

# Identification of novel drug targets for the risk and prognosis of COVID-19

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**Background:** Since the epidemic continues, there is a pressing need to improve our understanding of coronavirus disease 2019 (COVID-19). Mendelian randomization (MR) studies provide us with a method to explore the causality between circulating proteins and COVID-19 susceptibility and severity. We aim to find new perspectives on the pathological mechanism of the disease and possible drug targets for treatment based on this study.

**Methods:** We conducted a phenome-wide MR study to prioritize circulating proteins causally associated with COVID-19 susceptibility, which was defined as "patients tested positive for COVID-19 vs. population controls", and severity, which was defined as "patients hospitalized with COVID-19 vs. population controls". And we repeated the analysis for different definition of COVID-19 susceptibility, severity and control groups.

**Results:** Association of three circulating proteins with COVID-19 susceptibility and severity were demonstrated via our study. C-C motif chemokine 4 (OR =1.887, 95% CI: 1.608–2.165, P=8.04×10<sup>-6</sup>) and 2'-5'-oligoadenylate synthase 1 (OR =0.511, 95% CI: 0.266–0.757, P=8.51×10<sup>-8</sup>) were found respectively positively and negatively correlated with increased COVID-19 severity. Tissue factor, contrary to previous studies, was found associated with decreased COVID-19 susceptibility (OR =0.667, 95% CI: 0.484–0.850, P=1.47×10<sup>-5</sup>) and decreased COVID-19 severity (OR =0.459, 95% CI: 0.132–0.786, P=3.01×10<sup>-6</sup>).

**Conclusions:** Genetic evidence supports C-C motif chemokine 4 as a risk factor for COVID-19 severity, and 2'-5'-oligoadenylate synthase 1 as a protective factor for COVID-19 severity. The causal association between tissue factor and COVID-19 is contrary to the previous studies, needing further analyses. Further research is warranted to assess the viability of C-C motif chemokine 4 and 2'-5'-oligoadenylate synthase 1 as well as their downstream pathways as drug targets for anti-inflammatory and anti-virus treatment in severe cases.

Keywords: Mendelian randomization (MR); coronavirus disease 2019 (COVID-19); proteomics

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#### Introduction

Known as coronavirus disease 2019 (COVID-19), the pneumonia caused by SARS-CoV-2 infection has spread to 220 countries with 153,187,889 confirmed cases including 3,209,109 deaths reported to World Health Organization (WHO) as of 4:20 pm CEST, 4 May 2021, leading to widespread social and economic disruption (1). With a wide spectrum of clinical manifestations, high heterogeneity in both susceptibility and severity of SARS-CoV2 infection was shown. Common symptoms of COVID-19 include fever or chills, cough, headache et cetera, while severe cases can have shortness of breath or difficulty breathing, persistent pain or pressure in the chest, confusion, inability to wake or stay awake and even acute respiratory distress syndrome (ARDS).

To date, a number of vaccines against SARS-CoV-2 have been licensed and used. However, it still takes time to achieve the aim of 70 percent of the world population being vaccinated, and vaccine to prevent multi-generational transmission of the virus has not yet been developed. It remains unknown how long the immunity can be formed after infection with the virus or vaccination. Thus, to develop new and better treatments against the disease is still necessary. Mendelian randomization (MR) is a strategy for assessing the causal effect of modifiable exposures on disease using human genetic variation known to influence the exposures. With the introduction of instrumental variables (IV), which are innately determined genetic variants, MR offers a way to avoid the influence of confounding factors. Within detection for circulating proteins that correlate with susceptibility and severity of SARS-CoV2 infection, we may be able to find new perspectives on the pathological mechanism of the disease, and possible drug targets for treatment. This becomes feasible since recent technological advances in high-throughput protein quantification have enabled genome-wide association studies (GWAS) of genetic determinants of blood proteins, and COVID-19 GWAS meta-analyses are being performed worldwide.

Here in this study, we used MR approach to assess the relationship between circulating proteins derived from six biomarker GWAS analyses and COVID-19 susceptibility and severity. We present the following article in accordance with the STREGA reporting checklist (available at https://atm.amegroups.com/article/ view/10.21037/atm-21-6612/rc).

# **Methods**

# Characterizing genetic instruments for proteins

Briefly, we combined six different biomarker GWAS analyses, of which genome-wide summary statistics were publicly available [Cardiovascular Risk in Young Finns Study/FINRISK (YFS/ FINRISK) (2); IMPROVE (3); INTERVAL (4); FHS (5); AGES (6); KORA F4/OMDiab (7)]. Genetic determinants of circulating biomarker levels were derived. Biomarker testing was conducted in blood samples in the six study samples consisted of Caucasians. Various high-multiplex protein assays were used to conduct biomarker testing in the six study samples. Specifically, YFS/FINRISK analvzed 41 cytokines via bead-based immunoassays. IMPROVE analyzed 83 proteins via modified antibodies conjugated to ligonucleotides. FHS analyzed 71 proteins via modified enzyme-linked immunosorbent assay sandwich method. KORA F4/QMDiab, INTERVAL and AGES analyzed 1,124 proteins, 2,994 proteins and 4,137 proteins respectively via SOMAmers. For further details, please refer to Table S1. Among all the biomarkers, uncorrelated  $(r^2 < 0.001)$  single-nucleotide polymorphisms associated with the corresponding exposure trait at genome-wide significance  $(P < 5 \times 10^{-8})$  were retained as instrumental variables. Information of all the included identified biomarkers are available in Table S1.

### Characterizing COVID-19 susceptibility and severity

The COVID-19 Host Genetics Initiative where we extracted the data from is a bottom-up collaborative aims to provide a platform for sharing resources, organizing analytical activities and sharing results of such studies to identify genetic determinants of COVID-19 susceptibility and severity. Summary statistics from the third round of GWAS meta-analysis, shared publicly on July 2, 2020, which were available via the platform, were used to test the genetic instruments aforementioned against COVID-19 outcomes.

For our two primary analyses, we selected two samples with the largest number of cases from the above platform. For susceptibility analysis, we chose COVID-19 positive patients diagnosed by RNA PCR, serologic testing, or clinician diagnosis by chart review or ICD-coding (N=6,696) *vs.* population controls (N=1,073,072). And for severity analysis, we chose Hospitalized COVID-19 positive patients

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diagnosed by RNA PCR, serologic testing, or clinician diagnosis by chart review or ICD-coding (N=3,199) vs. population controls (N=897,488). The population controls were defined as any person who was not a case, which means who were tested negative, were never tested, or had an unknown testing status.

Four remained available outcomes from the platform were used to determine whether statistically significant results from the primary analyses were consistent across different definitions for COVID-19 susceptibility, severity, and control groups. For susceptibility: (I) COVID-19 positive by RNA PCR, serologic testing, or clinician diagnosis by chart review or ICD-coding (N=3,523) vs. lab/self-reported negative (N=36,634); (II) predicted COVID-19 from self-reported symptoms (N=1,865) vs. predicted or self-reported non-COVID-19 (N=29,174). For severity: (III) critical cases of COVID-19 defined by death, intubation, continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP), continued external negative pressure (CNP), or very high flow positive end expiratory pressure oxygen in patients with COVID-19 by RNA PCR or serologic testing (N=536) vs. population control (N=329,391); (IV) hospitalized COVID-19 positive (N=928) vs. non-hospitalized COVID-19 positive (N=2,028). The information of the above COVID-19 GWAS is available in Table S2.

#### Statistics analyses

The Wald ratio method was chosen for estimating the causal association between each exposure with each outcome since most of the exposures contained only one SNP. Suppose we have an IV (we can think of IV as a single nucleotide polymorphism) with value of 1 or 0, the entire population can be divided into two genetic groups based on this. Two of the three subgroups can be combined according to a dominant or recessive model, or if there are only a few individuals in a genetic subgroup (minor homozygotes), it can also be combined. According to the hypothesis, if both exposure distributions and outcome distributions of the two genetic subgroups differs from each other, it supports that the exposure has a causal relationship with the outcome. The ratio is the coefficient of the genetic variant in the regression of the outcome divided by the coefficient of the genetic variant in the regression of the exposure (8). Other methods including inverse variance weighted (IVW), MRegger and median weighted MR were also employed.

A Bonferroni-corrected P value threshold accounting

for both the number of biomarkers and outcomes analyzed was implemented [since two outcomes were used in our primary analyses, we set  $P=1.98 \times 10^{-5}=0.05/(1,263 \times 2)$ ]. We defined significant results as those with  $P<1.98 \times 10^{-5}$  (after Bonferroni correction), and suggestive associations as those with  $1.98 \times 10^{-5} < P < 0.05$ . We then performed standard sensitivity analyses including Wald ratio method and the others to assess the validity of the MR findings. Each exposure was tested with each outcome like the above operation. All the MR testing were performed using the "MRBase for TwoSample MR" package (version 0.4.09). The detailed process is available in *Figure 1*.

# Ethical statement

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The current analyses are based on publicly available summary data and therefore do not require ethical approval. Original studies have been approved by ethic committees and written informed consent was obtained from study participants or caregivers.

### Results

#### Selection of genetic instruments for exposures

For our primary analyses, after excluding variants that  $r^2>0.001$  and those with weak P values (P>5×10<sup>-8</sup>), 1,258 proteins were tested for the correlation with COVID-19 susceptibility, and 1,263 proteins were estimated for whether to be causally associated with COVID-19 severity. Contributing studies included in these exposure GWAS meta-analyses were predominantly of Caucasians.

# Causal effect of each exposure on COVID-19 susceptibility and severity

Significant results were defined as those with  $P<1.98\times10^{-5}$  (after Bonferroni correction), whereas those with  $1.98\times10^{-5}$ <br/>P<0.05 were defined as suggestive associations. MR results were presented in *Figures 2,3*. Traits were shown in the figure if Wald ratio or MR-IVW or MR-Weighted-Median showed nominally significant (P<0.05) results. Detail information is available in Table S3.

Of all the exposures, we observed tissue factor (TF) to be causally associated with COVID-19 susceptibility, while both TF and C-C motif chemokine 4 were found to have

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Figure 1 Study design of this MR study of the plasma proteome with COVID-19 susceptibility and severity. This study includes selection of genetic instruments, outcome selection, MR analyses for COVID-19 susceptibility and severity, and sensitivity analyses. MR, mendelian randomization; COVID-19, coronavirus disease 2019.

causal relationship with COVID-19 severity. Specifically, for susceptibility, we found that TF was negatively related to diagnosis of COVID-19 (Wald ratio, OR =0.667, 95% CI: 0.484-0.850, P= $1.47\times10^{-5}$ ). For severity, we found that TF was significantly associated with lower risk of hospitalization (Wald ratio, OR =0.459, 95% CI: 0.132-0.786, P= $3.01\times10^{-6}$ ). Whereas C-C motif chemokine 4 showed association with higher risk of COVID-19 hospitalization (Wald ratio, OR =1.887, 95% CI: 1.608-2.165, P= $8.04\times10^{-6}$ ).

The evidence indicated that TF might be a protective

factor of COVID-19, while C-C motif chemokine 4 might be a risk factor. Other 38 proteins were exhibited suggestive association with COVID-19 susceptibility whereas 70 proteins were exhibited suggestive association with COVID-19 severity. The complete information is available in Table S3.

# Sensitivity analyses

To demonstrate whether different definition of COVID-19 susceptibility and severity and control groups would



**Figure 2** COVID-19 susceptibility: COVID-19 positive *vs.* population controls. This figure shows the causal effect of each exposure on COVID-19 susceptibility. Traits were shown in the figure if Wald ratio or MR-IVW or MR-Weighted-Median showed nominally significant (P<0.05) results. MR, mendelian randomization; COVID-19, coronavirus disease 2019; IVW, inverse variance weighted.

influence on the results, we then repeated the analyses using the four other outcomes obtained from the COVID-19 Host Genetics Initiative.

As aforementioned, for susceptibility, 1,264 proteins were tested with the outcome of COVID-19 positive cases diagnosed by RNA PCR, serologic testing, or clinician diagnosis by chart review or ICD-coding vs. lab/self-reported negative cases (Bonferroni correction:  $P=3.96\times10^{-5}=0.05/1,264$ , those with  $P<3.96\times10^{-5}$  were defined as significant results), and 1,216 proteins were tested with the outcome of predicted COVID-19 cases from self-reported symptoms vs. predicted or selfreported non-COVID-19 cases (Bonferroni correction:  $P=4.11\times10^{-5}=0.05/1,216$ , those with  $P<4.11\times10^{-5}$ were defined as significant results). For severity, 1,279 proteins were tested with the outcome of critical cases of COVID-19 vs. population control (Bonferroni correction:  $P=3.91\times10^{-5}=0.05/1,279$ , those with  $P<3.91\times10^{-5}$  were defined as significant results), and 1,261 proteins were tested with the outcome of hospitalized COVID-19 positive cases vs. non-hospitalized COVID-19 positive cases (Bonferroni

correction:  $P=3.97 \times 10^{-5}=0.05/1,261$ , those with  $P<3.97 \times 10^{-5}$  were defined as significant results). MR results of sensitivity analyses are presented in https://cdn.amegroups.cn/static/public/atm-21-6612-1.docx.

Of all the exposures, only 2'-5'-oligoadenylate synthase 1 was found to be negatively associated with increased risk of confirmed COVID-19 with critical respiratory illness (IVW, OR =0.511, 95% CI: 0.266–0.757, P= $8.51 \times 10^{-8}$ ). Other 107 proteins were exhibited suggestive association with COVID-19 susceptibility whereas 124 proteins were exhibited suggestive association with COVID-19 severity. The complete information is available in https://cdn. amegroups.cn/static/public/atm-21-6612-1.docx.

# Summary findings

In summary, association of three circulating proteins with COVID-19 susceptibility and severity were demonstrated via our study. The most consistent finding was tentative evidence which revealed C-C motif chemokine 4 as a risk factor for COVID-19 severity, and 2'-5'-oligoadenylate



**Figure 3** COVID-19 severity: hospitalization *vs.* population controls. This figure shows the causal effect of each exposure on COVID-19 severity. Traits were shown in the figure if Wald ratio or MR-IVW or MR-Weighted-Median showed nominally significant (P<0.05) results. MR, mendelian randomization; COVID-19, coronavirus disease 2019; IVW, inverse variance weighted.

synthase 1 as a protective factor for COVID-19 severity. TF was found to be a possible protective factor for both COVID-19 susceptibility and severity, which was contrary to the previous studies, needing further analyses. A brief summary of the findings is present in *Figure 4*.

### Discussion

In this study, MR was applied to estimate the causal association between blood proteome and COVID-19 susceptibility and severity. In our primary analyses, 1,258 circulating proteins were tested for the correlation with COVID-19 susceptibility, and 1,263 proteins were tested for the correlation with COVID-19 severity. TF was identified as a possible protective factor for both COVID-19 susceptibility and severity, whereas C-C motif chemokine 4 was identified as a risk factor for COVID-19 severity. MR was further applied to perform sensitivity analyses, and 2'-5'-oligoadenylate synthase 1 was found to be negatively correlated with COVID-19 severity. The different proteins we found causally correlated with COVID-19 susceptibility and severity in our primary analyses and sensitivity analyses indicate that different definition of COVID-19 susceptibility and severity might have influence on the



Figure 4 Brief summary of the results of this study. This figure briefly shows the main results of the study.

result of the analyses.

The evidences revealed the causal relationship between C-C motif chemokine 4 and 2'-5'-oligoadenylate synthase 1 and COVID-19 severity are the most important findings of this study. As no previous study has shown that C-C motif chemokine 4 is correlated to COVID-19 severity, our study first indicates that increase of blood C-C motif chemokine 4 leads to a higher risk of COVID-19 hospitalization, and the possible mechanism might be related to the role it plays in the overexpression of inflammatory factors and inflammatory injury in the lungs. C-C motif chemokine 4 expresses in granulocyte and 180 other tissues. The function of the chemotactic cytokine family it belongs to is to induce direct chemotaxis in nearby responsive cells, recruiting cells of the immune system to a site of infection during immune response (9). The chemokine signal is transduced by G-protein coupled receptors expressed on the immune cells. Receptor activation leads to the dissociation of the  $\alpha$  and  $\beta$ - $\gamma$ -subunits of G protein, activating diverse downstream pathways such as Jak-STAT signaling pathway, MAPK signaling pathway PLC/PKC signaling pathway and etcetera, resulting in cellular growth and differentiation, cellular polarization, apoptosis and degranulation, NO induction and ROS production, and actin reorganization (refer to chemokine signaling pathway map in KEGG: Kyoto Encyclopedia of Genes and Genomes). We suppose that C-C motif chemokine 4 participates in the aggravation of patients' condition with COVID-19 through these pathways, since COVID-19 is characterized by an overexuberant inflammatory response, and excessive level of oxidative stress has been found in critically ill patients with COVID-19 (10). In fact, anti-inflammatory treatments have been applied in clinical trials. Previous study has found that Baricitinib, as a selective JAK inhibitor, has both antiviral and anti-inflammatory properties via a particularly high affinity for AAK1 and a vital regulator of clathrin-mediated endocytosis, while other JAK inhibitors do not have the predicted inhibition of clathrin-mediated endocytosis at a dose that patient can tolerate (11). Our study confirms the causal association between the C-C motif chemokine 4 and the severity of the disease, which indicates other possible therapeutic targets among the downstream pathways aforementioned besides Jak-STAT signaling pathway.

The critical function of oligoadenylate synthetases (OAS)/RNase L system in antiviral defense is well known, and our study demonstrates that it also plays its part during the process of COVID-19. 2'-5'-oligoadenylate synthase 1 is an interferon-induced, dsRNA-activated antiviral enzyme playing an important role in cellular innate antiviral response (12,13). The previous study has shown that 2'-5'-oligoadenylate synthase 1 has the function of anti-respiratory-syncytial-virus infection via interferon-

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gamma inhibition (14), and displays antiviral effect against vesicular stomatitis virus (VSV), herpes simplex virus type 2 (HSV2), and encephalomyocarditis virus (EMCV) via the classical RNase L-dependent pathway or an alternative antiviral pathway independent of RNase L. Our study indicates that high level of 2'-5'-oligoadenylate synthase 1 leads to a decreased risk of COVID-19 positive with critical respiratory illness. Refer to the previous study, we can speculate that the possible mechanism of how 2'-5'-oligoadenylate synthase works in the anti-SARS-CoV-2 response is that activated OAS catalyzes the oligomerization of ATP into 2',5'-linked oligoadenylate (2-5A) which can bind to and activate the latent RNase L (15). Activated RNase L then restricts viral propagation through both direct and indirect mechanisms including viral genome degradation, viral mRNA degradation, cellular mRNA and rRNA degradation and amplification of IFN signaling (15). Thus, this finding indicates potential implication of OAS1 activity as therapeutic target in critically ill COVID-19 patients.

The previous study on the inhibition of OAS/RNase L system by other viruses, on the other hand, remind us the possibility and potential mechanism how SARS-CoV-2 may counteract the antiviral activity of OAS/RNase L. Several methods are known used by other viruses at either upstream or downstream of the pathway, including dsRNA sequestration by a certain viral protein, expression of viral mRNA decapping enzymes, 2-5A degradation by a viral phosphodiesterase, production of inactive or inhibitory 2-5A, increased RLI/ABCE expression, inhibition of RNase L activation through direct binding to the enzyme, competitive inhibition of ribonuclease activity, and escape from RNase L cleavage through genome adaptation (14). Those possible escape mechanisms should be taken into account during future development of anti-SARS-CoV-2 treatments.

The other tentative finding of our study is that TF might be a protective factor of both COVID-19 susceptibility and severity, which is contrary to previous studies. TF is a transmembrane glycoprotein found express high level in bronchial mucosa and alveolar epithelial cells in the lungs. Following inflammatory injury in the lung, combined with FVII(a), TF is known to be correlated with the expression of several immunoregulatory genes in the lung and fibrin formation, coupled with increased cytokine production and cell migration and activation, leading to acute lung injury, for example, acute respiratory distress syndrome (ARDS) (16).

In contrary to our study, evidences in previous studies support that TF is positively related to the severity of COVID-19. Previous studies detected increased level of TF activity in COVID-19, which was correlated with the inflammatory injury and fibrin formation in the lungs of the COVID-19 patients, associated with COVID-19 severity and mortality (17,18). The previous cohort study demonstrated increased platelet activation and plateletmonocyte aggregate formation in severe COVID-19 patients, inducing TF expression in monocytes. Increased platelet activation and monocyte TF expression were associated with higher fibrinogen and D-dimers level in severe cases and could be inhibited by platelet P-selectin neutralization or integrin  $\alpha$ IIb/ $\beta$ 3 blocking with the aggregation inhibitor abciximab (10). Another study demonstrated higher TF expression in neutrophils in severe cases, which could be disrupted by complement C3 inhibition with compstatin Cp40, and showed that thrombotic activity of HAECs was induced by TF-bearing NETs (9).

Our study, however, shows a total different result, demonstrates the causal association between blood TF level and the decrease of COVID-19 susceptibility and severity, indicating that TF might be a protective factor of COVID-19. The possible explanation is that we might have not ruled out a clear effect of TF on COVID-19 owing to the low variance explained by only 1 genetic instrument. Whether TF has such causal association with COVID-19 susceptibility and severity need more genetic instruments to carry out further analyses.

Our study findings have several implications. First, anti-inflammatory treatment is supported since the proinflammatory protein (C-C motif chemokine 4) is found causally associated with the severity of COVID-19. Second, additional drug targets may be uncovered as biomarker testing becomes more comprehensive. Since OAS1 is found to be a protective factor of COVID-19 severity, it can be used as a target for further development of anti-virus drugs.

The interpretation and generalizability of study findings are limited by several factors. First, most study participants were Europeans due to limitations in data availability. Thus, further study based on non-European biomarker GWAS is necessary. Second, in our primary analyses, those who were broadly defined as not being a case were chosen to be controls. However, the control group could have been contaminated with people who had contracted COVID-19, particularly those with only mild or no viral symptoms without universal testing, which may influence the estimates

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in some degree. Third, the low variance explained by only 1 genetic instrument might make it hard for us to rule out a clear association between some of the blood proteins and COVID-19 susceptibility and severity. Forth, MR itself has certain limitations. The IVs are hypothesized to satisfy 3 assumptions: the IV is associated with the exposure; the IV is not associated with confounders; and the IV influences the outcome only through the exposure (19). However, due to the existence of complex biological effects, pleiotropy of the variants is usually inevitable. By using multivariable mendelian randomization (MVMR), the causal effects of each of the confounding factors can be estimated (20). However, we don't have access to clinical data needed, so we are unable to discuss their influence on the study results.

#### Conclusions

Systematic MR analysis of the circulating proteome revealed C-C motif chemokine 4 as a risk factor for COVID-19 severity, and 2'-5'-oligoadenylate synthase 1 as a protective factor for COVID-19 severity. The causal association between TF and COVID-19 is contrary to the previous studies, which need further analyses. Further research is warranted to assess the viability of C-C motif chemokine 4 and 2'-5'-oligoadenylate synthase 1 as well as their downstream pathways as drug targets for anti-inflammatory and anti-virus treatment in severe cases.

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#### Footnote

*Reporting Checklist:* The authors have completed the STREGA reporting checklist. Available at https://atm.

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*Conflicts of Interest*: All authors have completed the ICMJE uniform disclosure form (available at https://atm. amegroups.com/article/view/10.21037/atm-21-6612/coif). JTY serves as an unpaid Associate Editor-in-Chief of *Annals of Translational Medicine* from June 2019 to May 2024. The other authors have no conflicts of interest to declare.

*Ethical Statement*: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The current analyses are based on publicly available summary data and therefore do not require ethical approval. Original studies have been approved by ethic committees and written informed consent was obtained from study participants or caregivers.

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# Supplementary

GWAS	Sample size	Number of proteins	Measurement methods
YFS/FINRISK	8,293 Caucasians	41 cytokines	Bead-based immunoassays
IMPROVE	3,394 Caucasians	83 cardiovascular disease-related proteins	Modified antibodies conjugated to oligonucleotides
KORA F4/QMDiab	1,000 Caucasians	1,124 proteins	Slow off-rate modified aptamers (SOMAmers)
INTERVAL	3,301 Caucasians	2,994 proteins	SOMAmers
FHS	6,861 Caucasians	71 cardiovascular disease-related proteins	Modified enzyme-linked immunosorbent assay sandwich method
AGES	5,457 Caucasians	4,137 proteins	SOMAmers

# Table S1 Demographic characteristics of included Proteome GWASs used in the present MR analysis

Table S2 Demographic characteristics of included COVID-19 GWAS used in the present MR analysis (round 3)

GWAS	Sample information	
Susceptibility		
C1	COVID (N=3,523) vs. lab/self-reported negative (N=36,634)	
C2	COVID (N=6,696) vs. population (N=1,073,072)	
D1	Predicted COVID from self-reported symptoms (N=1,865) vs. predicted or self-reported non-COVID (N=29,174)	
Severity		
A2	Very severe respiratory confirmed COVID (N=536) vs. population (N=329,391)	
B1	Hospitalized COVID (N=928) vs. not hospitalized COVID (N=2,028)	
B2	Hospitalized COVID (N=3,199) vs. population (N=897,488)	

Table S3 Genetic correlation betwee	n proteome and COVID-19 susceptibility and severity
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	Stanogenhatiy (2)     Trans frame     Web at the     1     0.007     0.044     0.045       A distringting protein     Web at the     1     0.957     0.514     1.007       A distringting protein     Web at the     1     0.767     0.842     0.822     0.821       A bin-Metrio protein     Web at the     1     0.767     0.822     0.831       Carlinge actor protein     Web at the     1     0.842     0.831     0.841       Carlinge actor protein     Web at the     1     0.842     0.842     0.842       Carlinge actor protein     Web at the     1     0.847     0.845     0.845       Carlinge actor back     Protein Actor back     1     0.847     0.845	P value       1.47E-03       0.049       0.012       0.004       0.007       0.001       0.048       0.02       0.015       0.011       0.015       0.011       0.015       0.011       0.015       0.011       0.015       0.011       0.012       0.037       0.034       0.041       0.022       0.031       0.041       0.022       0.033       0.021       0.033       0.011       0.023       0.030       0.031       0.032       0.033       0.031       0.032       0.033       0.031       0.032       0.033       0.034
	Hunchsgundin multi     94011-130     1     0.707     0.107     0.107     0.107     0.107     0.107     0.002     0.002       Apha-synublen     Webi rate     1     0.707     0.002     0.001       Cartegain A     Webi rate     1     0.002     0.001     0.0	0.012 0.004 0.007 0.001 0.048 0.02 0.006 0.017 0.015 0.014 0.015 0.014 0.002 0.048 0.002 0.041 0.022 0.041 0.022 0.037 0.034 0.041 0.022 0.031 0.021 0.012 0.013 0.021 0.012
	alpha FargenonNild rate10.7870.0290.039Alpha sequenciesWald rate10.7750.020.031Cartiga calcip portenWald rate10.1630.031Cartiga calcip portenWald rate10.4370.031Cartiga calcip portenWald rate10.4350.631Correlationer CalcipacitiWald rate10.4350.631Correlationer CalcipacitiWald rate10.4350.631Correlationer CalcipacitiWald rate10.4350.631Correlationer CalcipacitiWald rate10.4350.631Correlationer CalcipacitiWald rate10.4350.631CalcipicaMalter rate0.4310.4310.4310.431CalcipicaMalter rate0.4310.4310.4310.431CalcipicaMalter rate0.4310.4310.4310.431CalcipicaMalter rateMalter rate0.4310.4310.431CalcipicaMalter rateMalter rate0.4310.4310.431CalcipicaMalter rateMalter rate0.4310.4310.431CalcipicaMalter rateMalter rate0.4310.4310.431CalcipicaMalter rateMalter rate0.4310.4310.431CalcipicaMalter rateMalter rate0.4310.4310.431CalcipicaMalter rateMalter rate0.4310.431	0.004 0.007 0.001 0.048 0.02 0.006 0.017 0.015 0.011 0.015 0.014 0.002 0.041 0.022 0.041 0.042 0.041 0.042 0.037 0.034 0.041 0.022 0.013 0.021 0.012 0.012 0.013 0.011
	Alpha-synchelinWat ratio10.7890.8290.831Carlings and cyminWat ratio10.7810.420.001Carlings and cyminWat ratio10.8610.001Carlings and cyminWat ratio10.8510.983Carlings and cyminWat ratio10.8510.983Carlings and cyminWat ratio10.8510.983Carlysinemi factor H-related pratiniWat ratio10.8610.993Carlysinemi factor H-related pratiniWat ratio10.8910.993Carlysinemi factor H-related pratiniWat ratio10.8910.993Carlysinemi factor H-related pratiniWat ratio10.8910.993Carlysinemi factor H-related pratiniWat ratio10.8910.993Carlysine infinition factor HWat ratio10.8910.993Carlysine infinition factor HWat ratio10.8910.993Galessin-4Wat ratio10.8910.9930.993Inter-caline-7Wat ratio10.8910.9930.993Inter-caline-7Wat ratio10.8930.9930.993Inter-caline-7Wat ratio10.8930.9930.993Inter-caline-7Wat ratio10.8930.9930.993Inter-caline-7Wat ratio10.8930.9930.993Inter-caline-7Wat ratio10.8930.993I	0.007 0.01 0.048 0.02 0.006 0.017 0.015 0.011 0.015 0.014 0.002 0.048 0.002 0.041 0.022 0.041 0.042 0.037 0.034 0.041 0.022 0.031 0.021 0.012 0.013 0.021 0.012 0.013 0.021
	Cartinge actilic protein 1Wald ratio11.0851.0971.078C.C. motil Chernolit 25Wald ratio10.0510.0780.078C.C. motil Chernolit 25Wald ratio10.0510.0780.078Complement C. That publicorporationWald ratio10.1601.0280.078Complement C. C. Addit function 2Wald ratio11.0201.0281.028Complement C. C. Addit is companieWald ratio10.0610.0781.028Elevoid L. Growth Lator 10Wald ratio10.0610.0781.028Colig methanes porteinWald ratio10.0610.0781.028Generin 4Wald ratio10.0610.0781.028Growth Lator 10Wald ratio10.0610.0280.028Growth Lator 11Wald ratio10.0580.0280.028Intercubar-27 suburt algoraNW20.0550.0280.028Intercubar-27 suburt algoraNW20.0570.0280.028Intercubar-27 suburt algoraNW20.0570.0280.028Intercubar-28Wald ratio10.0780.0280.028Intercubar-28Wald ratio10.0370.0280.028Intercubar-28Wald ratio10.0370.0280.028Intercubar-28Wald ratio10.0280.0280.028Intercubar-28Wald ratio10.028<	0.048 0.02 0.006 0.017 0.015 0.011 0.015 0.014 0.002 0.048 0.002 0.041 0.041 0.022 0.037 0.034 0.041 0.022 0.031 0.021 0.012 0.003 0.011 0.012 0.003 0.011
	Cathegoin H     Waid ratio     1     1.043     1.076       C. Confer domonion 20     Waid ratio     1     0.453     0.683     0.983       Complement factor H-related priori     Waid ratio     1     0.503     0.493     0.493       Complement factor H-related priori     Waid ratio     1     1.030     1.011     1.030       Complement factor H-related priori     Waid ratio     1     1.030     1.011     1.030       Complement factor H-related priori     Waid ratio     1     1.030     1.011     1.030       Giad control     Waid ratio     1     1.030     1.011     1.030       Giad control     Waid ratio     1     1.021     1.021     1.021       Giad control     Waid ratio     1     1.023     1.021     1.021       Interrackin-27     INW     2     0.055     0.736     1.021       Interrackin-27     INW     2     0.055     0.736     1.021       Interrackin-27     INW     2     0.050     0.735     0.736     0.73	0.02 0.006 0.017 0.015 0.011 0.015 0.014 0.002 0.048 0.002 0.041 0.042 0.037 0.034 0.041 0.022 0.031 0.021 0.012 0.013 0.021 0.012 0.003 0.011
	CD1B8 andigen     Wald ratio     1     DBS     0.983     0.983       Compenent factor H-stated protein     Wald ratio     1     1.083     0.983     0.983       Compenent factor H-stated protein     Wald ratio     1     1.081     1.013     1.013     1.013       Compenent factor H-stated protein     Wald ratio     1     1.013     1.012     1.026       Ency-CoA split introduces 2     Wald ratio     1     1.013     1.026     1.024       Galecin-A     Wald ratio     1     1.014     1.026     1.024       Galecin-A     Wald ratio     1     1.028     1.026     1.024       Interfeable-tryppic inhibitor heavy chain     I/W     2     1.026     1.024     1.028       Interfeable-tryppic inhibitor heavy chain     I/W     2     1.026     1.024     1.024       Interfeable-tryppic inhibitor heavy chain     I/W     2     1.026     1.024     1.024       Interfeable-T/F abbotympic head     Wald ratio     1     0.026     0.026     0.026       Kuncr (Set)	0.017 0.015 0.011 0.015 0.014 0.002 0.048 0.002 0.041 0.042 0.037 0.034 0.041 0.022 0.013 0.021 0.012 0.013 0.021 0.012 0.003 0.011
	Complement suburitUbid ratio10.8370.8800.890Complement Couplement Couplement Couplement CouplementVaid ratio11.0301.011.081Couplement Couplement CouplementVaid ratio11.0301.011.0211.010Couplement CouplementVaid ratio11.0211.0101.0211.0101.0211.0101.0211.	0.015 0.011 0.015 0.014 0.002 0.048 0.002 0.041 0.042 0.037 0.034 0.041 0.022 0.031 0.021 0.012 0.003 0.011 0.019 0.023 0.030 0.030 0.031
	Complement factor H-related protein     Wald ratio     1     1.039     1.041     1.268       CXADDF-ike membrane protein     Wald ratio     1     1.251     1.111     1.39       Enropi Cas details commans     Wald ratio     1     1.251     1.111     1.39       Galactin-4     Wald ratio     1     1.251     1.111     1.39       Galactin-4     Wald ratio     1     1.561     1.088     1.254       Granulins     MW     6     0.921     0.885     0.708     1.254       Inter-subne-trypsin inhibitor heavy chain     NW     2     0.826     0.708     1.001       Inter-subin-27     Wald ratio     1     0.659     0.728     0.893       Inter-subin-27     Wald ratio     1     0.755     0.798     0.893       Inter-subin-27     Wald ratio     1     0.639     0.728     0.893       Inter-subin-27     Wald ratio     1     0.53     0.783     0.781       Inter-subin-27     Wald ratio     1     0.53     0.791 <td< td=""><td>0.015 0.014 0.002 0.048 0.002 0.041 0.042 0.037 0.034 0.041 0.022 0.013 0.021 0.012 0.012 0.003 0.011 0.019 0.023 0.030 0.030</td></td<>	0.015 0.014 0.002 0.048 0.002 0.041 0.042 0.037 0.034 0.041 0.022 0.013 0.021 0.012 0.012 0.003 0.011 0.019 0.023 0.030 0.030
	Encyl-CoA diella isomeratea 2     Waid ratio     1     1.000     1.091     1.500       Fibrobilat growth factor 10     Wald ratio     1     0.21     1.111     1.300       Galeciir-4     Wald ratio     1     0.161     0.722     0.090       Inter-sight-stypish inhibit or heavy chain     IVW     2     0.755     0.708     1.000       Inter-sight-stypish inhibit or heavy chain     IVW     2     0.855     0.708     0.708       Inter-sight-stypish inhibit or heavy chain     IVW     2     1.026     1.020     1.028       Inter-sight-stypish inhibit or heavy chain     IVW     2     1.026     0.708     0.898       Inter-sight-stypish inhibitor     Wald ratio     1     0.755     0.499     0.898       Kunitz-type potease inhibitor     Wald ratio     1     0.873     0.780     0.898       Muthey innu-ceglocaling growth factor     Wald ratio     1     0.873     0.780     0.898       Muthey innu-ceglocaling growth factor     Wald ratio     1     0.863     0.772     0.898       Mut	0.014 0.002 0.048 0.002 0.041 0.042 0.037 0.034 0.041 0.022 0.013 0.021 0.012 0.003 0.011 0.019 0.023 0.030 0.030
	Fbroblast growth factor 19     Wald ratio     1     1.251     1.111     1.39       Gelogi membrane protein     Wild ratio     1     1.061     1.062     1.023       Granuline     WW     8     0.929     0.854     0.898     1.002       Inter-alpha -trypini (mibbor heavy chain     IW     2     0.855     0.708     1.002       Inter-alpha -trypini (mibbor heavy chain     IW     2     1.028     1.002     1.053       Interleadin-27     WW     2     1.028     1.002     1.053       Interleadin-27     Weld ratio     1     0.006     0.228     0.984       Land like 1     Wald ratio     1     0.105     0.490     1.001       Land like 1     Wald ratio     1     0.105     0.490     1.001       Motopherinatio prophophata     Wald ratio     1     1.165     1.006     1.284       Matter Simotal prophophata     Wald ratio     1     0.837     0.760     0.996       Matter Simotal prophophata     Wald ratio     1     0.837	0.002 0.048 0.002 0.041 0.042 0.037 0.034 0.041 0.022 0.013 0.021 0.012 0.003 0.011 0.019 0.023 0.030 0.030
	Golgi membrane probin 1     Wald ratio     1     1.01     1.080     1.254       Granuline     NW     2     0.034     0.684     0.009       Inter-siphe trypsin inhibitor heavy chain     NW     2     0.035     0.709     1.002       Inter-siphe trypsin inhibitor heavy chain     NW     2     0.055     0.709     1.002       Inter-siphe trypsin inhibitor heavy chain     NW     2     0.056     0.029     0.981       Inter-siphe trypsin inhibitor heavy chain     Wald ratio     1     0.995     0.728     0.998       Kunitz-type protease inhibitor 1     Wald ratio     1     0.895     0.728     0.998       Mitopic norski polyshosythate     Wald ratio     1     1.055     0.696     0.998       NADP/H dedydrogramas (guinon)1     Wald ratio     1     0.873     0.790     0.998       NADP/H dedydrogramas (guinon)1     Wald ratio     1     0.837     0.790     0.998       NADP/H dedydrogramas (guinon)1     Wald ratio     1     0.837     0.791     0.868       NADP/H dedydrogramas (guin	0.002 0.041 0.042 0.037 0.034 0.041 0.022 0.013 0.021 0.012 0.003 0.011 0.019 0.023 0.030 0.030
	Granulins     IVW     6     0.942     0.844     0.909       Inter-exphratrypini inbibar heavy chain     IVW     2     0.853     0.708     1.002       Inter-exphratrypini inbibar heavy chain     IVW     2     0.853     0.708     1.002       Interleadin-27     IVW     2     0.853     0.708     0.864       Interleadin-7     Weld ratio     1     0.708     0.893     0.781       Interleadin-7     Weld ratio     1     0.705     0.893     0.781       Interleadin-7     Weld ratio     1     0.705     0.895     0.783     0.781 <td>0.041 0.042 0.037 0.034 0.041 0.022 0.013 0.021 0.012 0.003 0.011 0.019 0.023 0.030 0.030</td>	0.041 0.042 0.037 0.034 0.041 0.022 0.013 0.021 0.012 0.003 0.011 0.019 0.023 0.030 0.030
Nor-No	H1     Mathematical structure     Inter-adjuba-trypain inhibitor beavy chain     IVW     2     0.855     0.708     1.002       H6     Interleukin-27     IVW     2     1.025     1.056     1.004     1.008       Interleukin-27     Wald ratio     1     0.859     0.728     0.989       Kunitz-type protease inhibitor     Wald ratio     1     0.905     0.629     0.989       Kunitz-type protease inhibitor     Wald ratio     1     0.716     0.009     0.001       Low affinity immunoglobulin gamma Fo     Wald ratio     1     0.726     0.098     0.839     0.833     0.985       Mitochondrikal ubiquitin ligase activator     Wald ratio     1     0.766     0.986     0.786     0.788     0.893     0.878     0.898     0.878     0.980     0.893     0.878     0.798     0.980     1.012     1.068     1.020     1.030       NAD-dependent protein deacetylate     WW     3     0.837     0.729     0.945       NAD-dependent protein deacetylate     WW     1     0.887     <	0.037 0.034 0.041 0.022 0.013 0.021 0.012 0.003 0.011 0.019 0.023 0.030 0.001
	Inter-alpha-trypain intributor heavy chain     IVW     2     0.855     0.708     1.002       Interieukin-27     IVW     2     1.068     1.024     1.053       Interieukin-27     Wald ratio     1     0.659     0.728     0.989       Kurlt2-type totase hibitor 1     Wald ratio     1     0.705     0.499     1.001       Law diffuity immunoglobulin gamma Forgon receptor II-8     Wald ratio     1     0.716     0.499     0.853     0.895       Michorbondrial Libiquith ligase activator     Wald ratio     1     0.757     0.060     1.284     0.866     0.878     0.998       NAAD(PH debydrogenase [quinone]     Wald ratio     1     0.873     0.760     0.986       NAAD,PH debydrogenase [quinone]     Wald ratio     1     0.887     0.729     0.945       NAAD,PH debydrogenase [quinone]     Wald ratio     1     0.887     0.729     0.945       NAAD,PH debydrogenase [quinone]     Wald ratio     1     0.887     0.729     0.945       NABD,PH debydrogenase [quinone]     Wald ratio     1     0.	0.034 0.041 0.022 0.013 0.021 0.012 0.003 0.011 0.019 0.023 0.030 0.030
	Interleukin-27     IVW     2     1.028     1.002     1.033       Interleukin-27 suburi ajha     IVW     2     1.036     1.044     1.046       Kunit: type protease inhibtor 1     Wald ratio     1     0.689     0.689       Kunit: type protease inhibtor 1     Wald ratio     1     0.765     0.409       Law Clike 1     Wald ratio     1     0.755     0.683     0.883       Law Clike 1     Wald ratio     1     0.716     0.853     0.986       Mitchorndrial ubiquith ligaes activator     Wald ratio     1     0.873     0.760     0.986       NADI(P)H dehydrogenase (quinone) 1     Wald ratio     1     0.876     0.777     0.986       NADI(P)H dehydrogenase (quinone) 1     Wald ratio     1     1.188     1.038     1.338       N-terminal pro-BNP     Wald ratio     1     0.876     0.777     1.056       N-terminal pro-BNP     Wald ratio     1     0.889     0.822     0.833     1.131       Rot GPAse-activating protein     Wald ratio     1     0.890	0.041 0.022 0.013 0.021 0.012 0.003 0.011 0.019 0.023 0.030 0.030
	Interleduin-7     Wald ratio     1     0.899     0.728     0.989       Kunitz-type prolease inhibitor 1     Wald ratio     1     0.056     0.829     0.084       Law affinity immunoglobulin gamma Fo region receptor III-B     Wald ratio     1     0.716     0.409     1.001       Mitochondrial ubliquitin ligase activator     Wald ratio     1     1.165     1.066     1.264       Mutbple inositol polyphosphate     Wald ratio     1     0.476     0.769     0.989       NAD-OPH dehydrogenase (quinone)     Wald ratio     1     0.873     0.760     0.986       NAD-dependent protein deacetylase     IVW     3     0.338     0.878     0.999       Nut-minal pro-ENP     Wald ratio     1     1.168     1.022     1.308       Nut-minal pro-ENP     Wald ratio     1     1.082     1.012     1.168       Nut-minal pro-ENP     Wald ratio     1     1.082     1.033     1.111       Nut-minal pro-ENP     Wald ratio     1     1.084     1.082     1.033     1.131     1.065	0.022 0.013 0.021 0.012 0.003 0.011 0.019 0.023 0.030 0.030
	Kunitz-byse protease inhibitor 1     Wald ratio     1     0.906     0.829     0.984       Lan C like 1     Wald ratio     1     0.705     0.409     1.001       Low affinity immunoglobulin gamma Fc     Wald ratio     1     0.716     0.785     0.985       Matochondrial ubiquini ligase activator of NRKB 1     Wald ratio     1     1.165     1.066     1.284       Multiple incositol polythosphate phosphatase 1     Wald ratio     1     0.473     0.760     0.986       NAD(P)H detrydrogenase (quinone) 1     Wald ratio     1     0.437     0.729     0.945       NADP/H detrydrogenase (quinone) 1     Wald ratio     1     0.633     0.338     0.378     0.939       Namminal pro-BNP     Wald ratio     1     0.485     0.747     1.005       N-4emminal pro-BNP     Wald ratio     1     0.863     0.121     1.138       Protein FAMSD     Wald ratio     1     1.284     1.144     1.382       Protein FAMSD     Wald ratio     1     0.469     0.321     0.766       Semaphorin-36 </td <td>0.013 0.021 0.012 0.003 0.011 0.019 0.023 0.030 0.001</td>	0.013 0.021 0.012 0.003 0.011 0.019 0.023 0.030 0.001
Image: sectorNotionNo. <th< td=""><td>Low affinity immunoglobulin gamma Fo     Wald ratio     1     0.919     0.853     0.995       Mitochondral ubiquitin igase activator     Wald ratio     1     1.165     1.066     1.284       Mutple inositol polyphosphate     Wald ratio     1     0.175     0.760     0.998       NADC/PI4 delydrogenase (quinone)     Wald ratio     1     0.873     0.769     0.998       NAD-dependent protein deacetylase     IVW     3     0.936     0.878     0.993       anturi-2     Nurwxin-3-bata     Wald ratio     1     1.168     1.028     1.308       N-terminal pro-BNP     Wald ratio     1     1.243     1.012     1.882       Protein FAM163A     Wald ratio     1     1.248     1.012     1.188       Protein FAM163A     Wald ratio     1     1.882     1.468     1.012     1.168     1.028     1.446       Semaphorin-3G     Wald ratio     1     1.264     1.082     1.446       Semaphorin-3G     Wald ratio     1     1.698     1.012     1.779</td><td>0.012 0.003 0.011 0.019 0.023 0.030 0.001</td></th<>	Low affinity immunoglobulin gamma Fo     Wald ratio     1     0.919     0.853     0.995       Mitochondral ubiquitin igase activator     Wald ratio     1     1.165     1.066     1.284       Mutple inositol polyphosphate     Wald ratio     1     0.175     0.760     0.998       NADC/PI4 delydrogenase (quinone)     Wald ratio     1     0.873     0.769     0.998       NAD-dependent protein deacetylase     IVW     3     0.936     0.878     0.993       anturi-2     Nurwxin-3-bata     Wald ratio     1     1.168     1.028     1.308       N-terminal pro-BNP     Wald ratio     1     1.243     1.012     1.882       Protein FAM163A     Wald ratio     1     1.248     1.012     1.188       Protein FAM163A     Wald ratio     1     1.882     1.468     1.012     1.168     1.028     1.446       Semaphorin-3G     Wald ratio     1     1.264     1.082     1.446       Semaphorin-3G     Wald ratio     1     1.698     1.012     1.779	0.012 0.003 0.011 0.019 0.023 0.030 0.001
NetworksNote of the sectorNote of the se	region receptor III-B     Mitochonorial ubiquini ligase activator     Wald ratio     1     1.165     1.066     1.284       Multiple inositol polyphosphate     Wald ratio     1     0.175     1.064     1.380       NAD(PH dehydrogenase [quinone]     Wald ratio     1     0.873     0.760     0.986       NAD-dependent protein deacetylase aitruin-2     Wald ratio     1     0.873     0.729     0.945       Neuresin-3-beta     Wald ratio     1     0.837     0.729     0.945       N-terminal pro-ENP     Wald ratio     1     1.085     1.012     1.168       OX-2 membrane glycoprotein     Wald ratio     1     1.028     1.012     1.168       OX-2 membrane glycoprotein     Wald ratio     1     1.026     1.012     1.168       Protein FAMI63A     Wald ratio     1     1.028     1.018     1.028     1.033     1.131       Brotein FAMI63A     Wald ratio     1     1.024     1.082     1.685       C-C motif chemokine 4     Wald ratio     1     1.084     1.080     1.212	0.003 0.011 0.019 0.023 0.030 0.001
ortholdNormal of some of som	everity (B2)     Aluftiple inositol polyphrosphate phosphatase 1     Wald ratio     1     1.212     1.064     1.360       NAD-(P)H dehydrogenase [quinone] 1     Wald ratio     1     0.873     0.760     0.986       NAD-dependent protein deacetylase sitruin-2     V/W     3     0.367     0.729     0.945       N-terminal pro-BNP     Wald ratio     1     1.083     1.028     1.308       N-terminal prohomore of brain nattruretic peptide     V/W     2     0.876     0.747     1.005       OX-2 membrane glycoprotein     Wald ratio     1     1.248     1.114     1.382       Protein FAM3D     Wald ratio     1     1.085     1.012     1.138       Rho GTPase-activating protein     Wald ratio     1     1.882     1.486       Semaphorin-3G     Wald ratio     1     1.892     2.466       Stormitybraydrofolate cyclo-ligase     WW     2     1.113     1.018     1.209       Aspartylasparaginyl beta-hydroxylase     Wald ratio     1     1.026     1.121     1.79       Biotinidase     Wald rat	0.011 0.019 0.023 0.030 0.001
Particular interparts     Norm     1     0.00 </td <td>phosphatase 1     NAD(P)H dehydrogenase (quinone) 1     Wald ratio     1     0.873     0.760     0.986       NAD-(P)H dehydrogenase (quinone) 1     WW     3     0.936     0.878     0.9393       Inturin-2     Neuresin-3-beta     Wald ratio     1     1.168     1.028     1.308       N-terminal pro-BMP     Wald ratio     1     1.248     1.114     1.382       N-terminal prohormone of brain natriuretic peptide     WW     2     0.876     0.747     1.005       OX-2 membrane glycoprotein     Wald ratio     1     1.248     1.114     1.382       Protein FAMDS     Wald ratio     1     1.085     1.033     1.168       Protein FAMSD     Wald ratio     1     0.899     0.682     0.937       Xaa-Pro aminopeptidase 2     Wald ratio     1     1.808     2.165       C-C mutri chemokine 4     Wald ratio     1     1.470     1.218     1.721       Bata-1,4-galactosytransferase 2     Wald ratio     1     1.040     1.022     1.721       Bata-1,4-galactosytransferase 2</td> <td>0.019 0.023 0.030 0.001</td>	phosphatase 1     NAD(P)H dehydrogenase (quinone) 1     Wald ratio     1     0.873     0.760     0.986       NAD-(P)H dehydrogenase (quinone) 1     WW     3     0.936     0.878     0.9393       Inturin-2     Neuresin-3-beta     Wald ratio     1     1.168     1.028     1.308       N-terminal pro-BMP     Wald ratio     1     1.248     1.114     1.382       N-terminal prohormone of brain natriuretic peptide     WW     2     0.876     0.747     1.005       OX-2 membrane glycoprotein     Wald ratio     1     1.248     1.114     1.382       Protein FAMDS     Wald ratio     1     1.085     1.033     1.168       Protein FAMSD     Wald ratio     1     0.899     0.682     0.937       Xaa-Pro aminopeptidase 2     Wald ratio     1     1.808     2.165       C-C mutri chemokine 4     Wald ratio     1     1.470     1.218     1.721       Bata-1,4-galactosytransferase 2     Wald ratio     1     1.040     1.022     1.721       Bata-1,4-galactosytransferase 2	0.019 0.023 0.030 0.001
No	NAD-dependent protein deacetylase sirulin-2     IVW     3     0.936     0.878     0.993 1.308       Neurexin-3-beta     Wald ratio     1     1.168     1.028     1.308       N-terminal pro-BNP     Wald ratio     1     0.876     0.747     1.005       OX-2 membrane glycoprotein     Wald ratio     1     1.248     1.114     1.382       Protein FAMISA     Wald ratio     1     1.085     1.012     1.158       Protein FAMISA     Wald ratio     1     1.082     1.033     1.131       Rho GTPase-activating protein 1     Wald ratio     1     1.087     1.466     Semaphorin-3G     Wald ratio     1     1.887     1.608     2.168       Tissue factor     Wald ratio     1     1.887     1.608     2.168     1.114     1.320     0.766       5-formyttetrahydroletac cycle-ligase     VW     2     1.113     1.018     1.209       Aspartyl/asparaginy beta-hydroxytase     Wald ratio     1     1.096     1.121     1.179       Binatruretic peptides     Wald ratio	0.023 0.030 0.001
Burnelsion     Normelsion     Normel	airtuin-2     Neurexin-3-beta     Wald ratio     1     1.168     1.028     1.308       N-terminal pro-BNP     Wald ratio     1     0.837     0.729     0.945       N-terminal prob-BNP     Wald ratio     1     1.248     1.114     1.382       OX-2 membrane glycoprotein     Wald ratio     1     1.248     1.114     1.382       Protein FAM153A     Wald ratio     1     1.085     1.012     1.131       Rho GTPase-activating protein 1     Wald ratio     1     1.277     1.067     1.466       Semaphorin-3G     Wald ratio     1     1.887     1.608     2.163       Xaa-Pro aminopeptidase 2     Wald ratio     1     1.887     1.608     2.165       Tissue factor     Wald ratio     1     1.470     1.218     1.221       Aspartyl/asparaginyl beta-hydroxylase     Wald ratio     1     1.470     1.218     1.721       Biotriurets peptidase     Wald ratio     1     1.076     1.024     1.340       Beta-1/4-galactoxspytransferase 2     Wald ratio     1<	0.030 0.001
	N-terminal pro-BNP     Waid ratio     1     0.837     0.729     0.945       N-terminal prohormone of brain natriuretic peptide     IVW     2     0.876     0.747     1.005       OX-2 membrane glycoprotein     Waid ratio     1     1.028     1.012     1.158       Protein FAM3D     Waid ratio     1     1.022     1.033     1.131       Rho GTPase-activating protein 1     Waid ratio     1     1.264     1.062     1.033     1.131       Rho GTPase-activating protein 1     Waid ratio     1     1.264     1.062     1.466       Semaphorin-3G     Waid ratio     1     1.264     1.082     1.062     1.466       Semaphorin-3G     Waid ratio     1     1.264     1.062     1.466       Tissue factor     Waid ratio     1     0.459     0.132     0.768       S-formyItetrahydrofolate cyclo-ligase     IVW     2     1.113     1.018     1.204       Bata1-caglactosyltransferase 2     Waid ratio     1     0.473     0.49     1.032       Biotinidase     Wai	0.001
NameNotNoN	N-terminal prohormone of brain natriuretic peptide     IVW     2     0.876     0.747     1.005       OX-2 membrane glycoprotein     Wald ratio     1     1.248     1.114     1.382       Protein FAM163A     Wald ratio     1     1.085     1.002     1.131       Rho GTPase-activating protein 1     Wald ratio     1     1.022     1.032     1.131       Rho GTPase-activating protein 1     Wald ratio     1     1.264     1.082     0.862     0.937       Xaa-Pro aminopeptidase 2     Wald ratio     1     1.264     1.082     1.688     2.165       Tissue factor     Wald ratio     1     0.459     0.682     0.937       Asparty/Lasparaginyl beta-hydroxylase     Wald ratio     1     1.470     1.218     1.721       Beta-1,4-galactosyltransferase 2     Wald ratio     1     0.409     1.032     1.032       Biotinidase     Wald ratio     1     0.747     0.449     1.038       Biotinidase     Wald ratio     1     0.757     0.449     1.032       Cation-dependent man	
Order without one of the set of the s	OX-2 membrane glycoprotein     Wald ratio     1     1.248     1.114     1.382       Protein FAM163A     Wald ratio     1     1.085     1.012     1.158       Protein FAM3D     Wald ratio     1     1.082     1.033     1.131       Rho GTPase-activating protein 1     Wald ratio     1     1.082     1.032     1.465       Semaphorin-3G     Wald ratio     1     1.887     1.608     2.616       Semaphorin-3G     Wald ratio     1     1.887     1.608     2.616       Tissue factor     Wald ratio     1     1.470     1.218     1.721       Bata-1,4-galactosyltransferase 2     Wald ratio     1     1.049     1.040     1.340       Bata-ricroseminoprotein     Wald ratio     1     1.026     1.173     1.179       Binatriuretic peptides     Wald ratio     1     1.006     1.012     1.174       Carboxypeptidase B     Wald ratio     1     0.059     1.012     1.124       Cathepsin H     Wald ratio     1     0.462     1.422 <td< td=""><td></td></td<>	
Number of the state of the	Protein FAM163A     Wald ratio     1     1.085     1.012     1.158       Protein FAM3D     Wald ratio     1     1.082     1.033     1.131       Rho GTPase-activating protein 1     Wald ratio     1     1.277     1.087     1.466       Semaphorin-3G     Wald ratio     1     1.264     1.082     1.446       Semaphorin-3G     Wald ratio     1     1.264     1.082     1.446       Semaphorin-3G     Wald ratio     1     1.264     1.082     1.446       Semaphorin-3G     Wald ratio     1     1.468     2.165     1.121     1.218     1.218     1.218     1.221     1.218     1.221     1.218     1.221     1.218     1.221     1.218     1.221     1.218     1.221     1.218     1.221     1.218     1.221     1.218     1.221     1.218     1.221     1.218     1.221     1.218     1.221     1.217     1.218     1.221     1.179     1.330     1.310     1.221     1.175     1.450     1.212     1.218     1.224 <td>0.001</td>	0.001
ProceedingsNumber of the second o	Rho GTPase-activating protein 1     Wald ratio     1     1.277     1.087     1.466       Semaphorin-3G     Wald ratio     1     0.809     0.682     0.937       Xaa-Pro aminopeptidase 2     Wald ratio     1     1.264     1.082     1.446       everity (B2)     C-C motif chemokine 4     Wald ratio     1     1.867     1.608     2.165       Tissue factor     Wald ratio     1     0.459     0.132     0.786       5-formyltetrahydrofolate cyclo-ligase     IWW     2     1.113     1.018     1.209       Aspartyl/asparaginyl beta-hydroxylase     Wald ratio     1     1.470     1.218     1.721       Beta-microseminoprotein     Wald ratio     1     1.040     1.340       Biotnidase     Wald ratio     1     1.026     1.175       Carboxypeptidase B     Wald ratio     1     0.63     1.022     1.123       Cathepsin H     Wald ratio     1     0.63     1.021     1.126       Cathepsin H     Wald ratio     1     0.63     1.022     1.125<	0.001
Amagenesis<	Semaphorin-3G     Wald ratio     1     0.809     0.682     0.937       Xaa-Pro aminopeptidase 2     Wald ratio     1     1.264     1.082     1.446       everity (B2)     C-C motif chemokine 4     Wald ratio     1     1.867     1.608     2.165       Tissue factor     Wald ratio     1     0.459     0.132     0.786       5-formyltetrahydrofolate cyclo-ligase     IVW     2     1.113     1.018     1.209       Asparty//asparaginyl beta-hydroxylase     Wald ratio     1     1.470     1.218     1.721       Beta-nicroseminoprotein     Wald ratio     1     1.096     1.012     1.179       Binatriuretic peptides     Wald ratio     1     1.076     1.012     1.179       Binatriuretic peptides     Wald ratio     1     0.743     0.449     1.032       Carboxypeptidase B     Wald ratio     1     0.767     0.49     1.024       Cathopsin H     Wald ratio     1     1.626     1.142     1.782       Cathopsin H     Wald ratio     1     1	0.002 0.011
Counter worksingCounter worksingWorksingNo. <td>everity (B2)     C-C motif chemokine 4     Wald ratio     1     1.887     1.608     2.165       Tissue factor     Wald ratio     1     0.459     0.132     0.786       5-formyltetrahydrofolate cyclo-ligase     IVW     2     1.113     1.018     1.209       Aspartyl/asparaginyl beta-hydroxylase     Wald ratio     1     1.470     1.218     1.721       Beta-1,4-galactosyltransferase 2     Wald ratio     1     1.096     1.012     1.179       Binatriuretic peptides     Wald ratio     1     0.743     0.449     1.038       Biotinidase     Wald ratio     1     0.757     0.49     1.024       Cathopsin H     Wald ratio     1     0.757     0.49     1.024       Cathop-dependent mannose-6- phosphate receptor     Wald ratio     1     1.063     1.002     1.173       Collagen alpha-1(XV) chain     Wald ratio     1     1.462     1.142     1.782       Collagen alpha-1(XV) chain     Wald ratio     1     1.426     1.125     1.788       Subcomponent-binding protein,<br <="" td=""/><td>0.011</td></td>	everity (B2)     C-C motif chemokine 4     Wald ratio     1     1.887     1.608     2.165       Tissue factor     Wald ratio     1     0.459     0.132     0.786       5-formyltetrahydrofolate cyclo-ligase     IVW     2     1.113     1.018     1.209       Aspartyl/asparaginyl beta-hydroxylase     Wald ratio     1     1.470     1.218     1.721       Beta-1,4-galactosyltransferase 2     Wald ratio     1     1.096     1.012     1.179       Binatriuretic peptides     Wald ratio     1     0.743     0.449     1.038       Biotinidase     Wald ratio     1     0.757     0.49     1.024       Cathopsin H     Wald ratio     1     0.757     0.49     1.024       Cathop-dependent mannose-6- phosphate receptor     Wald ratio     1     1.063     1.002     1.173       Collagen alpha-1(XV) chain     Wald ratio     1     1.462     1.142     1.782       Collagen alpha-1(XV) chain     Wald ratio     1     1.426     1.125     1.788       Subcomponent-binding protein, <td>0.011</td>	0.011
Tisse factorWarnelNumber of 2Number of 2N	Tissue factor     Wald ratio     1     0.459     0.132     0.786       5-formyltetrahydrofolate cyclo-ligase     IWW     2     1.113     1.018     1.209       Aspartyl/asparaginyl beta-hydroxylase     Wald ratio     1     1.470     1.218     1.721       Beta-1,4-galactosyltransferase 2     Wald ratio     1     1.096     1.012     1.179       Binatriuretic peptides     Wald ratio     1     0.743     0.449     1.038       Biotinidase     Wald ratio     1     0.757     0.49     1.024       Cathoxypeptidase B     Wald ratio     1     0.757     0.49     1.024       Cathor-dependent mannose-6-phosphate receptor     Wald ratio     1     1.030     1.075     1.565       phosphate receptor     IVW     2     1.204     1.030     1.378       Chondroitin sulfate N-acetylgalactosam     Wald ratio     1     0.807     0.599     1.016       Complement component 1 Q     Wald ratio     1     1.456     1.125     1.788       Subcomponent-binding protein, mitochondrial	0.012 8.04F-06
Asson of segregations between segregations     Water and     I     I. 4.00     I.000     I.0000     I.000	Aspartyl/asparaginyl beta-hydroxylase   Wald ratio   1   1.470   1.218   1.721     Beta-1,4-galactosyltransferase 2   Wald ratio   1   1.190   1.040   1.340     Beta-microseminoprotein   Wald ratio   1   1.096   1.012   1.179     Binatriuretic peptides   Wald ratio   1   0.743   0.449   1.038     Biotinidase   Wald ratio   1   0.757   0.49   1.024     Cathopypeptidase B   Wald ratio   1   1.063   1.002   1.123     Cathopendent mannose-6- phosphate receptor   Wald ratio   1   1.320   1.075   1.565     Chondroitin sulfate N-acetylgalactosam inyltransferase 2   IVW   2   1.204   1.030   1.378     Chondroitin sulfate N-acetylgalactosam inyltransferase 2   Wald ratio   1   1.462   1.142   1.782     Collagen alpha-1(XV) chain   Wald ratio   1   0.807   0.599   1.016     Complement component 1 Q subcomponent-binding protein, mitochondrial   Wald ratio   1   1.456   1.125   1.788     CXADR-like membrane protein   Wald ratio	8.04E-00
Densel , regarding sequencesWind now1101.00	Beta-1,4-galactosyltransferase 2   Wald ratio   1   1.190   1.040   1.340     Beta-microseminoprotein   Wald ratio   1   1.096   1.012   1.179     Binatriuretic peptides   Wald ratio   1   0.743   0.449   1.038     Biotinidase   Wald ratio   1   1.000   1.026   1.175     Carboxypeptidase B   Wald ratio   1   0.757   0.49   1.024     Cathepsin H   Wald ratio   1   1.063   1.002   1.123     Cation-dependent mannose-6- phosphate receptor   Wald ratio   1   1.462   1.142   1.782     C-C motif chemokine 28   IVW   2   1.204   1.030   1.378     Chondroitin sulfate N-acetylgalactosam inyltransferase 2   Wald ratio   1   1.462   1.142   1.782     Collagen alpha-1(XV) chain   Wald ratio   1   0.807   0.599   1.016     Complement component 1 Q subcomponent-binding protein, mitochondria   Wald ratio   1   1.426   1.113   1.739     Cytoskeleton-associated protein 2   Wald ratio   1   1.426   1.113 <td>0.028</td>	0.028
Dimensione suppose     Wale ratio     1     0.703     0.804     0.103 <td>Binatriuretic peptidesWald ratio10.7430.4491.038BiotinidaseWald ratio11.1001.0261.175Carboxypeptidase BWald ratio10.7570.491.024Cathepsin HWald ratio11.0631.0021.123Cation-dependent mannose-6- phosphate receptorWald ratio11.3201.0751.565C-C motif chemokine 28IVW21.2041.0301.378Chondroitin sulfate N-acetylgalactosam inyltransferase 2Wald ratio10.8070.5991.016Collagen alpha-1(XV) chainWald ratio10.8070.5991.016CxADR-like membrane protein, mitochondrial11.4261.1131.739Disintegrin and metalloproteinase domain-containing protein 19Wald ratio11.4261.1131.736Dual specificity protein phosphatase 4Wald ratio11.4051.0731.736Dynactin-associated proteinWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio11.5131.1221.905Endothelial monocyte-activating polypeptide 2Wald ratio10.8240.6341.014</td> <td>0.003 0.023</td>	Binatriuretic peptidesWald ratio10.7430.4491.038BiotinidaseWald ratio11.1001.0261.175Carboxypeptidase BWald ratio10.7570.491.024Cathepsin HWald ratio11.0631.0021.123Cation-dependent mannose-6- phosphate receptorWald ratio11.3201.0751.565C-C motif chemokine 28IVW21.2041.0301.378Chondroitin sulfate N-acetylgalactosam inyltransferase 2Wald ratio10.8070.5991.016Collagen alpha-1(XV) chainWald ratio10.8070.5991.016CxADR-like membrane protein, mitochondrial11.4261.1131.739Disintegrin and metalloproteinase domain-containing protein 19Wald ratio11.4261.1131.736Dual specificity protein phosphatase 4Wald ratio11.4051.0731.736Dynactin-associated proteinWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio11.5131.1221.905Endothelial monocyte-activating polypeptide 2Wald ratio10.8240.6341.014	0.003 0.023
Oversides     Wind ratio     1     1.000     1.000     1.710     1.000	BiotinidaseWald ratio11.1001.0261.175Carboxypeptidase BWald ratio10.7570.491.024Cathepsin HWald ratio11.0631.0021.123Cation-dependent mannose-6- phosphate receptorWald ratio11.3201.0751.565C-C motif chemokine 28IVW21.2041.0301.378Chondroitin sulfate N-acetylgalactosam inyltransferase 2Wald ratio10.8070.5991.016Collagen alpha-1(XV) chainWald ratio10.8070.5991.016Complement component 1 Q subcomponent-binding protein, mitochondrialWald ratio11.3421.1051.579Cytoskeleton-associated protein 2Wald ratio11.4261.1131.739Disintegrin and metalloproteinase domain-containing protein 19Wald ratio11.4051.0731.736Dynactin-associated proteinWald ratio10.6710.3191.023Dynactin-associated proteinWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio10.8240.6341.014polypeptide 21.0140.02641.014	0.033
Carbon-promotine monoportWork mode1Local <td>Cathepsin HWald ratio11.0631.0021.123Cation-dependent mannose-6- phosphate receptorWald ratio11.3201.0751.565C-C motif chemokine 28IVW21.2041.0301.378Chondroitin sulfate N-acetylgalactosam inyltransferase 2Wald ratio11.4621.1421.782Collagen alpha-1(XV) chainWald ratio10.8070.5991.016Complement component 1 Q subcomponent-binding protein, mitochondrialWald ratio11.4561.1251.788CXADR-like membrane proteinWald ratio11.3421.1051.5791.579Cytoskeleton-associated protein 2Wald ratio11.4261.1131.739Disintegrin and metalloproteinase domain-containing protein 19Wald ratio11.4051.0731.736Dynactin-associated proteinWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio10.8240.6341.014polypeptide 21.0141.0141.014</td> <td>0.048 0.012</td>	Cathepsin HWald ratio11.0631.0021.123Cation-dependent mannose-6- phosphate receptorWald ratio11.3201.0751.565C-C motif chemokine 28IVW21.2041.0301.378Chondroitin sulfate N-acetylgalactosam inyltransferase 2Wald ratio11.4621.1421.782Collagen alpha-1(XV) chainWald ratio10.8070.5991.016Complement component 1 Q subcomponent-binding protein, mitochondrialWald ratio11.4561.1251.788CXADR-like membrane proteinWald ratio11.3421.1051.5791.579Cytoskeleton-associated protein 2Wald ratio11.4261.1131.739Disintegrin and metalloproteinase domain-containing protein 19Wald ratio11.4051.0731.736Dynactin-associated proteinWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio10.8240.6341.014polypeptide 21.0141.0141.014	0.048 0.012
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picepties require     WW     2     NM     1.00     1.00     1.070     0.070       Concreation windlaw Neeroldy auxonam     War rule     1     0.007     0.008     0.008       Collages at department or generol in the consol of the consol interconsol	phosphate receptorC-C motif chemokine 28IVW21.2041.0301.378Chondroitin sulfate N-acetylgalactosamWald ratio11.4621.1421.782inyltransferase 2Collagen alpha-1(XV) chainWald ratio10.8070.5991.016Complement component 1 Q subcomponent-binding protein, mitochondrialWald ratio11.4561.1251.788CXADR-like membrane proteinWald ratio11.3421.1051.579Cytoskeleton-associated protein 2Wald ratio11.4261.1131.739Disintegrin and metalloproteinase domain-containing protein 19Wald ratio11.4051.0731.736Dual specificity protein phosphatase 4Wald ratio11.4051.0311.2321.095Dynein light chain 2, cytoplasmicWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio10.8240.6341.014polypeptide 2Wald ratio10.8240.6341.014	0.049
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Calegor apple 10% channer     Nach meine     1     0.400     0.400     0.400     0.400       Calegor apple 10% channer prohen     Wei meine     1     1.428     1.100     1.779     0.700       CARDER-Hole manner prohen     Wei meine     1     0.428     1.000     1.428     1.000     0.429       Data seguritation projection 10     Wei meine     1     0.467     0.733     1.729     0.726       Data seguritation projection 10     Wei meine     1     0.467     0.733     1.729     0.726       Data seguritation projection 10     Wei meine     1     0.467     0.733     1.724     0.426       Data seguritation projection 10     Wei meine     1     1.733     1.724     0.742       Data seguritation projection 10     Wei meine     1     1.738     1.728     0.728       Data seguritation projection 11     Wei meine     1     1.738     1.728     1.728     0.728       Data seguritation 11     Wei meine     1     0.718     0.728     0.728     0.728     0.728  <	Collagen alpha-1(XV) chainWald ratio10.8070.5991.016Complement component 1 Q subcomponent-binding protein, mitochondrialWald ratio11.4561.1251.788CXADR-like membrane proteinWald ratio11.3421.1051.579Cytoskeleton-associated protein 2Wald ratio11.4261.1131.739Disintegrin and metalloproteinase domain-containing protein 19Wald ratio11.2551.0601.450Dual specificity protein phosphatase 4Wald ratio11.4051.0731.736Dynactin-associated proteinWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio10.8240.6341.014polypeptide 2SaleSale1.0141.0451.014	0.037
Component component 1 0     Natic ratio     1     1.42     1.72     1.72     0.72       Control of all component function protein     Natic ratio     1     1.42     1.11     1.73     0.72       Control of all component function protein     Natic ratio     1     1.42     1.11     1.73     0.72       Dest specificity protein function protein     Natic ratio     1     0.47     0.31     1.22     1.25     0.26       Dynamic account of protein     Natic ratio     1     0.43     0.24     0.24     0.25     0.24       Experision protein fractorent     Natic ratio     1     0.43     0.24	Complement component 1 Q subcomponent-binding protein, mitochondrialWald ratio11.4561.1251.788CXADR-like membrane proteinWald ratio11.3421.1051.579Cytoskeleton-associated protein 2Wald ratio11.4261.1131.739Disintegrin and metalloproteinase domain-containing protein 19Wald ratio11.2551.0601.450Dual specificity protein phosphatase 4Wald ratio11.4051.0731.736Dynactin-associated proteinWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio10.8240.6341.014polypeptide 2Vald ratio10.8240.6341.014	0.044
millocinoxiali     Number of the second sec	mitochondrialCXADR-like membrane proteinWald ratio11.3421.1051.579Cytoskeleton-associated protein 2Wald ratio11.4261.1131.739Disintegrin and metalloproteinase domain-containing protein 19Wald ratio11.2551.0601.450Dual specificity protein phosphatase 4Wald ratio11.4051.0731.736Dynactin-associated proteinWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio11.5131.1221.905Endothelial monocyte-activating polypeptide 2Wald ratio10.8240.6341.014	0.026
Operating and matrix protects     Water ratio     1     1.405     1.135     1.200     1.400     0.002       Dard spectricity protects inprotects     Water ratio     1     1.405     1.000     1.400     0.002       Dymen ingrit charm 2, cyteptizamic     Water ratio     1     1.401     0.101 <td>Cytoskeleton-associated protein 2Wald ratio11.4261.1131.739Disintegrin and metalloproteinase domain-containing protein 19Wald ratio11.2551.0601.450Dual specificity protein phosphatase 4Wald ratio11.4051.0731.736Dynactin-associated proteinWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio11.5131.1221.905Endothelial monocyte-activating polypeptide 2Wald ratio10.8240.6341.014</td> <td></td>	Cytoskeleton-associated protein 2Wald ratio11.4261.1131.739Disintegrin and metalloproteinase domain-containing protein 19Wald ratio11.2551.0601.450Dual specificity protein phosphatase 4Wald ratio11.4051.0731.736Dynactin-associated proteinWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio11.5131.1221.905Endothelial monocyte-activating polypeptide 2Wald ratio10.8240.6341.014	
Discrete DistributionMade ratio11.551.0001.6500.021Data socialization (SM 19 Dynath associated protein Dynath associated protein Dynath associated protein Dynath associated protein Dynath associated protein Dynath associated protein Dynath associated protein Made ratio10.4501.0731.7390.078Dynath associated protein Dynath as	Disintegrin and metalloproteinase domain-containing protein 19Wald ratio11.2551.0601.450Dual specificity protein phosphatase 4Wald ratio11.4051.0731.736Dynactin-associated proteinWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio11.5131.1221.905Endothelial monocyte-activating polypeptide 2Wald ratio10.8240.6341.014	0.015
Dard specificity variation photogenetation     Wold ratio     1     1.400     1.730     1.730     0.024       Dynamin light charge yorksman     Wald ratio     1     0.024     0.024     0.044       Explorining and reading yorksman     Wald ratio     1     1.056     1.044     0.044       Explorining and reading yorksman     Wald ratio     1     1.056     1.044     0.040       Explorining and reading yorksman     Wald ratio     1     1.041     1.042     1.040       Explorining and reading yorksman     Wald ratio     1     1.041     1.042     1.040     1.042     1.040     1.042     1.040     1.042     1.040     1.042     1.040	Dual specificity protein phosphatase 4Wald ratio11.4051.0731.736Dynactin-associated proteinWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio11.5131.1221.905Endothelial monocyte-activatingWald ratio10.8240.6341.014polypeptide 211.0141.0141.014	0.020
Dynamin direction 2, synthesing     Waid ratio     1     0.571     0.339     1.023     0.023       Dynamin direction 2, synthesing     Naid ratio     1     1.535     1.024     1.035       Ephon byse direction 2     Waid ratio     1     1.335     1.047     1.042     1.043     0.042     1.043     0.042     1.043     0.042     1.043     0.042     1.043     0.042     1.043     0.042     1.043     0.042     1.043     0.042     1.043     0.042     1.043     0.042     1.043     0.042     1.043     0.042     1.043     0.042     1.043     0.042     1.044     1.042     0.043     1.044     1.044     1.04	Dynactin-associated proteinWald ratio10.6710.3191.023Dynein light chain 2, cytoplasmicWald ratio11.5131.1221.905Endothelial monocyte-activating polypeptide 2Wald ratio10.8240.6341.014	0.045
Endetbelia     Produce 1     0.824     0.034     1.04     0.044       Ephrin Syste Tarcsopter 8     Wald ratio     1     1.356     1.984     1.024     0.025       Ephrin Syste Tarcsopter 7     Wald ratio     1     0.016     0.184     0.024       Fibrobast growth factor 7     Wald ratio     1     0.016     0.184     0.024       Golg internorane protein 1     Wald ratio     1     0.101     0.192     1.778     0.024       Hebroopencour nuclear     Wald ratio     1     0.491     0.192     1.191     0.022     1.191     0.022     1.191     0.022     1.191     0.022     1.191     0.022     1.191     0.022     1.191     0.022     1.191     0.022     1.191     0.022     1.191     0.022     1.191     0.022     1.191     0.022     1.191     0.023     0.021     0.021     0.021     0.021     0.021     0.021     0.021     0.021     0.021     0.021     0.021     0.021     0.021     0.021     0.021     0.021     0	Endothelial monocyte-activating Wald ratio 1 0.824 0.634 1.014 polypeptide 2	0.026
potypeticie 2       Ephren byse Prosoprof     Wald ratio     1     1.326     1.047     1.022       Ephecidest growth factor 19     Wald ratio     1     0.051     0.012     0.022       Ephecidest growth factor 19     Wald ratio     1     0.016     0.018     0.014     0.028       Flamm-A     Wald ratio     1     0.011     0.119     0.524     0.028       Calgorinentificatione protein botin     Wald ratio     1     0.429     1.029     0.222     0.226       Interdución-7 branchoto statumi botin     Wald ratio     1     0.236     0.021     0.022     0.226       Interdución-7 branchoto statumi botin     Wald ratio     1     0.236     0.027     0.026       Kallaren-14     WW     2     1.124     0.011     0.025     0.027     0.026       Kallaren-14     WW     2     1.144     0.101     0.025     0.027     0.026       Kallaren-14     WW     2     1.144     0.161     0.028     0.027       Kallaren-14     WW <td>polypeptide 2</td> <td>0.038 0.046</td>	polypeptide 2	0.038 0.046
Epini-B1     Wald ratio     1     1.356     1.897     1.824     0.022       Hincheast growth factor 19     Wald ratio     1     0.0416     0.0416     0.0426	Ephrin type-R recentor 6 Wold ratio	
Fibrables growth factor 7     Wald ratio     1     0.616     0.184     1.040     0.027       Filamin A     Wald ratio     1     0.701     0.898     1.041     0.041       Golg membrane proten     Wald ratio     1     1.200     1.042     1.378     0.022       Heterogeneous cubars     Wald ratio     1     0.552     0.181     0.832     4.155-       Interioukin - 10 receptor suburit beta     Wald ratio     1     0.552     0.191     0.832     0.114       Interioukin - 20 receptor suburit beta     Wald ratio     1     0.552     0.191     0.832     0.014       Kalliterin-14     WV     2     1.134     0.111     1.256     0.022     0.387     0.022       Kalliterin-14     WV     2     1.144     1.406     0.438     0.021     0.038     0.729     0.86     0.822     0.022       Kalliterin-18     Wald ratio     1     0.453     1.55     0.424     0.001       Macrophage Intermologiculum and protein     Wald ratio     1     0.		0.023 0.026
Filamin-A     Weid ratio     1     0.701     0.888     1.014     0.022       Coigi membrane protein 1     Waid ratio     1     1.191     1.013     1.042     0.202       Hest social principant bales 1     Weid ratio     1     0.402     1.728     0.022     4.1875       Hestopancus rucles     Weid ratio     1     0.261     0.041     0.021     0.021     1.228     0.021		0.046
Heat shack protein bate-1     Waid ratio     1     1.209     1.502     1.766     0.202       Heerogeneos nucles     Waid ratio     1     1.66     1.125     1.78     0.202       Interlevice/17 Orceptor suburit beta     Waid ratio     1     0.512     0.191     0.882     4.154-       Kalikeen-13     Waid ratio     1     0.566     0.721     0.494     0.021       Kalikeen-13     Waid ratio     1     0.588     0.75     1.001     0.236       Kalikeen-14     WW     2     1.134     1.011     1.256     0.041       Kalikeen-14     WW     2     1.144     1.040     0.022       Low andriny immunoglobulin gamma Ec     Waid ratio     1     0.683     0.982     0.002       Macrophage infarmatory protein-11     WW     2     1.144     1.040     1.041     0.040       Macrophage infarmatory protein-12     Waid ratio     1     0.141     1.468     0.033     0.033     0.033     0.033     0.033     0.033     0.033     0.041		0.028 0.026
Heterogeneeue nueleer     Veid ratio     1     1.466     1.25     1.789     0.226       inbenoukin-27 aubunt apha     WW     2     1.129     1.121     1.22     1.034     1.496       Intereukin-27 aubunt apha     WW     2     1.124     1.034     1.048     1.048     1.048     1.048     1.048     1.048     1.048     1.048     1.048     1.048     1.048     1.048     1.048     1.048     1.048     1.048     1.048     1.048     0.032       Kallkerin-14     WW     2     1.141     1.011     1.250     0.047     0.022       Kallkerin-14     WW     2     1.144     1.041     1.033     0.375     1.001     0.032       Macrophage informatory protein-11     WW     2     1.144     1.441     1.041     1.441     1.043     1.033     0.032       Macrophage informatory protein-12     Wald ratio     1     0.319     1.033     0.033     0.049       Macrophage informatory protein-12     Wald ratio     1     0.141 <td< td=""><td>Golgi membrane protein 1 Wald ratio 1 1.191 1.019 1.364</td><td>0.046</td></td<>	Golgi membrane protein 1 Wald ratio 1 1.191 1.019 1.364	0.046
Interleadin-10 receptor subunit beta   Waid ratio   1   0.512   0.191   0.832   4.195-4     Interleadin-27 subunit atpha   WW   2   1.128   1.020   1.226   0.044     Kallkrein-13   Waid ratio   1   0.855   0.721   0.99   0.022     Kallkrein-14   WW   2   1.034   1.011   1.226   0.044     Kitligand   Waid ratio   1   0.838   0.875   1.001   0.033     Low affinity immonglobuli gamma Fc   Waid ratio   1   0.838   0.875   1.001   0.033     Maccophage infiltminatory protein-10   VW   2   1.144   1.046   1.241   0.046     Maccophage infiltminatory protein-12   WW   2   1.144   1.048   0.041     Maccophage infiltminatory protein-14   Wuid ratio   1   0.475   0.319   1.033   0.431     Maccophage indepotein 24   Wuid ratio   1   0.476   0.499   0.967   0.000     Machana - 1.24   Wuid ratio   1   0.478   0.498   0.972   0.0001     Multipl		0.026 0.026
Interferencies     Status     INV     2     1.129     1.032     1.248     0.013       Kallikerin-14     Wild ratio     1     1.266     1.041     1.498     0.013       Kallikerin-14     IVW     2     1.134     1.011     1.266     0.024       Killigand     Wald ratio     1     1.636     1.29     1.783     66-0       Low efficity immunoglobulin-like domains protein 3     Wald ratio     1     0.833     0.720     0.997     0.022       Macropolage inflammatory protein-18     Wuld ratio     1     0.853     0.721     0.86     0.892     0.001       Macropolage inflammatory protein-19     WV     2     1.144     1.046     1.047     0.002       Macropolage inflammatory protein-19     WV     2     1.041     1.131     1.497     0.002       Macropolage inflammatory protein 24     Wald ratio     1     0.576     0.319     1.033     0.491       Macropolage inflammatory protein 24     Wald ratio     1     0.76     0.319     1.033     0.491 <td>ribonucleoproteins C1/C2</td> <td></td>	ribonucleoproteins C1/C2	
Kallikrein-13     Waki ratio     1     0.855     0.721     0.99     0.022       Kallikrein-14     VW     2     1.134     1.011     1.286     0.044       Kit ligand     Waki ratio     1     0.683     0.675     1.001     0.034       Low affinity immooglobulin-like domains potein 3     Waki ratio     1     0.883     0.675     0.097     0.022       Macrophage inflarmatory protein-1/j     VW     2     1.144     1.046     1.241     0.046     0.492     0.022       Macrophage inflarmatory protein-1/j     VW     2     1.144     1.046     1.241     0.046     0.492     0.002       Matrophorial origo protein 24     Waki ratio     1     0.576     0.319     1.033     0.497     0.026       Matrophorial protein goutorie protein 24     Waki ratio     1     0.576     0.319     1.033     0.497     0.036       Neuroni growth regulator     Waki ratio     1     0.576     0.591     0.006     0.007     0.036     0.044     0.355     0.044     0.035<		4.15E-0
Kalikovain-14     VW     2     1.134     1.011     1.256     0.044       Kit igand     Waid ratio     1     1.538     1.29     1.783     BE-0       Low diffiction repeats and immunoglobuline-like domains protein 3     Waid ratio     1     0.833     0.675     1.001     0.033       Low affinity immunoglobulin gamma For region receptors II-B     Waid ratio     1     0.853     0.720     0.987     0.022       Mances-of-log-cascharids 1.2-alpha- menonicidase IB     Waid ratio     1     0.921     0.86     0.982     0.005       Metabrona-derived growth regulatory protein     Waid ratio     1     0.921     0.86     0.982     0.005       Metabrona-derived growth regulator     Waid ratio     1     0.131     1.147     0.003       Matchondrinal Libguith Tigges activator     Waid ratio     1     0.133     0.031     0.031       Mutobrondrinal Libguith Tigges activator     Waid ratio     1     0.133     0.032       Mutobrondrina Libguith Tigges activator     1     0.133     0.041     0.0457     0.002       Mu		0.012
Leucine-rich repeats and Immunoglobulin-like comains protein 3     Wald ratio     1     0.838     0.757     1.001     0.024       Low affinity immunoglobulin-like comains protein -1µ     Wald ratio     1     0.863     0.720     0.997     0.025       Macrophage inflammatory protein -1µ     I/W     2     1.144     1.466     1.241     0.496     0.005       Manneys-folgeaccharide 1_2-alpha- mannosidase IB     Wald ratio     1     0.921     0.86     0.982     0.005       Metanoma-derived growth regulatory of NFKB 1     Wald ratio     1     0.131     1.1417     0.002       Multiple inositol polyphosphate phosphatase 1     Wald ratio     1     1.314     1.1497     0.002       NADD[PH delydrogenase [quinone] 1     Wald ratio     1     0.733     0.499     0.967     0.005       NADD[PH delydrogenase [quinone] 1     Wald ratio     1     0.733     0.499     0.967     0.005       Neurotimin     Wald ratio     1     0.760     0.539     1.013     0.035       Nearchal probormone of brain nutrinetic poptide     I/Wald ratio     1		0.022 0.046
Immunoglobulini Barna For     Wald ratio     1     0.953     0.720     0.987     0.024       Macrophage inflammatory protein-10     VW     2     1.144     1.046     1.241     0.007       Macrophage inflammatory protein-10     VW     2     1.144     1.046     1.241     0.007       Mannosyl-Olgoasacharide 1.2-alpha- mannosidase IS     Wald ratio     1     0.576     0.319     1.033     0.031       Methyltransferase-like protein 24     Wild ratio     1     1.314     1.131     1.447     0.002       Multiple inositol polyhosphate phosphatase 1     Wald ratio     1     0.573     0.499     0.967     0.003       NKG2D ligand 3     Wald ratio     1     0.533     1.013     0.049       Neuronial growth regulator 1     Wald ratio     1     0.539     1.013     0.033       Nearceining incellane     Wald ratio     1     0.768     0.588     0.942       Nearceining incellane     Wald ratio     1     0.768     0.575     0.637     0.632     0.007       Nearceining incellanes	Kit ligand Wald ratio 1 1.536 1.29 1.783	6E-04
region mocaptage inflammatory protein-16     VW     2     1.141     1.046     1.241     0.007       Mannosyl-oligosaccharida 1.2-alpha- mennosidase IB     Waid ratio     1     0.921     0.86     0.982     0.005       Melanoma-derived growth regulatory     Waid ratio     1     0.921     0.86     0.982     0.005       Methyltransferase-like protein     Waid ratio     1     0.476     0.319     1.033     0.031       Mittochondrial ubiquitin ligase activator     Waid ratio     1     1.319     1.644     1.585     0.041       Modifyle insistel potyhosphate     Waid ratio     1     0.733     0.499     0.967     0.005       NAD(PH dehydrogenase [quinone]     Waid ratio     1     0.684     0.305     1.063     0.494       Neuronal growth regulator     Waid ratio     1     0.776     0.539     1.013     0.032       Neuronal growth regulator     Waid ratio     1     0.776     0.539     1.013     0.032       Nectorianal prohemone of brain     VW     2     1.219     1.219     1.219	· ·	0.034
Macrophage inflammatory protein-1       VW     2     1.144     1.046     1.241     0.007       Mannosy-Gilgosacharide 1.2-alpha- mannosidase IB     Wald ratio     1     1.269     1.041     1.496     0.044       Melanoma-derived growth regulatory protein     Wald ratio     1     0.921     0.86     0.982     0.005       Methythansferase-like protein 24     Wald ratio     1     1.314     1.131     1.497     0.003       Mottpjelionsitol polyphosphate     Wald ratio     1     1.319     1.654     1.565     0.041       NAU[PH dehydrogenase [quinone]     Wald ratio     1     0.733     0.499     0.967     0.002       Neurotrimin     Wald ratio     1     0.453     1.033     0.049       Non-secretory ribonuclease     Wald ratio     1     0.453     1.033     0.049       Naterminal pro-BNP     Wald ratio     1     0.765     0.537     0.532     0.000       Neterminal pro-BNP     Wald ratio     1     0.457     0.586     0.974     0.012       N-terminal pro-BNP		0.020
mannosidae IB     Malanoma-derived growth regulatory protein     Wald ratio     1     0.921     0.86     0.982     0.005       Methyltransferase-like protein 24     Wald ratio     1     0.676     0.319     1.033     0.031       Mitochondrial ubiquitir ligase activator of NFKB 1     Wald ratio     1     1.314     1.131     1.497     0.002       NADP[H derivg/orgenase [quinone]     Wald ratio     1     0.733     0.499     0.967     0.003       Nauprint fegulator 1     Wald ratio     1     0.433     0.499     0.967     0.004       Nauprint fegulator 1     Wald ratio     1     0.433     0.499     0.967     0.005       Nauprint fegulator 1     Wald ratio     1     0.453     1.033     0.045       Nucrotrimin     Wald ratio     1     0.457     0.892     0.006       N-terminal pro-BNP     Wald ratio     1     0.451     0.457     0.852     0.007       Nterminal prohomone of brain natriuretic poptide     IVW     2     1.219     1.207     1.410     0.401		0.007
protein     Metrytransferae-like protein 24     Wald ratio     1     0.676     0.319     1.033     0.031       Mttochondral Lubiquitin ligase activator     Wald ratio     1     1.314     1.131     1.497     0.032       Multiple inositol polyphosphate     Wald ratio     1     1.319     1.064     1.585     0.041       NAD(P)H dehydrogenase (quinone)     Wald ratio     1     0.733     0.499     0.967     0.006       Neuronal growth regulator 1     Wald ratio     1     0.684     0.305     1.063     0.049       NKG2D ligand 3     Wald ratio     1     0.683     0.395     0.002       Neurotrimin     Wald ratio     1     0.776     0.539     1.013     0.036       N-terminal pro-BNP     Wald ratio     1     0.78     0.586     0.974     0.0101       N-terminal pro-BNP     Wald ratio     1     0.511     0.106     0.316     0.0316       Out at first potain homolog     Wald ratio     1     0.451     0.735     0.982     0.0161       Protein dis		0.04
Methyltransferase-like protein 24     Wald ratio     1     0.676     0.319     1.033     0.031       Mitochondrial ubiquitin ligase activator of NFKB 1     Wald ratio     1     1.314     1.131     1.497     0.003       Multiple inositol polyphosphate phosphatase 1     Wald ratio     1     0.733     0.499     0.967     0.006       Neuronal growth regulator 1     Wald ratio     1     0.678     0.395     1.063     0.494       Neurotrimin     Wald ratio     1     0.674     0.395     1.063     0.0967       Non-secretory ribonuclease     Wald ratio     1     0.763     0.499     0.702     0.955     0.004       Nt-Group and probormone of brain natriuretic peptide     NW     2     0.705     0.457     0.952     0.006       Ostaoclast-associated immunoglobulin- like receptor     Wald ratio     1     0.161     0.735     0.974     0.0151       Out at first protein homolog     Wald ratio     1     0.684     0.375     0.992     0.0161       Poly(U)-specific endoribonuclease     Wald ratio     1		0.009
of NFKB 1     Multiple inositol polyphosphate phosphatase 1     Wald ratio     1     1.319     1.054     1.585     0.041       NAD(P)H dehydrogenase [quinone] 1     Wald ratio     1     0.733     0.499     0.967     0.005       Neuronal growth regulator 1     Wald ratio     1     0.684     0.305     1.063     0.049       Neurotrimin     Wald ratio     1     0.453     0.499     0.702     0.955     0.002       NKG2D ligand 3     Wald ratio     1     0.453     1.300     1.775     0.033       N-terminal pro-BNP     Wald ratio     1     0.768     0.974     0.012       N-terminal prohomone of brain natriuretic peptide     IVW     2     0.705     0.457     0.952     0.006       Out at first protein homolog     Wald ratio     1     0.511     0.106     0.916     0.001       Ukt areceptor     IVW     2     1.219     1.027     1.410     0.043     1       Potein disulfide-isomerase-like     IVW     2     1.212     1.075     1.349     0.006	Methyltransferase-like protein 24 Wald ratio 1 0.676 0.319 1.033	0.031
phosphatase 1     NAQDPH dehydrogenase [quinone] 1     Wald ratio     1     0.733     0.499     0.967     0.005       Neuronal growth regulator 1     Wald ratio     1     0.684     0.305     1.063     0.045       Neuronal growth regulator 1     Wald ratio     1     0.453     1.130     1.775     0.025       Neurochrimin     Wald ratio     1     0.453     1.130     0.339     1.013     0.036       N-terminal pro-BNP     Wald ratio     1     0.776     0.586     0.974     0.011       N-terminal pro-bormone of brain     IVW     2     0.705     0.457     0.952     0.000       Otat first protein homolog     Wald ratio     1     0.511     0.106     0.916     0.001       Ike receptor     Otat first protein homolog     Wald ratio     1     0.464     0.375     0.992     0.016       Protini disulfide-isomerase A3     Wald ratio     1     1.494     1.129     1.899     0.037       Protein idsuufide-isomerase A3     Wald ratio     1     1.045     0.922		0.003
NADP     Hehydrogenase [quinone]     Wald ratio     1     0.733     0.499     0.967     0.005       Neuronal growth regulator     Wald ratio     1     0.684     0.305     1.063     0.044       Neurothinin     Wald ratio     1     0.429     0.702     0.955     0.004       Non-secretory ribonuclease     Wald ratio     1     0.766     0.539     1.013     0.305       Non-secretory ribonuclease     Wald ratio     1     0.776     0.558     0.074     0.012       N-terminal pro-BNP     Wald ratio     1     0.781     0.585     0.004     0.016     0.001       Osteoclast-associated immunoglobulin-     Wald ratio     1     0.661     0.735     0.987     0.016       Out at first protein homolog     Wald ratio     1     0.861     0.735     0.992     0.016       Poly(U)-specific endoribonuclease     Wald ratio     1     0.684     0.375     0.992     0.016       Protein fAM3D     Wald ratio     1     0.651     0.405     0.897     6E-04		0.041
Neurotrimin     Wald ratio     1     0.829     0.702     0.955     0.004       NKG2D ligand 3     Wald ratio     1     1.453     1.130     1.775     0.023       Non-secretory ribonuclease     Wald ratio     1     0.776     0.539     1.013     0.036       N-terminal pro-BNP     Wald ratio     1     0.776     0.556     0.974     0.012       N-terminal pro-BNP     Wald ratio     1     0.757     0.952     0.006       Oxteoclast-associated immunoglobulin- inktruetic peptide     Wald ratio     1     0.861     0.735     0.987     0.012       Out at first protein homolog     Wald ratio     1     0.684     0.375     0.992     0.016       Protein disulfide-isomerase A3     Wald ratio     1     0.684     0.375     0.992     0.016       Protein idsulfide-isomerase A3     Wald ratio     1     0.494     1.129     1.839     0.031       Protein idsulfide-isomerase A3     Wald ratio     1     1.494     1.349     0.026       Ras-related protein Rab-35     Wald		0.009
NKG2D ligand 3   Wald ratio   1   1.453   1.130   1.775   0.023     Non-secretory ribonuclease   Wald ratio   1   0.776   0.539   1.013   0.036     N-terminal pro-BNP   Wald ratio   1   0.78   0.586   0.974   0.012     N-terminal prohormone of brain   IVW   2   0.705   0.457   0.952   0.006     Osteoclast-associated immunoglobulin-   Wald ratio   1   0.511   0.106   0.916   0.001     Out at first protein homolog   Wald ratio   1   0.861   0.735   0.987   0.013     Peptidyl-prolyl cis-trans isomerase-like   IVW   2   1.219   1.027   1.410   0.043     Poly(U)-specific endoribonuclease   Wald ratio   1   0.684   0.375   0.992   0.016     Protein disulfide-isomerase A3   Wald ratio   1   1.494   1.129   1.859   0.031     Protein FAM3D   Wald ratio   1   0.061   0.75   0.386   0.046     Pyruvate kinase PKLR   Wald ratio   1   1.237   1.050   1.425		0.049
N-terminal pro-BNP     Wald ratio     1     0.78     0.586     0.974     0.012       N-terminal prohormone of brain natrivetic peptide     IVW     2     0.705     0.457     0.952     0.006       Osteoclast-associated immunoglobulin- like receptor     Wald ratio     1     0.511     0.106     0.916     0.001       Out at first protein homolog     Wald ratio     1     0.861     0.735     0.987     0.013       Peptidyl-prolyl cis-trans isomerase-like     IVW     2     1.219     1.027     1.410     0.043       1     0.484     0.375     0.992     0.016     0.014     1     1.494     1.129     1.859     0.031       Protyl(J)-specific endoribonuclease     Wald ratio     1     1.044     1.129     1.859     0.031       Protein disulfide-isomerase A3     Wald ratio     1     1.075     1.349     0.006       Protein FAM3D     Wald ratio     1     1.097     1.006     1.188     0.446       Pyruvate kinase PKLR     Wald ratio     1     1.405     1.200		0.023
N-terminal prohormone of brain natriuretic peptide     IVW     2     0.705     0.457     0.952     0.006       Osteoclast-associated immunoglobulin- like receptor     Wald ratio     1     0.511     0.106     0.916     0.016       Out at first protein homolog     Wald ratio     1     0.861     0.735     0.987     0.013       Peptidyl-protyl cis-trans isomerase-like     IVW     2     1.219     1.027     1.410     0.043       Poly(U)-specific endoribonuclease     Wald ratio     1     0.684     0.375     0.992     0.016       Protein disulfide-isomerase A3     Wald ratio     1     1.494     1.129     1.859     0.031       Protein rAM3D     Wald ratio     1     1.049     1.129     1.849     0.006       Protein FAM3D     Wald ratio     1     0.071     0.388     1.014     0.026       Ras-related protein Rab-35     Wald ratio     1     1.425     0.026       Sarcoplasmic/endoplasmic reticulum     Wald ratio     1     1.405     1.405     0.026       Semaphorin-4C     <		0.036
Osteoclast-associated immunoglobulin- like receptor     Wald ratio     1     0.511     0.106     0.916     0.001       Out at first protein homolog     Wald ratio     1     0.861     0.735     0.987     0.018       Peptidyl-prolyl cis-trans isomerase-like     IVW     2     1.219     1.027     1.410     0.043       1     Poly(U)-specific endoribonuclease     Wald ratio     1     0.684     0.375     0.992     0.016       Protein disulfide-isomerase A3     Wald ratio     1     1.494     1.129     1.859     0.031       Protein eva-1 homolog C     IVW     2     1.212     1.075     1.349     0.006       Protein FAM3D     Wald ratio     1     0.701     0.388     1.014     0.026       Sarcoplasmic/endoplasmic reticulum     Wald ratio     1     0.405     0.897     6E-04       Secreted frizzled-related protein 2     Wald ratio     1     1.400     1.103     1.696     0.026       Semphorin-4C     Wald ratio     1     1.456     1.220     1.790     0.006	N-terminal prohormone of brain IVW 2 0.705 0.457 0.952	0.012
like receptor     Out at first protein homolog   Wald ratio   1   0.861   0.735   0.987   0.019     Peptidyl-prolyl cis-trans isomerase-like   IVW   2   1.219   1.027   1.410   0.043     1   Poly(U)-specific endoribonuclease   Wald ratio   1   0.684   0.375   0.992   0.016     Protein disulfide-isomerase A3   Wald ratio   1   1.494   1.129   1.859   0.031     Protein eva-1 homolog C   IVW   2   1.212   1.036   1.889   0.046     Pyruvate kinase PKLR   Wald ratio   1   0.097   1.006   1.188   0.042     Ras-related protein Rab-35   Wald ratio   1   0.701   0.388   1.014   0.026     Sarcoplasmic/endoplasmic reticulum   Wald ratio   1   0.405   0.887   6E-04     Calcium ATPase 3   Secreted frizzled-related protein 2   Wald ratio   1   1.400   1.103   1.696   0.026     Semaphorin-4C   Wald ratio   1   1.405   1.200   1.790   0.006     Spondin-1   Wald ratio		0.001
Peptidyl-prolyl cis-trans isomerase-like     IVW     2     1.219     1.027     1.410     0.043       1     Poly(U)-specific endoribonuclease     Wald ratio     1     0.684     0.375     0.992     0.016       Protein disulfide-isomerase A3     Wald ratio     1     1.494     1.129     1.859     0.031       Protein eva-1 homolog C     IVW     2     1.212     1.075     1.349     0.006       Protein FAM3D     Wald ratio     1     0.071     0.388     1.014     0.026       Ras-related protein Rab-35     Wald ratio     1     0.701     0.388     1.014     0.026       Sarcoplasmic/endoplasmic reticulum     Wald ratio     1     0.651     0.405     0.897     6E-04       Calcium ATPase 3     Secreted frizzled-related protein 2     Wald ratio     1     1.495     1.200     1.790     0.006       Semaphorin-4C     Wald ratio     1     1.495     1.200     1.790     0.006       Sialic acid-binding Ig-like lectin 14     IVW     2     1.069     1.008     1.129	like receptor	
Poly(U)-specific endoribonuclease   Wald ratio   1   0.684   0.375   0.992   0.016     Protein disulfide-isomerase A3   Wald ratio   1   1.494   1.129   1.859   0.031     Protein eva-1 homolog C   IVW   2   1.212   1.075   1.349   0.006     Protein FAM3D   Wald ratio   1   1.097   1.006   1.188   0.046     Pyruvate kinase PKLR   Wald ratio   1   0.701   0.388   1.014   0.026     Ras-related protein Rab-35   Wald ratio   1   1.237   1.050   1.425   0.026     Sarcoplasmic/endoplasmic reticulum   Wald ratio   1   0.405   0.897   6E-04     Calcium ATPase 3   Wald ratio   1   1.405   1.200   1.790   0.006     Sernet frizzled-related protein 2   Wald ratio   1   1.495   1.200   1.790   0.006     Semaphorin-4C   Wald ratio   1   1.456   1.125   1.788   0.026     Sialic acid-binding Ig-like lectin 14   IVW   2   1.069   1.008   1.129   0.014  S	Peptidyl-prolyl cis-trans isomerase-like IVW 2 1.219 1.027 1.410	0.019 0.043
Protein disulfide-isomerase A3   Wald ratio   1   1.494   1.129   1.859   0.031     Protein eva-1 homolog C   IVW   2   1.212   1.075   1.349   0.006     Protein FAM3D   Wald ratio   1   1.097   1.006   1.188   0.046     Pyruvate kinase PKLR   Wald ratio   1   0.701   0.388   1.014   0.026     Ras-related protein Rab-35   Wald ratio   1   1.237   1.050   1.425   0.026     Sarcoplasmic/endoplasmic reticulum   Wald ratio   1   0.651   0.405   0.897   6E-04     calcium ATPase 3   Secreted frizzled-related protein 2   Wald ratio   1   1.400   1.103   1.696   0.026     Semaphorin-4C   Wald ratio   1   1.400   1.103   1.696   0.026     Sialic acid-binding lg-like lectin 14   IVW   2   1.069   1.008   1.129   0.31     Spondin-1   Wald ratio   1   1.456   1.125   1.788   0.026     Spondin-1   Wald ratio   1   1.456   1.125   1.841   0.006 </td <td></td> <td>0.016</td>		0.016
Protein FAM3D   Wald ratio   1   1.097   1.006   1.188   0.046     Pyruvate kinase PKLR   Wald ratio   1   0.701   0.388   1.014   0.026     Ras-related protein Rab-35   Wald ratio   1   1.237   1.050   1.425   0.026     Sarcoplasmic/endoplasmic reticulum   Wald ratio   1   0.651   0.405   0.897   6E-04     Secreted frizzled-related protein 2   Wald ratio   1   1.400   1.103   1.696   0.026     Semaphorin-4C   Wald ratio   1   1.400   1.103   1.696   0.026     Seine/threonine-protein kinase 16   Wald ratio   1   1.495   1.200   1.790   0.006     Sialic acid-binding lg-like lectin 14   IVW   2   1.069   1.038   1.129   0.031     Spondin-1   Wald ratio   1   1.456   1.125   1.788   0.006     Testis-expressed sequence 29 protein   Wald ratio   1   1.231   1.082   1.381   0.004     median   1   1.231   1.023   1.379   0.044     Test	Protein disulfide-isomerase A3 Wald ratio 1 1.494 1.129 1.859	0.031
Pyruvate kinase PKLR   Wald ratio   1   0.701   0.388   1.014   0.026     Ras-related protein Rab-35   Wald ratio   1   1.237   1.050   1.425   0.026     Sarcoplasmic/endoplasmic reticulum calcium ATPase 3   Wald ratio   1   0.651   0.405   0.897   6E-04     Secreted frizzled-related protein 2   Wald ratio   1   1.400   1.103   1.696   0.026     Semaphorin-4C   Wald ratio   1   1.400   1.103   1.696   0.026     Serine/threonine-protein kinase 16   Wald ratio   1   1.495   1.200   1.790   0.006     Sialic acid-binding lg-like lectin 14   IVW   2   1.069   1.008   1.129   0.031     Spondin-1   Wald ratio   1   1.314   1.046   1.582   0.046     Testis-expressed sequence 29 protein   Weighted ratio   1   1.314   1.046   1.582   0.046     Testis-expressed sequence 29 protein   IVW   3   1.196   1.041   1.350   0.024     Trypsin-2   IVW   2   0.848   0.687   1.010		0.006
Sarcoplasmic/endoplasmic reticulum   Wald ratio   1   0.651   0.405   0.897   6E-04     Secreted frizzled-related protein 2   Wald ratio   1   1.400   1.103   1.696   0.026     Semaphorin-4C   Wald ratio   1   1.495   1.200   1.790   0.006     Serine/threonine-protein kinase 16   Wald ratio   1   1.456   1.125   1.788   0.026     Sialic acid-binding Ig-like lectin 14   IVW   2   1.069   1.008   1.129   0.031     Spondin-1   Wald ratio   1   1.231   1.082   1.381   0.006     Testican-2   Wald ratio   1   1.314   1.046   1.582   0.046     Testis-expressed sequence 29 protein   Weighted median   3   1.201   1.023   1.379   0.043     Trypsin-2   IVW   3   1.196   1.041   1.350   0.024     Tumor necrosis factor receptor superfamily member 6   Wald ratio   1   1.279   1.124   1.434   0.002     Xaa-Pro aminopeptidase 2   Wald ratio   1   1.542   1.21   1.874		0.040
calcium ATPase 3     Secreted frizzled-related protein 2   Wald ratio   1   1.400   1.103   1.696   0.026     Semaphorin-4C   Wald ratio   1   1.495   1.200   1.790   0.008     Serine/threonine-protein kinase 16   Wald ratio   1   1.495   1.200   1.790   0.026     Sialic acid-binding Ig-like lectin 14   IVW   2   1.069   1.008   1.129   0.031     Spondin-1   Wald ratio   1   1.231   1.082   1.381   0.006     Testican-2   Wald ratio   1   1.314   1.046   1.582   0.043     Testis-expressed sequence 29 protein   Weighted median   3   1.201   1.023   1.379   0.043     Trypsin-2   IVW   3   1.196   1.041   1.350   0.024     Tumor necrosis factor receptor superfamily member 6   Wald ratio   1   1.279   1.124   1.434   0.002     Xaa-Pro aminopeptidase 2   Wald ratio   1   1.542   1.21   1.874   0.011		0.046 0.026
Semaphorin-4C   Wald ratio   1   1.495   1.200   1.790   0.008     Serine/threonine-protein kinase 16   Wald ratio   1   1.456   1.125   1.788   0.026     Sialic acid-binding lg-like lectin 14   IVW   2   1.069   1.008   1.129   0.031     Spondin-1   Wald ratio   1   1.231   1.082   1.381   0.006     Testican-2   Wald ratio   1   1.314   1.046   1.582   0.046     Testis-expressed sequence 29 protein   Weighted median   3   1.201   1.023   1.379   0.043     Testis-expressed sequence 29 protein   IVW   3   1.196   1.041   1.350   0.024     Trypsin-2   IVW   2   0.848   0.687   1.010   0.046     Tumor necrosis factor receptor superfamily member 6   Wald ratio   1   1.279   1.124   1.434   0.002     Xaa-Pro aminopeptidase 2   Wald ratio   1   1.542   1.21   1.874   0.011	calcium ATPase 3	0.026 0.026
Serine/threonine-protein kinase 16   Wald ratio   1   1.456   1.125   1.788   0.026     Sialic acid-binding lg-like lectin 14   IVW   2   1.069   1.008   1.129   0.031     Spondin-1   Wald ratio   1   1.231   1.082   1.381   0.006     Testican-2   Wald ratio   1   1.314   1.046   1.582   0.046     Testis-expressed sequence 29 protein   Weighted median   3   1.201   1.023   1.379   0.043     Testis-expressed sequence 29 protein   IVW   3   1.196   1.041   1.350   0.024     Trypsin-2   IVW   2   0.848   0.687   1.010   0.046     Tumor necrosis factor receptor superfamily member 6   Wald ratio   1   1.279   1.124   1.434   0.002     Xaa-Pro aminopeptidase 2   Wald ratio   1   1.542   1.21   1.874   0.011	·	0.026 0.026 6E-04
Spondin-1   Wald ratio   1   1.231   1.082   1.381   0.006     Testican-2   Wald ratio   1   1.314   1.046   1.582   0.046     Testis-expressed sequence 29 protein   Weighted median   3   1.201   1.023   1.379   0.043     Testis-expressed sequence 29 protein   IVW   3   1.196   1.041   1.350   0.024     Trypsin-2   IVW   2   0.848   0.687   1.010   0.046     Tumor necrosis factor receptor superfamily member 6   Wald ratio   1   1.279   1.124   1.434   0.002     Xaa-Pro aminopeptidase 2   Wald ratio   1   1.542   1.21   1.874   0.011		0.026 0.026 6E-04 0.026
Testican-2   Wald ratio   1   1.314   1.046   1.582   0.046     Testis-expressed sequence 29 protein   Weighted median   3   1.201   1.023   1.379   0.043     Testis-expressed sequence 29 protein   IVW   3   1.196   1.041   1.350   0.024     Trypsin-2   IVW   2   0.848   0.687   1.010   0.046     Tumor necrosis factor receptor superfamily member 6   Wald ratio   1   1.279   1.124   1.434   0.002     Xaa-Pro aminopeptidase 2   Wald ratio   1   1.542   1.21   1.874   0.011		0.026 0.026 6E-04
Testis-expressed sequence 29 proteinWeighted median31.2011.0231.3790.043Testis-expressed sequence 29 proteinIVW31.1961.0411.3500.024Trypsin-2IVW20.8480.6871.0100.046Tumor necrosis factor receptor superfamily member 6Wald ratio11.2791.1241.4340.002Xaa-Pro aminopeptidase 2Wald ratio11.5421.211.8740.011		0.026 0.026 6E-04 0.026 0.008 0.026 0.031
Testis-expressed sequence 29 protein   IVW   3   1.196   1.041   1.350   0.024     Trypsin-2   IVW   2   0.848   0.687   1.010   0.046     Tumor necrosis factor receptor superfamily member 6   Wald ratio   1   1.279   1.124   1.434   0.002     Xaa-Pro aminopeptidase 2   Wald ratio   1   1.542   1.21   1.874   0.011	Testis-expressed sequence 29 protein Weighted 3 1.201 1.023 1.379	0.026 0.026 6E-04 0.026 0.008 0.026
Tumor necrosis factor receptorWald ratio11.2791.1241.4340.002superfamily member 6Xaa-Pro aminopeptidase 2Wald ratio11.5421.211.8740.011		0.026 0.026 6E-04 0.026 0.008 0.026 0.031 0.006
superfamily member 6 Xaa-Pro aminopeptidase 2 Wald ratio 1 1.542 1.21 1.874 0.011		0.026 0.026 6E-04 0.026 0.008 0.026 0.031 0.006 0.046
		0.026 0.026 6E-04 0.026 0.008 0.026 0.031 0.006 0.046 0.043 0.024 0.024
Zinc-alpha-2-glycoprotein IVW 2 1.31 1.107 1.512 0.009		0.026 0.026 6E-04 0.026 0.008 0.026 0.031 0.006 0.046 0.043 0.024 0.046 0.002

Significant results after Bonferroni correction with  $P<1.98\times10^{-5}$  [0.05/(1,263×2)]. Suggestive associations (1.98×10<sup>-5</sup><P<0.05). Susceptibility: COVID vs. population (C2); severity: hospitalized COVID vs. population (B2).