***eLife’s* transparent reporting form**

We encourage authors to provide detailed information *within their submission* to facilitate the interpretation and replication of experiments. Authors can upload supporting documentation to indicate the use of appropriate reporting guidelines for health-related research (see [EQUATOR Network](http://www.equator-network.org/%20)), life science research (see the [BioSharing Information Resource](https://biosharing.org/" \t "_blank)), or the [ARRIVE guidelines](http://www.plosbiology.org/article/info:doi/10.1371/journal.pbio.1000412) for reporting work involving animal research. Where applicable, authors should refer to any relevant reporting standards documents in this form.

If you have any questions, please consult our Journal Policies and/or contact us: [editorial@elifesciences.org](mailto:editorial@elifesciences.org).

**Sample-size estimation**

* You should state whether an appropriate sample size was computed when the study was being designed
* You should state the statistical method of sample size computation and any required assumptions
* If no explicit power analysis was used, you should describe how you decided what sample (replicate) size (number) to use

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

No sample size calculation was performed. Sample sizes were chosen based on previous experience.

**Replicates**

* You should report how often each experiment was performed
* You should include a definition of biological versus technical replication
* The data obtained should be provided and sufficient information should be provided to indicate the number of independent biological and/or technical replicates
* If you encountered any outliers, you should describe how these were handled
* Criteria for exclusion/inclusion of data should be clearly stated
* High-throughput sequence data should be uploaded before submission, with a private link for reviewers provided (these are available from both GEO and ArrayExpress)

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

Information on replicates and number of independently performed experiments can be found in the respective figure legends.

**Statistical reporting**

* Statistical analysis methods should be described and justified
* Raw data should be presented in figures whenever informative to do so (typically when N per group is less than 10)
* For each experiment, you should identify the statistical tests used, exact values of N, definitions of center, methods of multiple test correction, and dispersion and precision measures (e.g., mean, median, SD, SEM, confidence intervals; and, for the major substantive results, a measure of effect size (e.g., Pearson's r, Cohen's d)
* Report exact p-values wherever possible alongside the summary statistics and 95% confidence intervals. These should be reported for all key questions and not only when the p-value is less than 0.05.

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

Information on statistical significance and tests used can be found in the respective figure legends.

(For large datasets, or papers with a very large number of statistical tests, you may upload a single table file with tests, Ns, etc., with reference to sections in the manuscript.)

**Group allocation**

* Indicate how samples were allocated into experimental groups (in the case of clinical studies, please specify allocation to treatment method); if randomization was used, please also state if restricted randomization was applied
* Indicate if masking was used during group allocation, data collection and/or data analysis

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

Details on group allocation of our genetic association data can be found in the respective section of the Methods, as well as in the table of Supplementary File 1.

**Additional data files (“source data”)**

* We encourage you to upload relevant additional data files, such as numerical data that are represented as a graph in a figure, or as a summary table
* Where provided, these should be in the most useful format, and they can be uploaded as “Source data” files linked to a main figure or table
* Include model definition files including the full list of parameters used
* Include code used for data analysis (e.g., R, MatLab)
* Avoid stating that data files are “available upon request”

Please indicate the figures or tables for which source data files have been provided:

Raw, unedited TIFFs of Western blots are provided as source data for Figures 1-5 and their respective Figure Supplements.

Raw PLINK results for the association analysis of local subjects are provided in Supplementary File 5; association data for the GenOMICC replication cohort is available as described in the primary publication (Pairo-Castineira et al., 2020).

Additional data on our local COVID-19 cohort is available upon request (KCerosaletti@benaroyaresearch.org). This is being done to protect the privacy of the subjects in this study as the data were obtained from samples recovered from the hospital clinical laboratory with IRB approval but without written consent. For commercial entities, availability of these data will be assessed on a case-by-case basis in conjunction with the Benaroya Research Institute business development office.

Association testing was performed using gPLINK v2.050 (<https://zzz.bwh.harvard.edu/plink/gplink.shtmlI>) by logistic regression adjusting for sex and ancestry (race/ethnicity); see Supplementary File 5. An Excel file with the summary statistics for the association analysis in our local cohort is provided in the source data associated with Figure 6.

Distribution of allelic frequency of rs10774671 (A/G) in the human population (<http://popgen.uchicago.edu/ggv/>) (Marcus and Novembre, 2017) is provided in the figure legend of Figure 1 – Figure Supplement 1.

GenBank identifiers for OAS1 ortholog sequence alignment is provided in the figure legend of Figure 1 – Figure Supplement 2.