susceptibility, *ACE2* represents an expected, albeit interesting, finding. *MUC5B*, *SFTPD* and *SLC22A31* are the three most interesting new loci associated with COVID-19 severity. Their relationship with lung function and lung diseases is consistent with loci previously associated with disease severity. The surfactant proteins secreted by alveolar cells, representing an emerging biological mechanism, maintain healthy lung function and facilitate the clearance of pathogens[13]. The protective effect of the *MUC5B* variant is unexpected given the otherwise risk-increasing, concordant effect between IPF and COVID-19 observed for other variants[9]. Nonetheless, this result aligns with the *MUC5B* promoter variant association that shows a twofold higher survival rate among patients with IPF[10]. In mice, *Muc5b* seems to be essential for effective mucociliary clearance and for controlling infection[14], which suggests that therapies to control mucin secretion may be beneficial in patients with COVID-19.

Expanding genomic research to include participants from around the world enabled us to test whether the effect of COVID-19-related genetic variants was markedly different across ancestry groups. We did not detect obvious heterogeneity between ancestry groups, and we attribute the observed heterogeneity in the effect of COVID-19-related genetic variants to the diverse inclusion criteria across studies in terms of COVID-19 severity. However, we also note that ascertainment differences across studies might mask true underlying differences in effect sizes between ancestry groups.

The biological insights gained by this expansion of the COVID-19 Host Genetic Initiative showed that increasing sample size and diversity remain a fruitful activity to better understand the human genetic architecture of COVID-19.

Reporting summary

Further information on research design is available in the Nature Research Reporting Summary linked to this paper.

Online content

Any methods, additional references, Nature Research reporting summaries, source data, extended data, supplementary information, acknowledgements, peer review information; details of author contributions and competing interests; and statements of data and code availability are available at https://doi.org/10.1038/s41586-022-04826-7.

Data availability

Summary statistics generated by COVID-19 Host Genetics Initiative are available online (https://www.covid19hg.org/results/r6/). The analyses described here use the freeze 6 data. The COVID-19 Host Genetics Initiative continues to regularly release new data freezes. Summary statistics for samples from individuals of non-European ancestry are not currently available owing to the small individual sample sizes of these groups, but the results for 23 loci lead variants are reported in Supplementary Table 3. Individual-level data can be requested directly from the authors of the contributing studies, listed in Supplementary Table 1. We used publicly available data from GTEx (https://gtexportal.org/home/), the Neale laboratory (http://www.nealelab.is/uk-biobank/), the Finucane laboratory (https://www.finucanelab.org), the FinnGen Freeze 4 cohort (https://www.finngen.fi/en/access_results) and eQTL catalogue release 3 (http://www.ebi.ac.uk/eqtl/).

Code availability

The code for summary statistics lift-over, the projection PCA pipeline including precomputed loadings and meta-analyses are available on GitHub (https://github.com/covid19-hg/), and the code for the Mendelian randomization and genetic correlation pipeline is available at GitHub (https://github.com/marcoralab/MRcovid). Codes for implementing the multivariable Mendelian randomization analysis and subtype analyses are available at GitHub (https://github.com/marcoralab/multivariate_MR and https://github.com/mjpirinen/covid19-hgi_subtypes).

1. The COVID-19 Host Genetics Initiative. The COVID-19 Host Genetics Initiative, a global initiative to elucidate the role of host genetic factors in susceptibility and severity of the SARS-CoV-2 virus pandemic. *Eu. J. Hum. Genet.* **28**, 715–718 (2020).
2. COVID-19 Host Genetics Initiative. Mapping the human genetic architecture of COVID-19. *Nature* **600**, 472–477 (2021).
3. Hobbs, B. D. et al. Genetic loci associated with chronic obstructive pulmonary disease overlap with loci for lung function and pulmonary fibrosis. *Nat. Genet.* **49**, 426–432 (2017).
4. Shrine, N. et al. New genetic signals for lung function highlight pathways and chronic obstructive pulmonary disease associations across multiple ancestries. *Nat. Genet.* **51**, 481–493 (2019).
5. Hsieh, M.-H. et al. Human surfactant protein D binds spike protein and acts as an entry inhibitor of SARS-CoV-2 pseudotyped viral particles. *Front. Immunol.* **12**, 641360 (2021).
6. Hediger, M. A. et al. The ABCs of solute carriers: physiological, pathological and therapeutic implications of human membrane transport proteins. *Pflugers Arch.* **447**, 465–468 (2004).
7. Deelen, P. et al. Improving the diagnostic yield of exome-sequencing by predicting gene-phenotype associations using large-scale gene expression analysis. *Nat. Commun.* **10**, 2837 (2019).
8. Seibold, M. A. et al. A common MUC5B promoter polymorphism and pulmonary fibrosis. *N. Engl. J. Med.* **364**, 1503–1512 (2011).
9. Fadista, J. et al. Shared genetic etiology between idiopathic pulmonary fibrosis and COVID-19 severity. *EBioMedicine* **65**, 103277 (2021).
10. Peljto, A. L. et al. Association between the MUC5B promoter polymorphism and survival in patients with idiopathic pulmonary fibrosis. *JAMA* **309**, 2232–2239 (2013).
11. Vuille-Dit-Bille, R. N. et al. Human intestine luminal ACE2 and amino acid transporter expression increased by ACE-inhibitors. *Amino Acids* **47**, 693–705 (2014).
12. Horowitz, J. E. et al. Common genetic variants identify targets for COVID-19 and individuals at high risk of severe disease. Preprint at *medRxiv* https://doi.org/10.1101/2020.12.14.20248176 (2021).
13. Wright, J. R. Immunoregulatory functions of surfactant proteins. *Nat. Rev. Immunol.* **5**, 58–68 (2005).
14. Roy, M. G. et al. Muc5b is required for airway defence. *Nature* **505**, 412–416 (2014).

Author contributions Detailed author contributions are integrated in the authorship list.

Competing interests A full list of competing interests is supplied as Supplementary Table 11.

Additional information

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41586-022-04826-7.

Correspondence and requests for materials should be addressed to Andrea Ganna.

Reprints and permissions information is available at http://www.nature.com/reprints.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit http://creativecommons.org/licenses/by/4.0/.

© The Author(s) 2022

COVID-19 Host Genetics Initiative
Leadership
Gita A. Pathak[1], Juha Karjalainen[2], Christine Stevens[3], Benjamin M. Neale[4], Mark Daly[2,3,5] & Andrea Ganna[2,3,5] ✉

Writing group
Writing group lead Gita A. Pathak[1], Shea J. Andrews[6], Masahiro Kanai[3], Mattia Cordioli[7] & Andrea Ganna[2,3,5]

Analysis group
Manuscript analyses team lead Juha Karjalainen[2]

Manuscript analyses team members: PHEWAS Gita A. Pathak[1] & Renato Polimanti[1]

Manuscript analyses team members: Mendelian randomization Shea J. Andrews[6] & Nadia Harerimana[8]

Manuscript analyses team members: methods development Mattia Cordioli[7] & Matti Pirinen[7]

Manuscript analyses team members: PC projection, gene prioritization Masahiro Kanai[3]

Project management group
Project management lead Christine Stevens[3] & Rachel G. Liao[3]

Project managment support Karolina Chwialkowska[9], Amy Trankiem[3] & Mary K. Balaconis[3]

Website development
Huy Nguyen[3] & Matthew Solomonson[3]

Scientific communication group
Scientific communication lead Kumar Veerapen[3] & Brooke Wolford[10]

AncestryDNA COVID-19 Research Study
Analysis Team Lead Genevieve Roberts[11]

Data collection lead Danny Park[11]

Admin team lead Catherine A. Ball[11]

Analysis team member Marie Coignet[11], Shannon McCurdy[11], Spencer Knight[11], Raghavendran Partha[11] & Brooke Rhead[11]

Data collection member Miao Zhang[11], Nathan Berkowitz[11], Michael Gaddis[11], Keith Noto[11], Luong Ruiz[11] & Milos Pavlovic[11]

Admin team member Eurie L. Hong[11], Kristin Rand[11], Ahna Girshick[11], Harendra Guturu[11] & Asher Haug Baltzell[11]

BelCovid
Analysis team lead Mari E. K. Niemi[12]

Data collection lead Souad Rahmouni[13] & Julien Guntz[14]

Admin team lead Yves Beguin[15]

Analysis team member Mattia Cordioli[16], Sara Pigazzini[12] & Lindokuhle Nkambule[17,18,19]

Data collection member Michel Georges[13], Michel Moutschen[20,21], Benoit Misset[20,21], Gilles Darcis[20,21], Julien Guiot[20,21], Samira Azarzar[20,21], Stéphanie Gofflot[15], Sabine Claassen[14], Olivier Malaise[20], Pascale Huynen[20], Christelle Meuris[20], Marie Thys[20], Jessica Jacques[20], Philippe Léonard[20], Frederic Frippiat[20], Jean-Baptiste Giot[20], Anne-Sophie Sauvage[20], Christian Von Frenckell[20], Yasmine Belhaj[13] & Bernard Lambermont[20]

Biobanque Quebec COVID-19
Analysis team lead Tomoko Nakanishi[22,23,24,25]

Data collection lead David R. Morrison[23]

Admin team lead Vincent Mooser[26] & J. Brent Richards[23,27,28]

Analysis team member Guillaume Butler-Laporte[23,29], Vincenzo Forgetta[23] & Rui Li[26]

Data collection member Biswarup Ghosh[23], Laetitia Laurent[23], Alexandre Belisle[26], Danielle Henry[23], Tala Abdullah[23], Olumide Adeleye[23], Noor Mamlouk[23], Nofar Kimchi[23], Zaman Afrasiabi[23], Nardin Rezk[23], Branka Vulesevic[23], Meriem Bouab[23], Charlotte Guzman[23], Louis Petitjean[23], Chris Tselios[23], Xiaoqing Xue[23], Jonathan Afilalo[23], Marc Afilalo[30,31], Maureen Oliveira[32], Bluma Brenner[33], Nathalie Brassard[34] & Madeleine Durand[35,36]

Admin team member Erwin Schurr[37], Pierre Lepage[26], Jiannis Ragoussis[26], Daniel Auld[26], Michaël Chassé[36,38], Daniel E. Kaufmann[36,39], G. Mark Lathrop[26] & Darin Adra[23]

CCHC COVID-19 GAWS
Analysis team lead Caroline Hayward[40], Joseph T. Glessner[41,42] & Douglas M. Shaw[43]

Data collection lead Archie Campbell[44,45] & Marcela Morris[46]

Admin team lead Hakon Hakonarson[41,42], David J. Porteous[44] & Jennifer Below[43]

Analysis team member Anne Richmond[40], Xiao Chang[41], Hannah Polikowski[43], Petty E. Lauren[43], Hung-Hsin Chen[43] & Zhu Wanying[43]

Data collection member Chloe Fawns-Ritchie[44,47]

Admin team member Kari North[48] & Joseph B. McCormick[46]

CHOP CAG
Data collection member Xiao Chang[49], Joseph R. Glessner[49,50] & Hakon Hakonarson[49,51,52]

The Colorado Center for Personalized Medicine
Analysis team lead Christopher R. Gignoux[53]

Data collection lead Stephen J. Wicks[53] & Kristy Crooks[53]

Admin team lead Kathleen C. Barnes[53]

Analysis team member Michelle Daya[53], Jonathan Shortt[53], Nicholas Rafaels[53] & Sameer Chavan[53]

Coronagenes
Analysis team lead Paul R. H. J. Timmers[54,55], James F. Wilson[54,55] & Albert Tenesa[54,56]

Admin team lead Shona M. Kerr[54]

Analysis team member Kenton D'Mellow[56]

Egypt hgCOVID hub
Analysis team lead Mari E. K. Niemi[12]

Data collection lead Doaa Shahin[57] & Yasser M. El-Sherbiny[57,58]

Admin team lead Kathrin Aprile von Hohenstaufen[59], Ali Sobh[60] & Madonna M. Eltoukhy[61]

Analysis team member Mattia Cordioli[7] & Lindokuhle Nkambul[17,62]

Data collection member Tamer A. Elhadidy[63], Mohamed S. Abd Elghafar[64], Jehan J. El-Jawhari[57,58], Attia A. S. Mohamed[61], Marwa H. Elnagdy[65], Amr Samir[66], Mahmoud Abdel-Aziz[67], Walid T. Khafaga[68], Walaa M. El-Lawaty[69], Mohamed S. Torky[69] & Mohamed R. El-shanshory[70]

Admin team member Amr M. Yassen[71], Mohamed A. F. Hegazy[66], Kamal Okasha[72], Mohammed A. Eid[73] & Hanteera S. Moahmed[69]

EraCORE
Analysis team lead Carolina Medina-Gomez[74]

Data collection lead M. Arfan Ikram[75]

Admin team lead Andre G. Uitterlinden[74,75]

Estonian Biobank
Analysis team lead Reedik Mägi[76]

Data collection lead Lili Milani[76]

Admin team lead Andres Metspalu[76]

Analysis team member Triin Laisk[76], Kristi Läll[76] & Maarja Lepamets[76]

Data collection member Tõnu Esko[76], Ene Reimann[76], Paul Naaber[77], Edward Laane[78,79], Jaana Pesukova[78], Pärt Peterson[80], Kai Kisand[80], Jekaterina Tabri[81], Raili Allos[81], Kati Hensen[81], Joel Starkopf[82], Inge Ringmets[83], Anu Tamm[84] & Anne Kallaste[84]

Admin team member Helene Alavere[76], Kristjan Metsalu[76] & Mairo Puusepp[76]

EXCEED
Analysis team lead Chiara Batini[85]

Data collection lead Martin D. Tobin[85,86]

Admin team lead Laura D. Venn[85]

Analysis team member Paul H. Lee[85], Nick Shrine[85] & Alexander T. Williams[85]
Data collection member Anna L. Guyatt[85], Catherine John[85], Richard J. Packer[85], Altaf Ali[85], Robert C. Free[87], Xueyang Wang[85], Louise V. Wain[85,86] & Edward J. Hollox[88]

Admin team member Catherine E. Bee[85] & Emma L. Adams[85]

FinnGen
Aarno Palotie[89]

Analysis team member Samuli Ripatti[3,90,91] & Sanni Ruotsalainen[90]

Data collection member Kati Kristiansson[92], Sami Koskelainen[92], Markus Perola[92,93], Kati Donner[7], Katja Kivinen[7] & Aarno Palotie[7]

Admin team member Mari Kaunisto[7]

Functional Host Genomics in Infectious Diseases (FHoGID)
Analysis team lead Carlo Rivolta[94,95]

Data collection lead Pierre-Yves Bochud[96], Stéphanie Bibert[97], Noémie Boillat[96], Semira Gonseth Nussle[98] & Werner Albrich[99]

Analysis team member Mathieu Quinodoz[94,95] & Dhryata Kamdar[94,95]

Data collection member Noémie Suh[100], Dionysios Neofytos[101], Véronique Erard[102] & Cathy Voide[103]

FHoGID Pierre-Yves Bochud[104], Carlo Rivolta[104], Stéphanie Bibert[104], Mathieu Quinodoz[104], Dhryata Kamdar[104], Dionysios Neofytos[104], Véronique Erard[104], Cathy Voide[104], R. Friolet[104], P. Vollenweider[104], J. L. Pagani[104], M. Oddo[104], F. Meyer zu Bentrup[104], A. Conen[104], O. Clerc[104], O. Marchetti[104], A. Guillet[104], C. Guyat-Jacques[104], S. Foucras[104], M. Rime[104], J. Chassot[104], M. Jaquet[104], R. Merlet Viollet[104], Y. Lannepoudenx[104] & L. Portopena[104]

RegCOVID P. Y. Bochud[105], P. Vollenweider[105], J. L. Pagani[105], F. Desgranges[105], P. Filippidis[105], B. Guéry[105], D. Haefliger[105], E. E. Kampouri[105], O. Manuel[105], A. Munting[105], M. Papadimitr iou-Olivgeris[105], J. Regina[105], L. Rochat-Stettler[105], V. Suttels[105], E. Tadini[105], J. Tschopp[105], M. Van Singer[105] & B. Viala[105]

P-PredictUs N. Boillat-Blanco[106], T. Brahier[106], O. Hügli[106], J. Y. Meuwly[106] & O. Pantet[106]

SeroCOVID S. Gonseth Nussle[107], M. Bochud[107], V. D'Acremont[107] & S. Estoppey Younes[107]

CRiPSI W. C. Albrich[108], N. Suh[108], A. Cerny[108], L. O'Mahony[108], C. von Mering[108], P. Y. Bochud[108], M. Frischknecht[108], G-R. Kleger[108], M. Filipovic[108], C. R. Kahlert[108], H. Wozniak[108], T. Rochat Negro[108], J. Pugin[108], K. Bouras[108], C. Knapp[108], T. Egger[108], A. Perret[108], P. Montillier[108], C. di Bartolomeo[108] & B. Barda[108]

GCAT Genomes For Life
Analysis team lead Rafael de Cid[109]

Data collection lead Anna Carreras[109], Victor Moreno[110] & Manolis Kogevinas[111,112,113,114]

Analysis team member Iván Galván-Femenía[109], Natalia Blay[109], Xavier Farré[109] & Lauro Sumoy[109]

Data collection member Beatriz Cortés[109], Josep Maria Mercader[115,116,117,278], Marta Guindo-Martinez[118], David Torrents[118], Judith Garcia-Aymerich[111,113,114], Gemma Castaño-Vin yals[111,112,113,114] & Carlota Dobaño[111,114]

GEN-COVID Multicenter Study
Analysis team lead Marco Gori[119,120] & Mari E. K. Niemi[12]

Data collection lead Alessandra Renieri[121,122,123], Francesca Mari[121,122,123], Mario Umberto Mondelli[124,125], Francesco Castelli[126], Massimo Vaghi[127], Stefano Rusconi[128,129], Francesca Montagnani[123,130], Elena Bargagli[131], Federico Franchi[132], Maria Antonietta Mazzei[133], Luca Cantarini[134], Danilo Tacconi[135], Marco Feri[136], Raffaele Scala[137], Genni Spargi[138], Cesira Nencioni[139], Maria Bandini[140], Gian Piero Caldarelli[141], Anna Canaccini[142], Agostino Ognibene[143], Antonella D'Arminio Monforte[144], Massimo Girardis[145], Andrea Antinori[146], Daniela Francisci[147,148], Elisabetta Schiaroli[147,148], Pier Giorgio Scotton[149], Sandro Panese[150], Renzo Scaggiante[151], Matteo Della Monica[152], Mario Capasso[153,154,155], Giuseppe Fiorentino[156], Marco Castori[157], Filippo Aucella[158], Antonio Di Biagio[159], Luca Masucci[160,161], Serafina Valente[162], Marco Mandalà[163], Patrizia Zucchi[164], Ferdinando Giannattasio[165], Domenico A. Coviello[166], Cristina Mussini[167], Luisa Tavecchia[168], Lia Crotti[169,170,171,172], Marco Rizzi[173], Maria Teresa La Rovere[174], Simona Sarzi-Braga[175], Maurizio Bussotti[176], Sabrina Ravaglia[177], Rosangela Artuso[178], Antonio Perrella[179], Davide Romani[180], Paola Bergomi[181], Emanuele Catena[181], Antonella Vincenti[182], Claudio Ferri[183], Davide Grassi[183], Gloria Pessina[184], Mario Tumbarello[123,185], Massimo Di Pietro[186], Ravaglia Sabrina[187] & Sauro Luchi[188]

Admin team lead Simone Furini[123] & Simona Dei[189]

Analysis team member Elisa Benetti[123], Nicola Picchiotti[119,190], Maurizio Sanarico[191], Stefano Ceri[192], Pietro Pinoli[192], Francesco Raimondi[193], Filippo Biscarini[194], Alessandra Stella[194], Kristina Zguro[123], Katia Capitani[123,195], Mattia Cordioli[16], Sara Pigazzini[12], Mattia Cordioli[16], Sara Pigazzini[12], Lindokuhle Nkambule[17,62] & Marco Tanfoni[119]

Data collection member Chiara Fallerini[121,123], Sergio Daga[121,123], Margherita Baldassarri[121,123], Francesca Fava[121,122,123], Elisa Frullanti[121,123], Floriana Valentino[121,123], Gabriella Doddato[121,123], Annarita Giliberti[121,123], Rossella Tita[122], Sara Amitrano[122], Mirella Bruttini[121,122,123], Susanna Croci[121,123], Ilaria Meloni[121,123], Maria Antonietta Mencarelli[122], Caterina Lo Rizzo[122], Anna Maria Pinto[122], Giada Beligni[121,123], Andrea Tommasi[147], Laura Di Sarno[121,123], Maria Palmieri[121,123], Miriam Lucia Carriero[121,123], Diana Alaverdian[121,123], Stefano Busani[145], Raffaele Bruno[124,125], Marco Vecchia[196], Mary Ann Belli[168], Stefania Mantovani[196], Serena Ludovisi[197], Eugenia Quiros-Roldan[126], Melania Degli Antoni[126], Isabella Zanella[198,199], Matteo Siano[129], Arianna Emiliozzi[146], Massimiliano Fabbiani[130], Barbara Rossetti[130], Laura Bergantini[131], Miriana D'Alessandro[131], Paolo Cameli[131], David Bennett[131], Federico Anedda[132], Simona Marcantonio[132], Sabino Scolletta[132], Susanna Guerrini[133], Edoardo Conticini[134], Bruno Frediani[134], Chiara Spertilli[135], Alice Donati[136], Luca Guidelli[137], Marta Corridi[138], Leonardo Croci[139], Paolo Piacentini[140], Elena Desanctis[140], Silvia Cappelli[140], Agnese Verzuri[142], Valentina Anemoli[142], Alessandro Pancrazzi[143], Maria Lorubbio[143], Federica Gaia Miraglia[144], Sophie Venturelli[145], Andrea Cossarizza[200], Alessandra Vergori[146], Arianna Gabrieli[129], Agostino Riva[128,129], Francesco Paciosi[148], Francesca Andretta[149], Francesca Gatti[151], Saverio Giuseppe Parisi[201], Stefano Baratti[201], Carmelo Piscopo[152], Roberta Russo[153,154], Immacolata Andolfo[153,154], Achille Iolascon[153,154], Massimo Carella[157], Giuseppe Merla[153,202], Gabriella Maria Squeo[202], Pamela Raggi[203], Carmen Marciano[203], Rita Perna[203], Matteo Bassetti[159,204], Maurizio Sanguinetti[160,161], Alessia Giorli[163], Lorenzo Salerni[163], Pierpaolo Parravicini[164], Elisabetta Menatti[205], Tullio Trotta[165], Gabriella Coiro[165], Fabio Lena[206], Enrico Martinelli[207], Sandro Mancarella[168], Chiara Gabbi[191], Franco Maggiolo[173], Diego Ripamonti[173], Tiziana Bachetti[208], Claudia Suardi[209], Gianfranco Parati[169,170], Giordano Bottà[210], Paolo Di Domenico[210], Ilaria Rancan[130], Francesco Bianchi[123,179], Riccardo Colombo[181], Chiara Barbieri[211], Donatella Acquilini[212], Elena Andreucci[178], Agostino Riva[128,129], Francesco Vladimiro Segala[213], Giusy Tiseo[211], Marco Falcone[211], Mirjam Lista[123,214], Monica Poscente[184], Oreste De Vivo[162], Paola Petrocelli[215], Alessandra Guarnaccia[160] & Silvia Baroni[216]

Generation Scotland
Analysis team lead Caroline Hayward[217]

Data collection lead David J. Porteous[218,219]

Admin team lead Chloe Fawns-Ritchie[47,218,219]

Analysis team member Anne Richmond[217]

Data collection member Archie Campbell[218,219]

Genes & Health
Analysis team lead David A. van Heel[220]

Data collection lead Karen A. Hunt[220]

Admin team lead Richard C. Trembath[221]

Analysis team member Qin Qin Huang[222] & Hilary C. Martin[222]

Data collection member Dan Mason[223], Bhavi Trivedi[224] & John Wright[223]

Admin team member Sarah Finer[225]

Genes & Health Research Team Shaheen Akhtar[226], Mohammad Anwar[226], Elena Arciero[226], Samina Ashraf[226], Gerome Breen[226], Raymond Chung[226], Charles J. Curtis[226], Maharun Chowdhury[226], Grainne Colligan[226], Panos Deloukas[226], Ceri Durham[226], Sarah Finer[226], Chris Griffiths[226], Qin Qin Huang[226], Matt Hurles[226], Karen A. Hunt[226], Shapna Hussain[226], Kamrul Islam[226], Ahsan Khan[226], Amara Khan[226], Cath Lavery[226], Sang Hyuck Lee[226], Robin Lerner[226], Daniel MacArthur[226], Bev MacLaughlin[226], Hilary Martin[226],

Dan Mason[226], Shefa Miah[226], Bill Newman[226], Nishat Safa[226], Farah Tahmasebi[226], Richard C. Trembath[226], Bhavi Trivedi[226], David A. van Heel[226], John Wright[226] & Christopher J. Griffiths[227]

Genes for Good
Analysis team lead Albert V. Smith[228]

Data collection member Andrew P. Boughton[228], Kevin W. Li[228], Jonathon LeFaive[228] & Aubrey Annis[228]

Genome-wide assessment of the gene variants associated with severe COVID-19 phenotype in Iran
Analysis team lead Mari E. K. Niemi[12] & Ahmadreza Niavarani[229]

Data collection lead Rasoul Aliannejad[230]

Analysis team member Mattia Cordioli[7], Lindokuhle Nkambul[17,62] & Bahareh Sharififard[229]

Data collection member Ali Amirsavadkouhi[231], Zeinab Naderpour[230], Hengameh Ansari Tadi[232], Afshar Etemadi Aleagha[233], Saeideh Ahmadi[234], Seyed Behrooz Mohseni Moghaddam[235], Alireza Adamsara[236], Morteza Saeedi[237], Hamed Abdollahi[238] & Abdolmajid Hosseini[239]

Host genetic factors in COVID-19 patients in relation to disease susceptibility, disease severity and pharmacogenomics
Analysis team lead Pajaree Chariyavilaskul[240,241]

Data collection lead Watsamon Jantarabenjakul[242,243]

Admin team lead Nattiya Hirankarn[244,245]

Analysis team member Monpat Chamnanphon[246,247], Thitima B. Suttichet[246], Vorasuk Shotelersuk[248,249], Monnat Pongpanich[250,251], Chureerat Phokaew[249,252,253] & Wanna Chetruengchai[249,253]

Data collection member Opass Putchareon[242,254], Pattama Torvorapanit[242,254], Thanyawee Puthanakit[243,255] & Pintip Suchartlikitwong[255,256]

Admin team member Voraphoj Nilaratanakul[257,258] & Pimpayao Sodsai[244,245]

HUNT
Analysis team lead Ben M. Brumpton[259,260,261]

Data collection lead Kristian Hveem[259,260] & Cristen Willer[262,263,264]

Analysis team member Brooke Wolford[262,263,264] & Wei Zhou[265,266]

Data collection member Tormod Rogne[267,268,269], Erik Solligard[267,269] & Bjørn Olav Åsvold[259,260,261]

Lifelines
Analysis team lead Lude Franke[270]

Data collection lead Marike Boezen[271]

Analysis team member Patrick Deelen[272], Annique Claringbould[270], Esteban Lopera[270], Robert Warmerdam[270], Judith. M. Vonk[273] & Irene van Blokland[270]

Data collection member Pauline Lanting[274] & Anil P. S. Ori[275,276]

Mass General Brigham-Host Vulnerability to COVID-19
Analysis team lead Yen-Chen Anne Feng[277] & Josep Mercader[116,117,278]

Data collection lead Scott T. Weiss[279], Elizabeth W. Karlson[280], Jordan W. Smoller[281], Shawn N. Murphy[282], James B. Meigs[283] & Ann E. Woolley[280]

Admin team lead Robert C. Green[284]

Data collection member Emma F. Perez[285]

Michigan Genomics Initiative
Analysis team lead Brooke Wolford[264]

Admin team lead Sebastian Zöllner[228]

Analysis team member Jiongming Wang[228] & Andrew Beck[228]

Mount Sinai Health System COVID-19 Genomics Initiative
Analysis team lead Laura G. Sloofman[6,286,287]

Data collection lead Steven Ascolillo[288], Robert P. Sebra[289,290], Brett L. Collins[291] & Tess Levy[291]

Admin team lead Joseph D. Buxbaum[291] & Stuart C. Sealfon[6]

Analysis team member Shea J. Andrews[6], Daniel M. Jordan[292,293], Ryan C. Thompson[288,294,295], Kyle Gettler[289], Kumardeep Chaudhary[293,296], Gillian M. Belbin[297], Michael Preuss[296,298], Clive Hoggart[6,299], Sam Choi[300] & Slayton J. Underwood[6,301]

Data collection member Irene Salib[289], Bari Britvan[291], Katherine Keller[291], Lara Tang[291], Michael Peruggia[291], Liam L. Hiester[291], Kristi Niblo[291], Alexandra Aksentijevich[291], Alexander Labkowsky[291], Avromie Karp[291], Menachem Zlatopolsky[291] & Marissa Zyndorf[289]

Admin team member Alexander W. Charney[302], Noam D. Beckmann[288], Eric E. Schadt[289,290], Noura S. Abul-Husn[297], Judy H. Cho[293,296], Yuval Itan[293,296], Eimear E. Kenny[297], Ruth J. F. Loos[296,298,303], Girish N. Nadkarni[295,296,304,305,306], Ron Do[293,296], Paul O'Reilly[300] & Laura M. Huckins[307]

MyCode Health Initiative
Analysis team lead Manuel A. R. Ferreira[308] & Goncalo R. Abecasis[308]

Data collection lead Joseph B. Leader[309] & Michael N. Cantor[308]

Admin team lead Anne E. Justice[310] & Dave J. Carey[311]

Analysis team member Geetha Chittoor[310], Navya Shilpa Josyula[310], Jack A. Kosmicki[308], Julie E. Horowitz[308] & Aris Baras[308]

Data collection member Matthew C. Gass[309] & Ashish Yadav[308]

Admin team member Tooraj Mirshahi[311]

Netherlands Twin Register
Analysis team lead Jouke Jan Hottenga[312]

Data collection lead Meike Bartels[312]

Admin team lead Eco E. J. C. de geus[312]

Analysis team member Michel M. G. Nivard[312]

Penn Medicine Biobank
Analysis team lead Anurag Verma[313] & Marylyn D. Ritchie[313]

Admin team lead Daniel Rader[313]

Analysis team member Binglan Li[314], Shefali S. Verma[313], Anastasia Lucas[313] & Yuki Bradford[313]

Saudi Human Genome Program - COVID19: Host Genomic markers predicting the severity and suitability to COVID-19 in highly consanguineous population
Analysis team lead Malak Abedalthagafi[315] & Manal Alaamery[316,317]

Data collection lead Abdulraheem Alsharef[318] & Mona Sawaji[319]

Admin team lead Salam Massadeh[316,317] & Abdulaziz AlMalik[320]

Analysis team member Saleh Alqahtani[321,322], Dona Baraka[323], Fawz Al Harthi[315], Ebtehal Alsolm[315], Leen Abu Safieh[315], Albandary M. Alowayn[315], Fatimah Alqubaishi[315], Amal Al Mutairi[315] & Serghei Mangul[324]

Data collection member Mansour Almutairi[316,317], Nora Aljawini[325], Nour Albesher[325], Yaseen M. Arabi[326], Ebrahim S. Mahmoud[326], Amin K. Khattab[327], Roaa T. Halawani[327], Ziab Z. Alahmadey[327], Jehad K. Albakri[327], Walaa A. Felemban[327], Bandar A. Suliman[318], Rana Hasanato[323], Laila Al-Awdah[328], Jahad Alghamdi[329], Deema AlZahrani[330], Sameera AlJohani[331], Hani Al-Afghani[332], Nouf AlDhawi[330], Hadeel AlBardis[315], Sarah Alkwai[325], Moneera Alswailm[325], Faisal Almalki[330], Maha Albeladi[330], Iman Almohammed[325], Eman Barhoush[333] & Anoud Albader[330]

Admin team member Sara Alotaibi[315], Bader Alghamdi[334], Junghyun Jung[335] & Mohammad S. fawzy[315]

Data collection member May Alrashed[336]

The genetic predisposition to severe COVID-19
Analysis team lead Mari E. K. Niemi[12]

Data collection lead Hugo Zeberg[337,338]

Analysis team member Mattia Cordioli[16], Sara Pigazzini[12] & Lindo Nkambul[3,17,339]

Data collection member Robert Frithiof[340], Michael Hultström[340,341], Miklos Lipcsey[340,342], Nicolas Tardif[343], Olav Rooyackers[343], Jonathan Grip[343] & Tomislav Maricic[338]

The Norwegian Mother, Father and Child Cohort Study
Analysis team lead Øyvind Helgeland[344]

Data collection lead Per Magnus[345] & Lill-Iren S. Trogstad[346]

Analysis team member Yunsung Lee[345]

Admin team member Jennifer R. Harris[344]

TwinsUK
Analysis team lead Massimo Mangino[347,348]

Data collection lead Tim D. Spector[347]

Data collection member Duncan Emma[347]

UK 100,000 Genomes Project (Genomics England)
Analysis team lead Loukas Moutsianas[349,350]

Data collection lead Mark J. Caulfield[349,350,351] & Richard H. Scott[349,352]

Analysis team member Athanasios Kousathanas[353], Dorota Pasko[353], Susan Walker[353], Alex Stuckey[353], Christopher A. Odhams[353] & Daniel Rhodes[353]

Data collection member Tom Fowler[353], Augusto Rendon[349,354], Georgia Chan[353] & Prabhu Arumugam[353]

UK Biobank
Analysis team lead Tomoko Nakanishi[22,23,24,25], Konrad J. Karczewski[5,19], Alicia R. Martin[5,19], Daniel J. Wilson[355] & Chris C. A. Spencer[356]

Data collection lead Derrick W. Crook[357], David H. Wyllie[357,358] & Anne Marie O'Connell[359]

Admin team lead J. Brent Richards[23,27,28]

Analysis team member Guillaume Butler-Laporte[23,29], Vincenzo Forgetta[23], Elizabeth G. Atkinson[5,19], Masahiro Kanai[5,19,360], Kristin Tsuo[5,19,361], Nikolas Baya[5,19], Patrick Turley[5,19], Rahul Gupta[5,19], Raymond K. Walters[5,19], Duncan S. Palmer[5,19], Gopal Sarma[5,19], Matthew Solomonson[5,19], Nathan Cheng[5,19], Wenhan Lu[5,19], Claire Churchhouse[5,19], Jacqueline I. Goldstein[5,19], Daniel King[5,19], Wei Zhou[5,19], Cotton Seed[5,19], Mark J. Daly[2,3,5], Benjamin M. Neale[5,19], Hilary Finucane[5,19], Sam Bryant[3], F. Kyle Satterstrom[5,19], Gavin Band[362], Sarah G. Earle[355], Shang-Kuan Lin[355], Nicolas Arning[355] & Nils Koelling[356]

Data collection member Jacob Armstrong[355] & Justine K. Rudkin[355]

Admin team member Shawneequa Callier[363], Sam Bryant[5,19] & Caroline Cusick[19]

UK Blood Donors Cohort
Analysis team lead Nicole Soranzo[364,365,366] & Jing Hua Zhao[367]

Data collection lead John Danesh[367,368,369,370,371] & Emanuele Di Angelantonio[367,368,369,370]

Analysis team member Adam S. Butterworth[367,368,369,370]

Million Veteran Program
Analysis team lead Yan V. Sun[372,373] & Jennifer E. Huffman[374]

Data collection lead Kelly Cho[375]

Admin team lead Christopher J. O'Donnell[374], Phil Tsao[376,377] & J. Michael Gaziano[375]

Analysis team member Gina Peloso[374,378]

Data collection member Yuk-Lam Ho[375]

Vanda COVID
Analysis team lead Sandra P. Smieszek[379]

Admin team lead Christos Polymeropoulos[379], Vasilios Polymeropoulos[379] & Mihael H. Polymeropoulos[379]

Analysis team member Bartlomiej P. Przychodzen[379]

Variability in immune response genes and severity of SARS-CoV-2 infection (INMUNGEN-CoV2 study)
Analysis team lead Israel Fernandez-Cadenas[380]

Data collection lead Anna M. Planas[381,382]

Analysis team member Jordi Perez-Tur[383,384,385], Laia Llucià-Carol[380,386], Natalia Cullell[380,387], Elena Muiño[380], Jara Cárcel-Márquez[380], Marta L. DeDiego[388] & Lara Lloret Iglesias[389]

Data collection member Alex Soriano[390], Veronica Rico[391], Daiana Agüero[391], Josep L. Bedini[391], Francisco Lozano[392], Carlos Domingo[391], Veronica Robles[391], Francisca Ruiz-Jaén[393], Leonardo Márquez[394], Juan Gomez[395], Eliecer Coto[395], Guillermo M. Albaiceta[395], Marta García-Clemente[395], David Dalmau[396], Maria J. Arranz[396], Beatriz Dietl[396], Alex Serra-Llovich[396], Pere Soler[397], Roger Colobrán[397], Andrea Martín-Nalda[397], Alba Parra Martínez[397], David Bernardo[398], Silvia Rojo[399], Aida Fiz-López[398], Elisa Arribas[398], Paloma de la Cal-Sabater[398], Tomás Segura[400], Esther González-Villa[400], Gemma Serrano-Heras[401], Joan Martí-Fàbregas[402], Elena Jiménez-Xarrié[402], Alicia de Felipe Mimbrera[403], Jaime Masjuan[403], Sebastian García-Madrona[403], Anna Domínguez-Mayoral[404], Joan Montaner Villalonga[404] & Paloma Menéndez-Valladares[404]

Women's Genome Health Stud
Analysis team lead Daniel I. Chasman[405,406]

Data collection lead Howard D. Sesso[405,406] & JoAnn E. Manson[405,406]

Admin team lead Julie E. Buring[405,406] & Paul M. Ridker[405,406]

Analysis team member Giulianini Franco[405]

Phenotype steering group
Lea Davis[43], Andrea Ganna[2,3,5], Sulggi Lee[407], James Priest[376], Marco Gori[119,120], Vijay G. Sankaran[3,408], David van Heel[220], Marike Boezen[271], J. Brent Richards[23,27,28], Tomoko Nakanishi[22,23,24,25], Les Biesecker[409], V. Eric Kerchberger[43] & J. Kenneth Baillie[40,56,410]

COVID-19 HGI corresponding authors
Benjamin M. Neale[4], Mark Daly[2,3,5] & Andrea Ganna[2,3,5]

[1]Yale University, New Haven, CT, USA. [2]Institute for Molecular Medicine Finland (FIMM), University of Helsinki, Helsinki, Finland. [3]Broad Institute of MIT and Harvard, Cambridge, MA, USA. [4]Massachusetts General Hospital, Broad Institute of MIT and Harvard, Cambridge, MA, USA. [5]Analytic and Translational Genetics Unit, Massachusetts General Hospital, Boston, MA, USA. [6]Icahn School of Medicine at Mount Sinai, New York, NY, USA. [7]Institute for Molecular Medicine Finland (FIMM), University of Helsinki, Helsinki, Finland. [8]Icahn School of Medicine at Mount Sinai, Genetics and Genomic Sciences, York City, NY, USA. [9]Centre for Bioinformatics and Data Analysis, Medical University of Bialystok, Bialystok, Poland. [10]University of Michigan, Ann Arbor, MI, USA. [11]Ancestry, Lehi, UT, USA. [12]Institute for Molecular Medicine Finland (FIMM), Helsinki, Finland. [13]University of Liege, GIGA-Institute, Liège, Belgium. [14]CHC Mont-Légia, Liège, Belgium. [15]5BHUL (Liège Biobank), CHU of Liège, Liège, Belgium. [16]Institute for Molecular Medicine Finland, University of Helsinki, Helsinki, Finland. [17]Analytic & Translational Genetics Unit, Massachusetts General Hospital, Boston, MA, USA. [18]Stanley Center for Psychiatric Research, Broad Institute of MIT and Harvard, Cambridge, MA, USA. [19]Program in Medical and Population Genetics, Broad Institute of MIT and Harvard, Cambridge, MA, USA. [20]CHU of Liege, Liège, Belgium. [21]University of Liege, Liège, Belgium. [22]Department of Human Genetics, McGill University, Montreal, Quebec, Canada. [23]Lady Davis Institute, Jewish General Hospital, McGill University, Montreal, Quebec, Canada. [24]Kyoto-McGill International Collaborative School in Genomic Medicine, Graduate School of Medicine, Kyoto University, Kyoto, Japan. [25]Research Fellow, Japan Society for the Promotion of Science, Tokyo, Japan. [26]McGill Genome Centre and Department of Human Genetics, McGill University, Montreal, Quebec, Canada. [27]Department of Human Genetics, Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, Quebec, Canada. [28]Department of Twin Research, King's College London, London, UK. [29]Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montréal, Québec, Canada. [30]Department of Emergency Medicine, McGill University, Montreal, Quebec, Canada. [31]Emergency Department, Jewish General Hospital, McGill University, Montreal, Quebec, Canada. [32]McGill AIDS Centre, Department of Microbiology and Immunology, Lady Davis Institute for Medical Research, Jewish General Hospital, McGill University, Montreal, Quebec, Canada. [33]McGill Centre for Viral Diseases, Lady Davis Institute, Department of Infectious Disease, Jewish General Hospital, Montreal, Quebec, Canada. [34]Research Centre of the Centre Hospitalier de l'Université de Montréal, Montreal, Canada. [35]Department of Medicine, Research Centre of the Centre Hospitalier de l'Université de Montréal, Montreal, Canada. [36]Department of Medicine, Université de Montréal, Montreal, Canada. [37]Department of Medicine and Human Genetics, McGill University, Montreal, Quebec, Canada. [38]Department of Intensive Care, Research Centre of the Centre Hospitalier de l'Université de Montréal, Montreal, Quebec, Canada. [39]Division of Infectious Diseases, Research Centre of the Centre Hospitalier de l'Université de Montréal, Montreal, Quebec, Canada. [40]MRC Human Genetics Unit, Institute of Genetics and Cancer, University of Edinburgh, Western General Hospital, Edinburgh, UK. [41]Center for Applied Genomics, Children's Hospital of Philadelphia, Philadelphia, PA, USA. [42]Department of Pediatrics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA. [43]Vanderbilt University Medical Center, Nashville, TN, USA. [44]Centre for Genomic and Experimental Medicine, Institute of Genetics and Cancer,

University of Edinburgh, Western General Hospital, Edinburgh, UK. [45]Usher Institute, University of Edinburgh, Nine, Edinburgh Bioquarter, Edinburgh, UK. [46]University of Texas Health, Houston, TX, USA. [47]Department of Psychology, University of Edinburgh, Edinburgh, UK. [48]University of North Carolina at Chapel Hill, Chapel Hill, NC, USA. [49]Center for Applied Genomics, The Children's Hospital of Philadelphia, Philadelphia, PA, USA. [50]Division of Human Genetics, Department of Pediatrics, The Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA. [51]Divisions of Human Genetics and Pulmonary Medicine, Department of Pediatrics, The Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA. [52]Faculty of Medicine, University of Iceland, Reykjavik, Iceland. [53]University of Colorado - Anschutz Medical Campus, Aurora, CO, USA. [54]MRC Human Genetics Unit, Institute of Genetics and Cancer, University of Edinburgh, Western General Hospital, Edinburgh, UK. [55]Centre for Global Health Research, Usher Institute, University of Edinburgh, Teviot Place, Edinburgh, UK. [56]The Roslin Institute, The Royal (Dick) School of Veterinary Studies, University of Edinburgh, Edinburgh, UK. [57]Department of Clinical Pathology, Faculty of Medicine, Mansoura University, Mansoura, Egypt. [58]Department of Biosciences, School of Science and Technology, Nottingham Trent University, Nottingham, UK. [59]Genolier Innovation Network and Hub, Swiss Medical Network, Genolier Healthcare Campus, Genolier, Switzerland. [60]Department of Pediatrics, Faculty of Medicine, Mansoura University, Mansoura, Egypt. [61]Department of Clinical Pathology, Faculty of Medicine, Tanta University, Tanta, Egypt. [62]Stanley Center for Psychiatric Research & Program in Medical and Population Genetics, Broad Institute of MIT and Harvard, Cambridge, MA, USA. [63]Chest Department, Faculty of Medicine, Mansoura University, Mansoura, Egypt. [64]Anesthesia, Surgical Intensive Care & Pain Management Department, Faculty of Medicine, Tanta University, Tanta, Egypt. [65]Department of Medical Biochemistry, Faculty of Medicine, Mansoura University, Mansoura, Egypt. [66]Department of Surgery, Faculty of Medicine, Mansoura University, Mansoura, Egypt. [67]Department of Tropical Medicine, Faculty of Medicine, Mansoura University, Mansoura, Egypt. [68]pediatric and neonatology, Kafr Elzayat General Hospital, Kafr El-Zayat, Egypt. [69]Chest Department, Faculty of Medicine, Tanta University, Tanta, Egypt. [70]Pediatrics Department, Faculty of Medicine, Tanta University, Tanta, Egypt. [71]Department of Anaethesia and Critical Care, Faculty of Medicine, Mansoura University, Mansoura, Egypt. [72]Department of Internal Medicine, Faculty of Medicine, Tanta University, Tanta, Egypt. [73]Faculty of Science, Tanta University, Tanta, Egypt. [74]Department of Internal Medicine, Erasmus MC Rotterdam, Rotterdam, The Netherlands. [75]Department of Epidemiology, Erasmus MC Rotterdam, Rotterdam, The Netherlands. [76]Estonian Genome Centre, Institute of Genomics, University of Tartu, Tartu, Estonia. [77]SYNLAB Estonia, University of Tartu, Tartu, Estonia. [78]Kuressaare Hospital, Kuressaare, Estonia. [79]University of Tartu, Tartu, Estonia. [80]Institute of Biomedicine and Translational Medicine, University of Tartu, Tartu, Estonia. [81]West Tallinn Central Hospital, Tallinn, Estonia. [82]University of Tartu, Tartu University Hospital, Tartu, Estonia. [83]Estonian Health Insurance Fund, Tallinn, Estonia. [84]Tartu University Hospital, Tartu, Estonia. [85]Department of Health Sciences, University of Leicester, Leicester, UK. [86]Leicester NIHR Biomedical Research Centre, Leicester, UK. [87]Department of Respiratory Sciences, University of Leicester, Leicester, UK. [88]Department of Genetics and Genome Biology, University of Leicester, Leicester, UK. [89]FinnGen, Helsinki, Finland. [90]Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland. [91]Public Health, Faculty of Medicine, University of Helsinki, Helsinki, Finland. [92]Finnish Institute for Health and Welfare (THL), Helsinki, Finland. [93]University of Helsinki, Faculty of Medicine, Clinical and Molecular Metabolism Research Program, Helsinki, Finland. [94]Institute of Molecular and Clinical Ophthalmology Basel (IOB), Basel, Switzerland. [95]Department of Ophthalmology, University of Basel, Basel, Switzerland. [96]Infectious Diseases Service, Department of Medicine, University Hospital and University of Lausanne, Lausanne, Switzerland. [97]Infectious Diseases Service, Department of Medicine, University Hospital, University of Lausanne, Lausanne, Switzerland. [98]Centre for Primary Care and Public Health, University of Lausanne, Lausanne, Switzerland. [99]Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital St Gallen, St Gallen, Switzerland. [100]Division of Intensive Care, Geneva University Hospitals and the University of Geneva Faculty of Medicine, Geneva, Switzerland. [101]Infectious Disease Service, Department of Internal Medicine, Geneva University Hospital, Geneva, Switzerland. [102]Clinique de Médecine et spécialités, Infectiologie, HFR-Fribourg, Fribourg, Switzerland. [103]Infectious Diseases Division, University Hospital Centre of the Canton of Vaud, Hospital of Valais, Sion, Switzerland. [104]Functional Host Genomics of Infectious Diseases, University Hospital and University of Lausanne, Lausanne, Switzerland. [105]Registry COVID, University Hospital and University of Lausanne, Lausanne, Switzerland. [106]Pneumonia prediction using lung ultrasound, University Hospital and University of Lausanne, Lausanne, Switzerland. [107]Center for Primary Care and Public Health (Unisanté), University of Lausanne, Lausanne, Switzerland. [108]Covid-19 Risk Prediction in Swiss ICUs-Trial, Division of Infectious Diseases and Hospital Epidemiology, Cantonal Hospital St Gallen, St Gallen, Switzerland. [109]GCAT-Genomes for Life, Germans Trias i Pujol Health Sciences Research Institute (IGTP), Badalona, Spain. [110]Catalan Institute of Oncology, Bellvitge Biomedical Research Institute, Consortium for Biomedical Research in Epidemiology and Public Health and University of Barcelona, Barcelona, Spain. [111]ISGlobal, Barcelona, Spain. [112]IMIM (Hospital del Mar Medical Research Institute), Barcelona, Spain. [113]Universitat Pompeu Fabra (UPF), Barcelona, Spain. [114]CIBER Epidemiología y Salud Pública (CIBERESP), Madrid, Spain. [115]Barcelona Supercomputing Center, Centro Nacional de Supercomputación (BSC-CNS), Life & Medical Sciences, Barcelona, Spain. [116]Diabetes Unit and Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, USA. [117]Harvard Medical School, Boston, Massachusetts, USA. [118]Barcelona Supercomputing Center, Centro Nacional de Supercomputación (BSC-CNS), Life & Medical Sciences, Barcelona, Spain. [119]University of Siena, DIISM-SAILAB, Siena, Italy. [120]Université Côte d'Azur, Inria, CNRS, I3S, Maasai, Nice, France. [121]Medical Genetics, University of Siena, Siena, Italy. [122]Genetica Medica, Azienda Ospedaliero-Universitaria Senese, Siena, Italy. [123]Med Biotech Hub and Competence Center, Department of Medical Biotechnologies, University of Siena, Siena, Italy. [124]Division of Infectious Diseases and Immunology, Department of Medical Sciences and Infectious Diseases, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy. [125]Department of Internal Medicine and Therapeutics, University of Pavia, Pavia, Italy. [126]Department of Infectious and Tropical Diseases, University of Brescia and ASST Spedali Civili Hospital, Brescia, Italy. [127]Chirurgia Vascolare, Ospedale Maggiore di Crema, Crema, Italy. [128]III Infectious Diseases Unit, ASST-FBF-Sacco, Milan, Italy. [129]Department of Biomedical and Clinical Sciences Luigi Sacco, University of Milan, Milan, Italy. [130]Dept of Specialized and Internal Medicine, Tropical and Infectious Diseases Unit, Azienda Ospedaliera Universitaria Senese, Siena, Italy. [131]Unit of Respiratory Diseases and Lung Transplantation, Department of Internal and Specialist Medicine, University of Siena, Siena, Italy. [132]Dept of Emergency and Urgency, Medicine, Surgery and Neurosciences, Unit of Intensive Care Medicine, Siena University Hospital, Siena, Italy. [133]Department of Medical, Surgical and Neuro Sciences and Radiological Sciences, Unit of Diagnostic Imaging, University of Siena, Siena, Italy. [134]Rheumatology Unit, Department of Medicine, Surgery and Neurosciences, University of Siena, Policlinico Le Scotte, Siena, Italy. [135]Department of Specialized and Internal Medicine, Infectious Diseases Unit, San Donato Hospital Arezzo, Arezzo, Italy. [136]Dept of Emergency, Anesthesia Unit, San Donato Hospital, Arezzo, Italy. [137]Department of Specialized and Internal Medicine, Pneumology Unit and UTIP, San Donato Hospital, Arezzo, Italy. [138]Department of Emergency, Anesthesia Unit, Misericordia Hospital, Grosseto, Italy. [139]Department of Specialized and Internal Medicine, Infectious Diseases Unit, Misericordia Hospital, Grosseto, Italy. [140]Department of Preventive Medicine, Azienda USL Toscana Sud Est, Arezzo, Italy. [141]Clinical Chemical Analysis Laboratory, Misericordia Hospital, Grosseto, Italy. [142]Territorial Scientific Technician Department, Azienda USL Toscana Sud Est, Arezzo, Italy. [143]Clinical Chemical Analysis Laboratory, San Donato Hospital, Arezzo, Italy. [144]Department of Health Sciences, Clinic of Infectious Diseases, ASST Santi Paolo e Carlo, University of Milan, Milan, Italy. [145]Department of Anesthesia and Intensive Care, University of Modena and Reggio Emilia, Modena, Italy. [146]HIV/AIDS Department, National Institute for Infectious Diseases, IRCCS, Lazzaro Spallanzani, Rome, Italy. [147]Infectious Diseases Clinic, Department of Medicine 2, Azienda Ospedaliera di Perugia and University of Perugia, Santa Maria Hospital, Perugia, Italy. [148]Infectious Diseases Clinic, "Santa Maria" Hospital, University of Perugia, Perugia, Italy. [149]Department of Infectious Diseases, Treviso Hospital, Treviso, Italy. [150]Clinical Infectious Diseases, Mestre Hospital, Venezia, Italy. [151]Infectious Diseases Clinic, Belluno Hospital, Viale Europa, Belluno, Italy. [152]Medical Genetics and Laboratory of Medical Genetics Unit, A.O.R.N. "Antonio Cardarelli", Naples, Italy. [153]Department of Molecular Medicine and Medical Biotechnology, University of Naples Federico II, Naples, Italy. [154]CEINGE Biotecnologie Avanzate, Naples, Italy. [155]IRCCS SDN, Naples, Italy. [156]Unit of Respiratory Physiopathology, AORN dei Colli, Monaldi Hospital, Naples, Italy. [157]Division of Medical Genetics, Fondazione IRCCS Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo, Italy. [158]Department of Medical Sciences, Fondazione IRCCS Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo, Italy. [159]Infectious Diseases Clinic, Policlinico San Martino Hospital, IRCCS for Cancer Research, Genova, Italy. [160]Microbiology, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Catholic University of Medicine, Rome, Italy. [161]Department of Laboratory Sciences and Infectious Diseases, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy. [162]Department of Cardiovascular Diseases, University of Siena, Siena, Italy. [163]Otolaryngology Unit, University of Siena, Siena, Italy. [164]Department of Internal Medicine, ASST Valtellina e Alto Lario, Sondrio, Italy. [165]First Aid Department, Luigi Curto Hospital, Polla, Salerno, Italy. [166]U.O.C. Laboratorio di Genetica Umana, IRCCS Istituto G. Gaslini, Genova, Italy. [167]Infectious Diseases Clinics, University of Modena and Reggio Emilia, Modena, Italy. [168]U.O.C. Medicina, ASST Nord Milano, Ospedale Bassini, Cinisello Balsamo, Milan, Italy. [169]Department of Cardiovascular, Neural and Metabolic Sciences, Istituto Auxologico Italiano, IRCCS, San Luca Hospital, Milan, Italy. [170]Department of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy. [171]Istituto Auxologico Italiano, IRCCS, Center for Cardiac Arrhythmias of Genetic Origin, Milan, Italy. [172]Istituto Auxologico Italiano, IRCCS, Laboratory of Cardiovascular Genetics, Milan, Italy. [173]Unit of Infectious Diseases, ASST Papa Giovanni XXIII Hospital, Bergamo, Italy. [174]Department of Cardiology, Istituti Clinici Scientifici Maugeri IRCCS, Institute of Montescano, Pavia, Italy. [175]Istituti Clinici Scientifici Maugeri, IRCCS, Department of Cardiac Rehabilitation, Institute of Tradate (VA), Pavia, Italy. [176]Cardiac Rehabilitation Unit, Fondazione Salvatore Maugeri, IRCCS, Scientific Institute of Milan, Milan, Italy. [177]IRCCS C. Mondino Foundation, Pavia, Italy. [178]Medical Genetics Unit, Meyer Children's University Hospital, Florence, Italy. [179]Department of Medicine, Pneumology Unit, Misericordia Hospital, Grosseto, Italy. [180]Department of Preventive Medicine, Azienda USL Toscana Sud Est, Tuscany, Italy. [181]Department of Anesthesia and Intensive Care Unit, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Polo Universitario, University of Milan, Milan, Italy. [182]Infectious Disease Unit, Hospital of Massa, Massa, Italy. [183]Department of Clinical Medicine, Public Health, Life and Environment Sciences, University of L'Aquila, L'Aquila, Italy. [184]UOSD Laboratorio di Genetica Medica - ASL Viterbo, San Lorenzo, Italy. [185]Department of Medical Sciences, Infectious and Tropical Diseases Unit, Azienda Ospedaliera Universitaria Senese, Siena, Italy. [186]Unit of Infectious Diseases, S.M. Annunziata Hospital, Florence, Italy. [187]IRCCS Mondino Foundation, Pavia, Italy. [188]Infectious Disease Unit, Hospital of Lucca, Lucca, Italy. [189]Health Management, Azienda USL Toscana Sudest, Tuscany, Italy. [190]Department of Mathematics, University of Pavia, Pavia, Italy. [191]Independent Researcher, Milan, Italy. [192]Department of Electronics, Information and Bioengineering (DEIB), Politecnico di Milano, Milano, Italy. [193]Scuola Normale Superiore, Pisa, Italy. [194]CNR-Consiglio Nazionale delle Ricerche, Istituto di Biologia e Biotecnologia Agraria (IBBA), Milano, Italy. [195]Core Research Laboratory, ISPRO, Florence, Italy. [196]Division of Infectious Diseases and Immunology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy. [197]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy. [198]Department of Molecular and Translational Medicine, University of Brescia, Brescia, Italy. [199]Clinical Chemistry Laboratory, Cytogenetics and Molecular Genetics Section, Diagnostic Department, ASST Spedali Civili di Brescia, Brescia, Italy. [200]Department of Medical and Surgical Sciences for Children and Adults, University of Modena and Reggio Emilia, Modena, Italy. [201]Department of Molecular Medicine, University of Padova, Padua, Italy. [202]Laboratory of Regulatory and Functional Genomics, Fondazione IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo (Foggia), Foggia, Italy. [203]Clinical Trial Office, Fondazione IRCCS Casa Sollievo della Sofferenza Hospital, San Giovanni Rotondo, Italy. [204]Department of Health Sciences, University of Genova, Genova, Italy. [205]Oncologia Medica e Ufficio Flussi Sondrio, Sondrio, Italy. [206]Local Health Unit-Pharmaceutical Department of Grosseto, Toscana Sud Est Local Health Unit, Grosseto, Italy. [207]Department of Respiratory Diseases, Azienda Ospedaliera di Cremona, Cremona, Italy. [208]Direzione Scientifica, Istituti Clinici Scientifici Maugeri IRCCS, Pavia, Italy. [209]Fondazione per la ricerca Ospedale di Bergamo, Bergamo, Italy. [210]Allelica Inc, New York, NY, USA. [211]Department of Clinical and Experimental Medicine, Infectious Diseases Unit, University of Pisa, Pisa, Italy. [212]Infectious Disease Unit, Santo Stefano Hospital, AUSL Toscana Centro, Prato, Italy. [213]Clinic of Infectious Diseases, Catholic University of the Sacred Heart, Rome, Italy. [214]Medical Genetics, University of Siena, Siena, Italy. [215]Infectious Disease Unit, Hospital

of Lucca, Lucca, Italy. [216]Department of Diagnostic and Laboratory Medicine, Institute of Biochemistry and Clinical Biochemistry, Fondazione Policlinico Universitario A. Gemelli IRCCS, Catholic University of the Sacred Heart, Rome, Italy. [217]MRC Human Genetics Unit, IGC, University of Edinburgh, Edinburgh, UK. [218]Medical Genetics Section, Centre for Genomic and Experimental Medicine, IGC, University of Edinburgh, Edinburgh, UK. [219]Generation Scotland, Centre for Genomic and Experimental Medicine, IGC, University of Edinburgh, Edinburgh, UK. [220]Blizard Institute, Queen Mary University of London, London, UK. [221]School of Basic and Medical Biosciences, Faculty of Life Sciences and Medicine, King's College London, London, UK. [222]Medical and Population Genomics, Wellcome Sanger Institute, Hinxton, UK. [223]Bradford Institute for Health Research, Bradford Teaching Hospitals National Health Service (NHS) Foundation Trust, Bradford, UK. [224]Blizard Institute, Queen Mary University of London, London, UK. [225]Institute of Population Health Sciences, Queen Mary University of London, London, UK. [226]Genes & Health, Blizard Institute, Queen Mary University of London, London, UK. [227]Institute of Population Health Sciences, Queen Mary University of London, London, UK. [228]Department of Biostatistics, University of Michigan, Ann Arbor, MI, USA. [229]Digestive Oncology Research Center, Digestive Disease Research Institute, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran. [230]Department of Pulmonology, School of Medicine, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran. [231]Department of Critical Care Medicine, Noorafshar Hospital, Tehran, Iran. [232]Department of Emergency Intensive Care Unit, School of Medicine, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran. [233]Department of Anesthesiology, School of Medicine, Amir Alam Hospital, Tehran University of Medical Sciences, Tehran, Iran. [234]Department of Pulmonology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran. [235]Department of Pathology, Parseh Pathobiology and Genetics Laboratory, Tehran, Iran. [236]Department of Microbiology, Health and Family Research Center, NIOC Hospital, Tehran, Iran. [237]Department of Emergency Medicine, School of Medicine, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran. [238]Department of Anesthesiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran. [239]Department of Pathology, Faculty of Medicine, Tehran Azad University, Tehran, Iran. [240]Clinical Pharmacokinetics and Pharmacogenomics Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. [241]Department of Pharmacology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. [242]Thai Red Cross Emerging Infectious Diseases Clinical Centre, King Chulalongkorn Memorial Hospital, Bangkok, Thailand. [243]Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. [244]Immunology Division, Department of Microbiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. [245]Center of Excellence in Immunology and Immune-mediated Diseases, Department of Microbiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. [246]Clinical Pharmacokinetics and Pharmacogenomics Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. [247]Department of Pathology, Faculty of Medicine, Nakornnayok, Srinakharinwirot University, Bangkok, Thailand. [248]Center of Excellence for Medical Genomics, Medical Genomics Cluster, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. [249]Excellence Center for Genomics and Precision Medicine, King Chulalongkorn Memorial Hospital, The Thai Red Cross Society, Bangkok, Thailand. [250]Department of Mathematics and Computer Science, Faculty of Science, Chulalongkorn University, Bangkok, Thailand. [251]Omics Sciences and Bioinfomatics Center, Faculty of Science, Chulalongkorn University, Bangkok, Thailand. [252]Research Affairs, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. [253]Center of Excellence for Medical Genomics, Medical Genomics Cluster, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. [254]Division of Infectious Disease, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. [255]Center of Excellence in Pediatric Infectious Diseases and Vaccines, Chulalongkorn University, Bangkok, Thailand. [256]Department of Microbiology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. [257]Division of Infectious Diseases, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. [258]Healthcare-associated Infection Research Group STAR (Special Task Force for Activating Research), Chulalongkorn University, Bangkok, Thailand. [259]K.G. Jebsen Center for Genetic Epidemiology, Department of Public Health and Nursing, NTNU, Norwegian University of Science and Technology, Trondheim, Norway. [260]HUNT Research Center, Department of Public Health and Nursing, NTNU, Norwegian University of Science and Technology, Levanger, Norway. [261]Clinic of Medicine, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway. [262]Division of Cardiovascular Medicine, Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA. [263]Department of Computational Medicine and Bioinformatics, University of Michigan, Ann Arbor, MI, USA. [264]Department of Human Genetics, University of Michigan, Ann Arbor, MI, USA. [265]Analytic and Translational Genetics Unit, Massachusetts General Hospital, Boston, Massachusetts, USA. [266]Program in Medical and Population Genetics, Broad Institute of Harvard and MIT, Cambridge, Massachusetts, USA. [267]Gemini Center for Sepsis Research, Department of Circulation and Medical Imaging, NTNU, Norwegian University of Science and Technology, Trondheim, Norway. [268]Department of Chronic Disease Epidemiology and Center for Perinatal, Pediatric and Environmental Epidemiology, Yale School of Public Health, New Haven, CT, USA. [269]Clinic of Anaesthesia and Intensive Care, St. Olavs Hospital, Trondheim University Hospital, Trondheim, Norway. [270]Department of Genetics, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands. [271]Department of Epidemiology, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands. [272]Department of Genetics, University Medical Centre Groningen, University of Groningen / Department of Genetics, University Medical Centre Utrecht, Utrecht, The Netherlands. [273]Department of Epidemiology, University of Groningen, University Medical Center Groningen, Groningen, The Netherlands. [274]University of Groningen, University Medical Center Groningen, Department of Genetics, Groningen, The Netherlands. [275]Department of Genetics, University Medical Center Groningen, Groningen, The Netherlands. [276]Department of Psychiatry, University Medical Center Groningen, Groningen, The Netherlands. [277]Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, USA. [278]Programs in Metabolism and Medical and Population Genetics, Broad Institute of MIT and Harvard, Cambridge, MA, USA. [279]Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA. [280]Brigham and Women's Hospital, Boston, MA, USA. [281]Psychiatric and Neurodevelopmental Genetics Unit, Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, USA. [282]Department of Neurology, Massachusetts General Hospital, Boston, MA, USA. [283]Division of General Internal Medicine, Massachusetts General Hospital and Dpeartment of Medicine, Harvard Medical School and Program in Medical and Population Genetics, Broad Institute, Boston, MA, USA. [284]Division of Genetics, Department of Medicine, Brigham and Women's Hospital, Broad Institute of MIT and Harvard, Harvard Medical School, Boston, MA, USA. [285]Division of Genetics, Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA. [286]Seaver Autism Center for Research and Treatment, York City, NY, USA. [287]Department of Psychiatry, Icahn School of Medicine, New York, NY, USA. [288]Mount Sinai Clinical Intelligence Center, Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [289]Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [290]Sema4, a Mount Sinai venture, Stamford, CT, USA. [291]Seaver Autism Center for Research and Treatment, Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [292]Mount Sinai Clnical Intelligence Center, Charles Bronfman Institute for Personalized Medicine, New York, NY, USA. [293]Department of Genetics & Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [294]Icahn Institute of Data Science and Genomics Technology, New York, NY, USA. [295]Mount Sinai Clinical Intelligence Center, New York, NY, USA. [296]Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [297]Institute for Genomic Health, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [298]The Mindich Child Health and Development Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [299]Pamela Sklar Division of Psychiatric Genomics, Department of Psychiatry, Department of Genetic and Genomic Sciences, New York, NY, USA. [300]Pamela Sklar Division of Psychiatric Genomics, Department of Psychiatry, Department of Genetic and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [301]Seaver Autism Center for Research and Treatment, Department of Psychiatry, New York, NY, USA. [302]Mount Sinai Clinical Intelligence Center, Department of Psychiatry, Department of Genetic and Genomic Sciences, Icahn School of Medicine at Mount Sinai, Mount Sinai, NY, USA. [303]Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [304]The Hasso Plattner Institute of Digital Health at Mount Sinai, New York, NY, USA. [305]BioMe Phenomics Center, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [306]Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [307]Pamela Sklar Division of Psychiatric Genomics, Seaver Autism Center for Research and Treatment, Department of Psychiatry, Department of Genetic and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY, USA. [308]Regeneron Genetics Center, Tarrytown, NY, USA. [309]Phenomic Analytics & Clinical Data Core, Geisinger Health System, Danville, PA, USA. [310]Department of Population Health Sciences, Geisinger Health System, Danville, PA, USA. [311]Department of Molecular and Functional Genomics, Geisinger Health System, Danville, PA, USA. [312]Vrije Universiteit Amsterdam, Amsterdam, UK. [313]Department of Genetics, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, USA. [314]Department of Biomedical Data Science, Stanford University, Stanford, CA, USA. [315]Genomics Research Department, Saudi Human Genome Project, King Fahad Medical City and King Abdulaziz City for Science and Technology, Riyadh, Saudi Arabia. [316]Developmental Medicine Department, King Abdullah International Medical Research Center, King Saud Bin Abdulaziz University for Health Sciences, Ministry of National Guard- Health Affairs, Riyadh, Saudi Arabia. [317]Saudi Human Genome Project (SHGP), King Abdulaziz City for Science and Technology (KACST), Satellite Lab at King Abdulaziz Medical City (KAMC), Ministry of National Guard Health Affairs (MNG-HA), Riyadh, Saudi Arabia. [318]College of Applied Medical Sciences, Taibah University, Madina, Saudi Arabia. [319]Developmental Medicine Department, King Abdullah International Medical Research Center, King Saud Bin Abdulaziz University for Health Sciences, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia. [320]Life Science and environmental institute, King Abdulaziz City for Science and Technology, Riyadh, Saudi Arabia. [321]The Liver Transplant Unit, King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia. [322]The Division of Gastroenterology and Hepatology, Johns Hopkins University, Baltimore, MD, USA. [323]Department of Pathology, College of Medicine, King Saud University, Riyadh, Saudi Arabia. [324]Titus Family Department of Clinical Pharmacy, USC School of Pharmacy University of Southern California, Los Angeles, CA, USA. [325]KACST-BWH Centre of Excellence for Biomedicine, Joint Centers of Excellence Program, King Abdulaziz City for Science and Technology (KACST), Riyadh, Saudi Arabia. [326]Ministry of the National Guard Health Affairs, King Abdullah International Medical Research Center and King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia. [327]Ohud Hospital, Ministry of Health, Madinah, Saudi Arabia. [328]Pediatric Infectious Diseases, Children's Specialized Hospital, King Fahad Medical City, Riyadh, Saudi Arabia. [329]The Saudi Biobank, King Abdullah International Medical Research Center, King Saud bin Abdulaziz University for Health Sciences, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia. [330]Developmental Medicine Department, King Abdullah International Medical Research Center, King Saud Bin Abdulaziz University for Health Sciences, King AbdulAziz Medical City, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia. [331]Department of Pathology and Laboratory Medicine, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, King Saud Bin Abdulaziz University for Health Sciences and King Abdullah International Medical Research Center, Riyadh, Saudi Arabia. [332]Laboratory Department, Security Forces Hospital, General Directorate of Medical Services, Ministry of Interior, Riyadh, Saudi Arabia. [333]King Abdulaziz City for Science and Technology (KACST), Riyadh, Saudi Arabia. [334]Department of Developmental Medicine, King Abdullah International Medical Research Center, King Saud Bin Abdulaziz University for Health Sciences, King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh, Saudi Arabia. [335]Titus Family Department of Clinical Pharmacy, USC School of Pharmacy, Los Angeles, CA, USA. [336]Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia. [337]Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden. [338]Max Planck Institute for Evolutionary Anthropology, Leipzig, Germany. [339]Stanley Center for Psychiatric Research & Program in Medical and Population Genetics, Cambridge, MA, USA. [340]Anaesthesiology and Intensive Care Medicine, Department of Surgical Sciences, Uppsala University, Uppsala, Sweden. [341]Integrative Physiology, Department of Medical Cell Biology, Uppsala University, Uppsala, Sweden. [342]Hedenstierna Laboratory, CIRRUS, Anaesthesiology and Intensive Care Medicine, Department of Surgical Sciences, Uppsala University, Uppsala, Sweden. [343]Division Anesthesiology and Intensive Care, CLINTEC, Karolinska Institutet, Stockholm, Sweden. [344]Department of Genetics and Bioinformatics, Norwegian Institute of Public Health, Oslo, Norway. [345]Centre for Fertility and Health, Norwegian Institute of Public Health, Oslo, Norway.

[346]Department of Method Development and Analytics, Norwegian Institute of Public Health, Oslo, Norway. [347]King's College London, Department of Twin Research and Genetic Epidemiology, London, UK. [348]NIHR Biomedical Research Centre at Guy's and St Thomas' Foundation Trust, London, UK. [349]Genomics England, London, UK. [350]Queen Mary University, London, UK. [351]William Harvey Research Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, UK. [352]UCL Great Ormond Street Institute of Child Health, London, UK. [353]Genomics England, London, UK. [354]University of Cambridge, London, United Kingdom. [355]Big Data Institute, Nuffield Department of Population Health, University of Oxford, Li Ka Shing Centre for Health Information and Discovery, Old Road Campus, Oxford, UK. [356]Genomics PLC, King Charles House, Oxford, UK. [357]Nuffield Department of Medicine, Experimental Medicine Division, University of Oxford, John Radcliffe Hospital, Oxford, UK. [358]Public Health England, Field Service, Addenbrooke's Hospital, Cambridge, UK. [359]Public Health England, Data and Analytical Services, National Infection Service, London, UK. [360]Program in Bioinformatics and Integrative Genomics, Harvard Medical School, Boston, MA, USA. [361]Program in Biological and Biomedical Sciences, Harvard Medical School, Boston, MA, USA. [362]Wellcome Centre for Human Genetics, University of Oxford, Roosevelt Drive, Oxford, UK. [363]Department of Clinical Research and Leadership, George Washington University, Washington, DC, USA. [364]Department of Human Genetics, The Wellcome Sanger Institute, Wellcome Genome Campus, Hinxton, Cambridge, UK. [365]The National Institute for Health Research Blood and Transplant Unit in Donor Health and Genomics, University of Cambridge, Strangeways Research Laboratory, Wort's Causeway, Cambridge, UK. [366]Department of Haematology, University of Cambridge, Cambridge Biomedical Campus, Long Road, Cambridge, UK. [367]British Heart Foundation Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK. [368]British Heart Foundation Centre of Research Excellence, University of Cambridge, Cambridge, UK. [369]National Institute for Health Research Blood and Transplant Research Unit in Donor Health and Genomics, University of Cambridge, Cambridge, UK. [370]Health Data Research UK Cambridge, Wellcome Genome Campus and University of Cambridge, Cambridge, UK. [371]Department of Human Genetics, Wellcome Sanger Institute, Hinxton, UK. [372]Department of Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA, USA. [373]Atlanta CA Health Care System, North Druid Hills, GA, USA. [374]Center for Population Genomics, MAVERIC, VA Boston Healthcare System, Boston, MA, USA. [375]MAVERIC, VA Boston Healthcare System, Boston, MA, USA. [376]Stanford University, Stanford, CA, USA. [377]Palo Alto VA Healthcare System, Stanford, CA, USA. [378]Department of Biostatistics, Boston Univeristy School of Public Health, Boston, MA, USA. [379]Vanda Pharmaceuticals Inc., Washington, DC, USA. [380]Stroke Pharmacogenomics and Genetics, Biomedical Research Institute Sant Pau, Sant Pau Hospital, Barcelona, Spain. [381]Institute for Biomedical Researhc of Barcelona (IIBB), National Spanish Research Council (CSIC), Madrid, Spain. [382]Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain. [383]Institute of Biomedicine of Valencia (IBV), CSIC, València, Spain. [384]Network Center for Biomedical Research on Neurodegenerative Diseases (CIBERNED), València, Spain. [385]Neurology and Genetic Mixed Unit, La Fe Helath Research Institute, València, Spain. [386]Institute for Biomedical Research of Barcelona (IIBB), National Spanish Research Council (CSIC), Barcelona, Spain. [387]Department of Neurology, Hospital Universitari MútuaTerrassa, Fundació Docència i Recerca MútuaTerrassa, Terrassa, Spain. [388]Department of Molecular and Cell Biology, Centro Nacional de Biotecnología (CNB-CSIC), Campus Universidad Autónoma de Madrid, Madrid, Spain. [389]Instituto de Física de Cantabria (IFCA-CSIC), Santander, Spain. [390]Hospital Clínic, IDIBAPS, Barcelona, Spain. [391]Hospital Clínic, Barcelona, Spain. [392]Hospital Clínic, IDIBAPS, School of Medicine, University of Barcelona, Barcelona, Spain. [393]IDIBAPS, Barcelona, Spain. [394]IIBB-CSIC, Barcelona, Spain. [395]Servicio de Salud del Principado de Asturias, Oviedo, Spain. [396]Hospital Mutua de Terrassa, Terrassa, Spain. [397]Hospital Valle Hebrón, Barcelona, Spain. [398]Instituto de Biomedicina y Genética Molecular (IBGM), CSIC-Universidad de Valladolid, Valladolid, Spain. [399]Hospital Clínico Universitario de Valladolid (SACYL), Valladolid, Spain. [400]Department of Neurology, University Hospital of Albacete, Albacete, Spain. [401]Research Unit, University Hospital of Albacete, Albacete, Spain. [402]Department of Neurology, Biomedical Research Institute Sant Pau (IIB Sant Pau), Hospital de la Santa Creu i Sant Pau, Barcelona, Spain. [403]Hospital Universitario Ramón Y Cajal, IRYCIS, Madrid, Spain. [404]Institute de Biomedicine of Seville, IBiS/Hospital Universitario Virgen del Rocío/CSIC/University of Seville & Department of Neurology, Hospital Universitario Virgen Macarena, Seville, Spain. [405]Brigham and Women's Hospital, Boston, USA. [406]Harvard Medical School, Boston, MA, USA. [407]University of California San Francisco, San Francisco, CA, USA. [408]Boston Children's Hospital, Boston, MA, USA. [409]National Institutes of Health, Bethesda, MD, USA. [410]Intensive Care Unit, Royal Infirmary of Edinburgh, Edinburgh, UK. ✉e-mail: aganna@broadinstitute.org

nature portfolio

Corresponding author(s): Andrea Ganna

Last updated by author(s): Nov 14, 2021

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our Editorial Policies and the Editorial Policy Checklist.

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒ A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☐	☒ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☐	☒ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	No code was used to collect data in the study.
Data analysis	Each individual study that contributed genetic-phenotype association summary statistics to the consortium carried out their association analyses independently of the consortium (study-specific information outlined in Supplementary Table 1). However, the consortium did release phenotyping and analysis guidelines as a recommendation (https://www.covid19hg.org/). For quality control of genotype data we recommended using the Ricopili pipeline (PMID: 31393554). For genotype phasing and imputation we recommended the TopMed Imputation Server (PMID: 27571263) or Michigan Imputation Server (PMID: 27571263). For genome-wide association study (GWAS), we recommended SAIGE (PMID: 30104761), but some studies used PLINK (PMID: 17701901). Each study then submitted their GWAS summary statistics to the consortium for meta-analysis. LD score regression v 1.0.1 [PMID: 25642630] was used for heritability and partitioned heritability analyses. Variants for Mendelian randomization instruments were selected using PLINK version 1.90b6.18 (PMID: 17701901). Exposure and outcome datasets were harmonized, and MR statistical analysis conducted using R version 4.0.3. with the R-package TwoSampleMR version 0.5.5 (PMID: 29846171) (which included Fixed-effects IVW analysis (PMID: 24114802), weighted median estimator (WME) (PMID: 27061298), weighted mode based estimator (WMBE) and MR Egger regression (PMID: 26050253)) and additionally MR-PRESSO version 1.0 (PMID: 29686387). Code availability statement: The code for summary statistics liftover, projection PCA pipeline including precomputed loadings and metaanalysis are available at https://github.com/covid19-hg/ , the code for Mendelian randomization and genetic correlation pipeline at https://github.com/marcoralab/MRcovid , and code for Probabilistic assignment of variants into susceptibility vs. severity effects is at https://github.com/mjpirinen/covid19-hgi_subtypes

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

Summary statistics generated by COVID-19 HGI are available at https://www.covid19hg.org/results/r6/ . The analyses described here utilize the freeze 6 data. COVID-19 HGI continues to regularly release new data freezes. Summary statistics for non-European ancestry samples are not currently available due to the small individual sample sizes of these groups, but results for 23 loci lead variants are reported in Supplementary Table 4. Individual level data can be requested directly from contributing studies, listed in Supplementary Table 1. We used publicly available data from GTEx (https://gtexportal.org/home/), the Neale lab (http://www.nealelab.is/uk-biobank/), Finucane lab (https://www.finucanelab.org), FinnGen Freeze 4 cohort (https://www.finngen.fi/en/access_results), and eQTL catalogue release 3 (http://www.ebi.ac.uk/eqtl/).

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	The consortium meta-analysed genome-wide association study (GWAS) summary statistics from any individual study that had included a minimum of 50 cases and 50 controls in their analysis. The cutoff was aimed at reducing noise for the meta-analysis, but also to be inclusive of studies that had not yet accumulated large numbers of COVID-19 patient data. No statistical calculation for adequate sample size was performed, but the results identifying multiple genomic regions at genome-wide significance threshold indicates adequate power for genetic discovery.
Data exclusions	Individual level phenotype and genotype data exclusions were performed by each individual study, following the consortium analysis plan recommendations (www.covid19hg.org). Possible reasons for sample exclusion included removing genetic ancestry outliers within a study (using principal components analysis), poor quality of genetic data or lack of phenotypic data for a sample. The consortium manually examined GWAS summary statistics data submitted by each study (for each submitted analysis separately), including sample size used for analysis, allele frequency check against Gnomad reference panel, and distribution of test statistics. After meta-analysis, the results were checked for heterogeneity variant effects between contributing studies in SupplementaryTable 2
Replication	No replication was performed. The consortium meta-analysed GWAS summary statistics, bringing together as many studies as possible to achieve the largest possible sample size and statistical power for association. this meant that the consortium included most large studies of COVID-19 host genetics that have been performed to date, so it was not possible to perform replication analyses in external cohorts. Therefore we performed manual checks on each study contributing summary statistics before entering them into the meta-analysis. In addition, after meta-analysis, we performed a check for heterogeneity between variant association estimates across studies contributing data. This allowed us to better understand whether the variant effects differed much between individual studies.
Randomization	No randomization was performed because there was no allocation of samples to experimental groups
Blinding	Blinding was not relevant to the study. The case status and severity of symptoms was evaluated for each sample by investigators from each study respectively. The consortium recommended using covariates to control for confounding: age + age2 + sex + age*sex + 20 principal components (obtained using genetic data) + study specific covariates (if any). The consortium meta-analysed summary statistics from these case/control studies, not individual level data. Details of which variables each study used and how the calculated PCs for their analysis are available in Supplementary Table 1.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Human research participants

Policy information about studies involving human research participants

Population characteristics	Summary statistics from 60 independent studies were included in consortium meta-analyses. Mean age of cases across studies was 53.36 years. The effective sample size for genetic ancestry populations for Sars-CoV2 reported infection was: n=6147 Middle Eastern; n=23391 South Asian; 13152 East Asian; 39571 African; 39817 Ad-mixed American; 440696 European. Population characteristics regarding age, sex and exact case and control sample numbers for each contributing study are given in Supplementary Table 1.
Recruitment	The consortium pre-defined phenotype criteria for cases and controls, but the specific recruitment was carried out independently by each contributing study. COVID-19 disease status (critical illness, hospitalization status) was assessed following the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (PMID: 32358325). The critically ill COVID-19 group included patients who were hospitalized due to symptoms associated with laboratory-confirmed SARSCoV-2 infection and who required respiratory support or whose cause of death was associated with COVID-19. The hospitalized COVID-19 group included patients who were hospitalized due to symptoms associated with laboratoryconfirmed SARS-CoV-2 infection. The reported infection cases group included individuals with laboratory-confirmed SARSCoV-2 infection or electronic health record, ICD coding or clinically confirmed COVID-19, or self-reported COVID-19 (e.g. by questionnaire), with or without symptoms of any severity. Genetic ancestry-matched controls for the three case definitions were sourced from population-based cohorts, including individuals whose exposure status to SARS-CoV-2 was either unknown or infection- negative for questionnaire/electronic health record based cohorts.
Ethics oversight	Ethical statements for each contributing study are given in Supplementary Table 1.

Note that full information on the approval of the study protocol must also be provided in the manuscript.