Supplementary Methods

Healthy controls

Healthy controls were recruited in Australia during 2013 – 2015. Criteria for recruitment of healthy controls were as follows; (1) older than eighteen years old, (2) no prior or current history of significant medical conditions, (3) no recent influenza vaccination in the preceding three months and (4) no recent history of flu-like illness. The *IFI27* levels in healthy volunteers were used as baseline expression level to compare against patient samples. These *IFI27* baseline levels were first determined in the healthy volunteers in the discovery cohort (n=18) and subsequently validated in two additional groups of healthy volunteers (first cohort n=37, second cohorts n=85).

Discovery Cohorts

The discovery cohorts consisted of three case-control studies (Supplementary Table S1). Two studies were multi-center studies (Australia and Canada) and one was a single-center study (Germany). In the Australian and Canadian cohorts, all patients had the following features; (1) influenza virus infection confirmed by rapid-antigen assay or viral PCR performed on nasopharyngeal samples/bronchoalveolar lavage, (2) admission to intensive care unit. In the German cohort, all patients had the following features; (1) influenza virus infection confirmed by rapid-antigen assay/viral PCR performed on nasopharyngeal samples, (2) admission to hospital. The Australian and Canadian cohorts consisted of severely infected patients because 90% patients developed respiratory failure which required mechanical ventilation. The German cohort consisted of moderately to severely infected patients because only 17% patients received mechanical ventilation (Supplementary Table S1).

In all cohorts, a blood sample (2.5ml) was collected at the time of enrolment into the study. The sample was placed into PAXgene Blood RNA tubes (BD systems, NJ, USA) and was kept in storage at -20°C. RNA extraction was later performed using the standard protocol (PAXgene^{TM} Blood RNA kit - Qiagen). Microarray analysis was performed in two cohorts (Australia and Germany). Quantitative real-time PCR of the *IFI27* gene (described below) was performed in all three cohorts.

In the Australian cohort, two additional groups of patients were included. They included (1) patients with severe community acquired pneumonia caused by bacterial pathogens (2) patients with systemic inflammatory response syndrome (SIRS). The SIRS patients were recruited from patients who fulfilled at least two of the four established SIRS criteria: (a) fever or hypothermia (temperature >38 degree Celsius [100.4-F] or <36 degree Celsius [96.8]); (b) tachycardia (>90 beats/min); (c) tachypnea (>20 breaths/min or $PaCO_2$ < 32 mmHg [4.3 kPa]) or the need for mechanical ventilation; (d) an altered white blood cell count of more than 12,000 cells/L, less than 4,000 cells/L, or the presence of more than 10% band forms. The recruited SIRS patients consisted of patients who had surgery, trauma, pancreatitis, cardiac and pulmonary conditions. None of the SIRS patients had evidence of infection, based on results from microbiological cultures (blood, urine, respiratory samples).

Prospective Validation Cohort

In this cohort, thirty-seven healthy volunteers and 402 patients were prospectively and consecutively recruited in a multicenter study during 2012 – 2016. Eligible patients included

adult patients (>18 years) who (1) presented with 'influenza-like' illness (see below), or (2) were assessed by clinicians to have a high likelihood of influenza infection.

Inclusion criteria

To be eligible, the patient needed to have at least one symptom from two or more symptoms categories. The symptom categories are as follows;

(1) Fever
(2) Constitutional symptoms (chill, headache, muscle ache)
(3) Respiratory symptoms (cough, sore throat, nasal congestion, dyspnea)

Blood sample

Venous blood was collected and placed into PAXgene as described above. RNA extraction was performed as per manufacturer's protocol. *IFI27* gene-expression was measured by quantitative real-time PCR (described below). Researchers who performed PCR assays were blinded to information regarding patient data or etiological diagnoses.

Microbiological investigation

Nasopharyngeal, sputum, urine and blood samples were obtained at admission. These samples were sent for standard microbiological testing including sputum Gram stain and culture, blood culture. In addition, urinary antigen test for *Streptococcus pneumoniae* was also performed. In patients admitted to intensive care unit, additional respiratory samples were obtained from bronchoalveolar lavage or tracheal aspirates. In addition to standard microbiological tests, testing for atypical respiratory pathogens (*Chlamydophila pneumoniae*, *Mycoplasma pneumoniae* and *Legionella pneumonphila*) was also performed in selected patients at the discretion of treating physicians. Respiratory viruses were tested in all patients using nucleic acid PCR in respiratory samples including sputum, nasopharyngeal or bronchoalveolar lavage (for patients in intensive care units). The PCR panel tested for influenza A, influenza B, respiratory syncytial virus, rhinovirus, parainfluenza virus and human metapneumovirus.

Follow-up

All patients were followed up on study completion. Researchers retrieved relevant information from medical records using a pre-specified data collection form including outcomes, laboratory results, treatments and microbiological reports. Telephone follow-up was performed where information was incomplete. Researchers who performed the follow-up were blinded to the *IFI27* levels or the results of the microarray analysis.

Biomarker

Whole blood sample was collected from each participant within 24 hours of presentation/admission to the hospital. Blood samples were placed into PAXgene tubes, a sample collection system commonly used for gene-expression measurement in clinical studies. Gene-expression measurements were by microarray analysis and PCR assay. In the discovery cohorts, microarray analysis was used initially and its finding was subsequently validated on PCR assay (Figure 1). In all studies, researchers who measured the biomarker level (either by PCR assays or microarray analyses) were blinded to the phenotype information (e.g. patient data or laboratory results). Similarly, researchers who collected the phenotype information or clinicians who recruited the study participants were blind to the

results of the PCR assays or microarray analyses. Detailed information on biomarker measurements (PCR assay and microarray analysis) is provided below.

Microarray analyses

Microarray analysis was performed by two teams (Australia and Germany). Each team used different microarray platforms and performed the analysis independently. Result from the German team is presented in Figure 2A and result from the Australian team is presented in Supplementary Figure S1. Findings from these two analyses were in agreement with each other.

German cohort: The integrity of the total RNA was first evaluated on a 2100 Bioanalyzer (Agilent Technologies; Waldbronn, Germany) to ensure optimal RNA quality. After this, 100 ng of total RNA were applied for Cy3-labelling reaction using the one color Quick Amp Labeling protocol (Agilent Technologies; Waldbronn, Germany). Labeled cRNA was hybridized to Agilent 8x60k Human V3 (Design ID: 072363) microarrays for 16 hours at 68°C and scanned using the Agilent DNA Microarray Scanner. Microarray data were then analyzed using the R software package.[22] Pre-processing steps included background correction, quantile normalization and annotation using the limma package and Agi4x44PreProcess.[23] Multi-group comparisons and identification of differentially expressed probe sets were performed using Benjamini and Hochberg correction for multiple testing.[24] Differentially expressed genes were identified based on an adjusted p-value of < 0.05 and exhibiting more than a two-fold difference in expression levels ($[\log^2]>1$). Pathway analysis was performed using Reactome enrichment analysis in R package (ReactomePA provided in the R package cluster profiler).[25]

Australian cohort: Before the microarray analysis, RNA quality was analyzed using a Agilent Bioanalyser to ensure optimal quality of samples. After this, sample amplification and labeling was carried out on 200ng of total RNA using an Illumina TotalPrep Amplification kit, in batches of 24 samples at a time (Ambion, Austin, TX). Amplified cRNA was assessed using the Agilent Bioanalyser, to ensure satisfactory amplification. The samples (750ng of each sample) were then immediately hybridized onto HT-12_v3_BeadChips. The hybridization and washing procedure was identical for each set of arrays processed and, after normalization, no significant batch effects were identified. Prior to analysis, each probe on the array was passed through a filter requiring a detection p-value of less than 0.0050 in at least one sample to be included in any further analyses. Of the 48,804 probes present on the Illumina HT 12 array, 24840 probes (henceforth referred to as genes) passed this criterion. Genes which passed the filtering were loaded into BRB ArrayTools where quantile normalisation and log transformation of the data was applied. Genes with low variance across all samples, defined to be less than the median, were removed from the dataset. P-values were adjusted for multiple testing using the Benjamani and Hochberg False Discovery Rate (FDR) method.[24] A FDR of 5% was used as the cut-off for genes deemed to be differentially expressed between the two classes. Pathway analysis was performed using Gene Set Enrichment Analysis.[23]

Data and materials availability: Microarray data generated in this study has been deposited in the NCBI Gene Expression Omnibus (GSE82050, GSE74077, GSE40012). This study also used microarray data from existing data sets (GSE6269, GSE42026, GSE68310 and GSE60244).

Quantitative real-time PCR

Quantitative real-time PCR was performed in discovery cohorts, the prospective validation cohort and all *in vitro* experiments.

The primers used for measurement of *IFI27* gene-expression level were:

5'-ACCTCATCAGCAGTGACCAGT-3' (forward),

5'-ACATCATCTTGGCTGCTATGG-3' (reverse).

cDNA was synthesized from RNA using qScript cDNA SuperMix (Quanta BioSciences) according to the manufacturer's protocol. Assays were run on a Rotor- Gene 3000 or 6000 platform (Qiagen) using the SYBR green protocol. All samples were normalized to GAPDH. Single PCR products were confirmed by both melt curve analysis and by observation of a single product when run on an ethidium bromide stained 2% agarose gel (Sigma-Aldrich) and visualized by Gel Doc EZ Imager (Bio Rad laboratories, Australia).

***In vitro* experiments**

We performed *in vitro* experiments to gain insight into the biology of the biomarker. In these experiments, we investigated immune cell subsets including monocytes, natural killer (NK) cells, B cells, plasmacytoid dendritic cells, myeloid dendritic cells, neutrophils, CD4 and CD8 lymphocytes. In each immune cell subset, we measured the biomarker response to different pathogens (e.g. virus vs. bacteria) and to activation of toll-like receptor (TLR), a pathogen recognition pathway used by immune cells to recognize virus and bacteria.

Isolation of immune cell subsets

Human cell types (monocytes, NK cells, B cells, pDCs, mDCs, $CD4^+$, $CD8^+$ T-cells and neutrophils) were purified from whole PBMCs. To isolate PBMC, 35ml of whole blood was loaded on 15ml of Ficoll in 50ml Falcon tubes and centrifuged at 400 x g for 30 min at 20^{o}C, with the brake off. The white layer located at the interface was extracted carefully and put into new Falcon tubes. The isolated PBMCs were washed twice with Dulbecco's Phosphate Buffer Saline without Ca^{2+} or Mg^{2+} (DPBS; Lonza, Walkersville, MD, USA). The number of nucleated cells was determined by staining with crystal violet. We used culture medium consisting of Gibco RPMI 1640 medium (Life Technologies, Australia Pty Ltd) supplemented with 10% fetal bovine serum (FBS; SAFC Biosciences, Victoria, Australia) 50 IU/ml penicillin, 50 µg/ml streptomycin and 2 mM L-glutamine. All cultured cells were maintained at 37^{o}C in a humidified atmosphere of 5% CO_2.

Isolation of Monocytes: Monocytes were isolated from fresh human PBMCs using EasySep Human Monocytes Enrichment Kit (negative selection-STEMCELL Technologies, Australia) by following the manufacturer's instructions. The kit depletes a small subset of CD+16 monocytes. Cells were fluorescently stained with CD14-FITC and analyzed by flow cytometry. The purity was always more than 92%.

Isolation of Natural Killer cells (NK cells): Natural killer cells were isolated from human PBMCs using EasySep human NK cell enrichment kit (negative selection-STEMCELL Technologies, Australia). The kit enriches NK cells by depletion of non-NK cells. Purity of NK cells was measured by flow cytometry after staining with CD56-PE.Cy7 and CD3-FITC. The purity was always more than 94%.

Isolation of B cells: B cells were enriched to >98% purity (CD19+) by magnetic cell separation (negative selection) using a Human B Cell Enrichment Kit (STEMCELL Technologies, Australia). The purity was always more than 90%.

Isolation of Myeloid Dendritic Cell (mDCs): mDCs were isolated from human PBMCs using the Myeloid Dendritic Cell Isolation Kit (negative selection, Miltenyi Biotec, N.S.W., Australia). mDCs are isolated by depletion of non-mDCs. Non-mDCs were indirectly magnetically labeled with a cocktail of biotin-conjugated antibodies before addition of

antibiotin-conjugated microbeads as a secondary labeling reagent. The magnetically labeled non-mDCs were depleted by retaining these cells on a MACS column. The unlabeled mDCs pass through the column. Cells were fluorescently stained with CD141 (BDCA-3)- FITC, CD1c (BDCA-1)- APC and analyzed by flow cytometry. The purity was more than 90%.

Isolation of Plasmacytoid Dendritic Cells (pDCs): pDCs were isolated from human PBMCs using EasySep Human plasmacytoid DC Enrichment Kit (negative selection-STEMCELL Technologies, Vic, Australia). The kit enriches pDCs from PBMCs by depletion of non-pDCs. Cells were fluorescently stained with CD304 (BDCA-4)-APC and HLA-DR- PerCP and analyzed by flow cytometry. The purity was always more than 92%.

Isolation of CD4+ T cells: CD4+ T cells were freshly isolated by negative selection (STEMCELL Technologies, Australia) according to the protocol provided by the manufacturer. The purity of CD3+/CD4+ T cells was ≥96%.

Isolation of CD8+ T cells: $CD8^+$ T cells were isolated by CD8 negative selection using the EasySep CD8 enrichment kit (STEMCELL Technologies, Australia). Purity of the CD3+/$CD8^+$ T cells was verified by flow cytometry (>95%).

Isolation of Neutrophils: A total of 10 to 20 mL human blood was obtained from healthy donors using heparin to prevent clotting. All subsequent steps were performed at 4°C or on ice. The blood was diluted 1:1 with Hank's Balanced Salt Solution (HBSS; Life Technologies, Victoria, Australia) containing 2% Dextran T500 (Pharmacia) and incubated for 30 minutes to sediment red blood cells. The upper phase was transferred to a new tube and density fractionated using Ficoll-Paque^{TM}PLUS (GE HealthCare, Australia and NZ). Neutrophils were recovered from the pellet and mononuclear cells were recovered from the interface. The pellet was transferred to a new tube and re-suspended in RBC lysis buffer (150mM ammonium Chloride, 1mM potassium bicarbonate, 0·1mM EDTA, pH 7·2) and then washed with RPMI 1640 supplemented with 10% low-endotoxin fetal bovine serum (FBS) and antibiotics. Typical recovery was three to five million neutrophils per milliliter of collected blood. Purity was more than 92%. Neutrophils were isolated before each experiment and used immediately.

Cell stimulation assay

Pure cell populations were re-suspended in RPMI 1640 containing 10% FBS, 2mM L-glutamine, 50 IU/ml penicillin, and 50µg/ml streptomycin at the density of 1-2x10^6 cells per ml. To determine the effect that different concentrations of stimulators have on *IFI27* expression, cells were incubated for 6, 12, and 24 hours at 37^{o}C with different concentrations of stimulators in media. For all treatments, a dose response was performed to define optimal stimulating conditions. Stimulators were used at the following concentrations unless otherwise noted: interferon alpha (IFNa:Roche products Pty limited, NSW, Australia); 10^3 U/ml, FluVax vaccine (CSL limited, Victoria, Australia); 0·225 µg/ml, A/California/7/2009-like (Pandemic H1N1); MOI 0·05, A/Perth/16/2009-like (H3N2) virus; MOI 0·05, B/Wisconsin/1/2010- like (Flu B); MOI 0.05, and human TLR1-9 agonists (InvivoGen, San Diego, CA, USA) which contained the following: TLR1/2, Pam3CSK4; 0.25µg/ml, TLR2, HKLM; 10^6 cells/ml, TLR3, Polyinosinic-polycytidylic acid (poly(I:C); 25 µg/ml, TLR4, lipopolysaccharide (LPS-EK); 1 µg/ml, TLR5, flagellin (FLA-ST); 1 µg/ml, TLR6/2, FSL-1 (Pam2CGDPKHPKSF); 0·1 µg/ml, TLR7, Imiquimod (R837); 0·5 µg/ml, TLR8, ssRNA40; 1µg/ml, and TLR9, CpG ODNs, 5µM. Cell viability before and after stimulation was measured by the method of Trypan blue exclusion (Sigma-Aldrich, St Louis, MO, USA).

Mouse infection

To validate the biomarker expression in an *in vivo* setting, we conducted mouse experiments

using Collaborative Cross strains, a well-established model in influenza research. In these experiments, we used virus strains known to cause different degree of infection severity, including PWK/PhJ strain (mild infection), C57BL/6J & 129S1/SvImJ strain (intermediate infection) and CAST/EiJ (severe infection).

The CC founder (C57BL/6J, 129S1/SvlmJ, CAST/EiJ, PWK/PhJ) were purchased from Jackson Laboratories (Bar Harbor, ME) and bred in the animal facility in Helmholtz Centre for Infection Research, Braunschweig, Germany for two to six generations depending on the respective strain. All mice were maintained under specific pathogen free conditions. All experiments in mice were approved by an external committee according to the national guidelines of the animal welfare law in Germany (BGBl. I S. 1206, 1313 and BGBl. I S. 1934). The protocol used in these experiments has been reviewed by an ethics committee (equivalent to US IACUC, according to the German law) and approved by the 'Niedersächsisches Landesamt für Verbraucherschutz und Lebensmittelsicherheit, Oldenburg, Germany' (Permit Numbers: 33.9.42502-04-051/09 and 3392 42502-04-13/1234). Details of the infection protocol and microarray analysis are described elsewhere. (reference: Leist SR,et al. Influenza H3N2 infection of the collaborative cross founder strains reveals highly divergent host responses and identifies a unique phenotype in CAST/EiJ mice. *BMC Genomics* 2016; 17: S73). The array data have been deposited at the gene expression data base GEO (GSE74077).

IFI27 diagnostic threshold

To choose the optimal *IFI27* diagnostic threshold, we used the established method by Metz and Zhou as implemented in the NCSS statistical software (see references below). This method searches for an optimal cut-off value (*IFI27* fold change) over a full range of diagnostic thresholds (10 – 6,000 fold changes). Within this range, each diagnostic threshold was analyzed and a corresponding cost-benefit ratio was computed.

The cost-benefit ratio provides an estimation of the average overall cost of four possible outcomes at each diagnostic threshold: true positive, true negative, false positive and false negative. In the NCSS software, four cost-benefit ratios are used: 0.5, 1.0, 1.5 and 2.0. The ratio 0.5 is used when the clinical decision is driven by a greater need to avoid false negatives (which may lead to missed diagnosis and delayed treatment) over the cost of three other possible outcomes. The ratio 2.0 is used when the clinical decision is driven by a greater need to avoid false positives (which could lead to over diagnosis, unnecessary treatment and drug toxicity) over the cost of three other possible outcomes.

We choose a cost-benefit ratio of 0.5 to reflect a clinical reality that a missed diagnosis could lead to a relatively higher clinical cost (i.e. delayed antiviral treatment, spreading of virus to healthy individuals and an increased risk of developing respiratory complications) compared to other possible outcomes. Based on the method by Metz and Zhou, the optimal diagnostic threshold is the one at which the computed cost-benefit ratio is maximized. In this case, a cost-benefit ratio of 0.5708 corresponds to an optimal diagnostic threshold of 74 fold change (see next page for the list of cutoff values). Diagnostic thresholds that are less than 74 fold change result in a decreasing cost-benefit ratio. Similarly, diagnostic thresholds greater than 74 fold change result in a decreasing cost-benefit ratio. At the 74 fold change, the negative predictive value is 94%, thereby fulfilling our requirement to minimize false negatives without excessively increasing false positives (actual data from 402 patients: 30 false positives, 19 false negatives).

The following conditions were also present in the calculation of the diagnostic threshold;

(1) The minimal interval between successive thresholds was 8.0 (i.e. in the increment of 10, 18, 26, 34, etc.). Computation was not possible for intervals less than 8.0.
(2) The calculation was performed using the empirical (non-parametric) method since the data did not follow a normal distribution.
(3) The diagnostic threshold was optimized in the discovery cohorts (training data) and then it was tested in the prospective validation cohort (test data).

Reference

(1) Metz, C.E. 1978. "Basic principles of ROC analysis." *Seminars in Nuclear Medicine*, Volume 8, No. 4, pages 283-298.
(2) Zhou, X., Obuchowski, N., McClish, D. 2002. *Statistical Methods in Diagnostic Medicine*. John Wiley & Sons, Inc. New York, New Yourk.

***IFI27* cutoff values in differentiating between influenza and bacterial infections**

IFI27 Cutoff Value	Sensitivity	Specificity	Cost - Benefit When Ratio = 0.5000	Cost - Benefit When Ratio = 1.0000	Cost - Benefit When Ratio = 1.5000	Cost - Benefit When Ratio = 2.0000
10.00	0.9175	0.7143	0.5842	0.2509	-0.0825	-0.4158
18.00	0.8969	0.7959	0.6588	0.4207	0.1826	-0.0555
26.00	0.8660	0.7959	0.6279	0.3898	0.1517	-0.0864
34.00	0.8557	0.7959	0.6176	0.3795	0.1414	-0.0967
42.00	0.8557	0.7959	0.6176	0.3795	0.1414	-0.0967
50.00	0.8247	0.7959	0.5866	0.3486	0.1105	-0.1276
58.00	0.8144	0.8163	0.6001	0.3859	0.1716	-0.0427
66.00	0.8144	0.8980	0.6954	0.5763	0.4573	0.3382
74.00	0.8041	0.8980	0.6851	0.5660	0.4470	0.3279
82.00	0.7835	0.8980	0.6645	0.5454	0.4264	0.3073
90.00	0.7629	0.8980	0.6438	0.5248	0.4057	0.2867
98.00	0.7526	0.8980	0.6335	0.5145	0.3954	0.2764
106.00	0.7526	0.9184	0.6573	0.5621	0.4669	0.3716
114.00	0.7423	0.9184	0.6470	0.5518	0.4566	0.3613
122.00	0.7320	0.9184	0.6367	0.5415	0.4462	0.3510
130.00	0.7010	0.9184	0.6058	0.5106	0.4153	0.3201
138.00	0.6598	0.9184	0.5646	0.4693	0.3741	0.2788
146.00	0.6082	0.9184	0.5130	0.4178	0.3225	0.2273
154.00	0.6082	0.9184	0.5130	0.4178	0.3225	0.2273
162.00	0.5979	0.9184	0.5027	0.4075	0.3122	0.2170
170.00	0.5670	0.9184	0.4718	0.3765	0.2813	0.1861
178.00	0.5670	0.9184	0.4718	0.3765	0.2813	0.1861
186.00	0.5464	0.9388	0.4750	0.4035	0.3321	0.2607
194.00	0.5464	0.9388	0.4750	0.4035	0.3321	0.2607
202.00	0.5361	0.9388	0.4647	0.3932	0.3218	0.2504
210.00	0.5258	0.9388	0.4543	0.3829	0.3115	0.2401
218.00	0.5155	0.9388	0.4440	0.3726	0.3012	0.2297
226.00	0.4948	0.9388	0.4234	0.3520	0.2806	0.2091
234.00	0.4845	0.9592	0.4369	0.3893	0.3417	0.2941
242.00	0.4639	0.9592	0.4163	0.3687	0.3211	0.2734
250.00	0.4639	0.9592	0.4163	0.3687	0.3211	0.2734
258.00	0.4227	0.9592	0.3751	0.3274	0.2798	0.2322
266.00	0.4227	0.9592	0.3751	0.3274	0.2798	0.2322
274.00	0.4227	0.9592	0.3751	0.3274	0.2798	0.2322
282.00	0.4124	0.9592	0.3648	0.3171	0.2695	0.2219
290.00	0.4124	0.9592	0.3648	0.3171	0.2695	0.2219
298.00	0.4124	0.9592	0.3648	0.3171	0.2695	0.2219
306.00	0.4124	0.9592	0.3648	0.3171	0.2695	0.2219
314.00	0.4124	0.9592	0.3648	0.3171	0.2695	0.2219
322.00	0.4124	0.9592	0.3648	0.3171	0.2695	0.2219
330.00	0.4124	0.9592	0.3648	0.3171	0.2695	0.2219
338.00	0.4021	0.9592	0.3544	0.3068	0.2592	0.2116
346.00	0.4021	0.9592	0.3544	0.3068	0.2592	0.2116
354.00	0.4021	0.9592	0.3544	0.3068	0.2592	0.2116
362.00	0.3814	0.9592	0.3338	0.2862	0.2386	0.1910
370.00	0.3814	0.9592	0.3338	0.2862	0.2386	0.1910
378.00	0.3814	0.9592	0.3338	0.2862	0.2386	0.1910
386.00	0.3814	0.9592	0.3338	0.2862	0.2386	0.1910
394.00	0.3814	0.9592	0.3338	0.2862	0.2386	0.1910
402.00	0.3814	0.9592	0.3338	0.2862	0.2386	0.1910

(Cut-off values > 402 are not shown due to space limitation).