

Supplementary information

The Serum Profile of Hypercytokinemia Factors Identified in H7N9-Infected

Patients can Predict Fatal Outcomes

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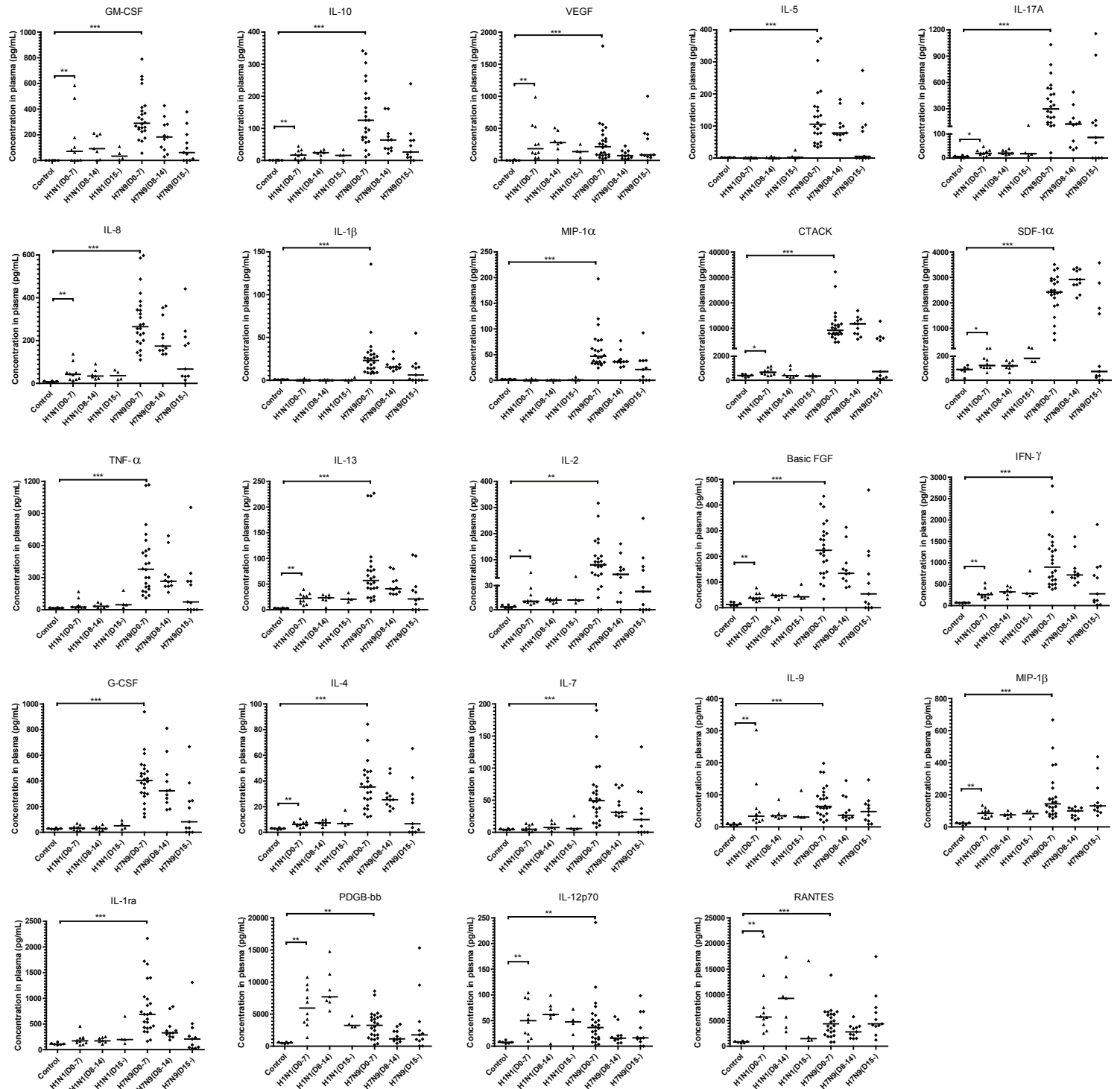
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Supplementary Figure 1

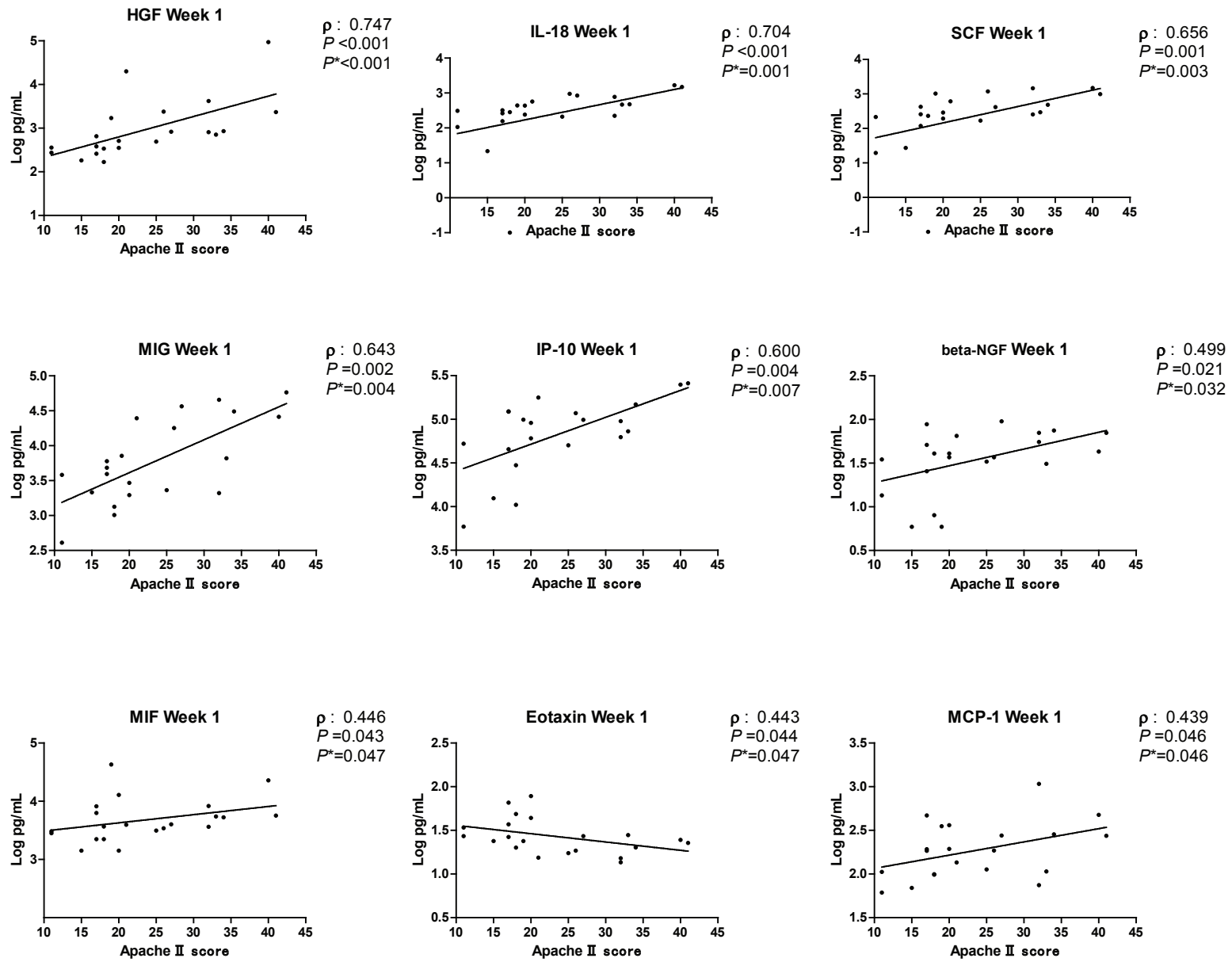


Supplementary Table 1. Cytokine/chemokine Comparison Among 6 healthy controls, 21 H1N1-infected patients and 46 H7N9-infected patients.

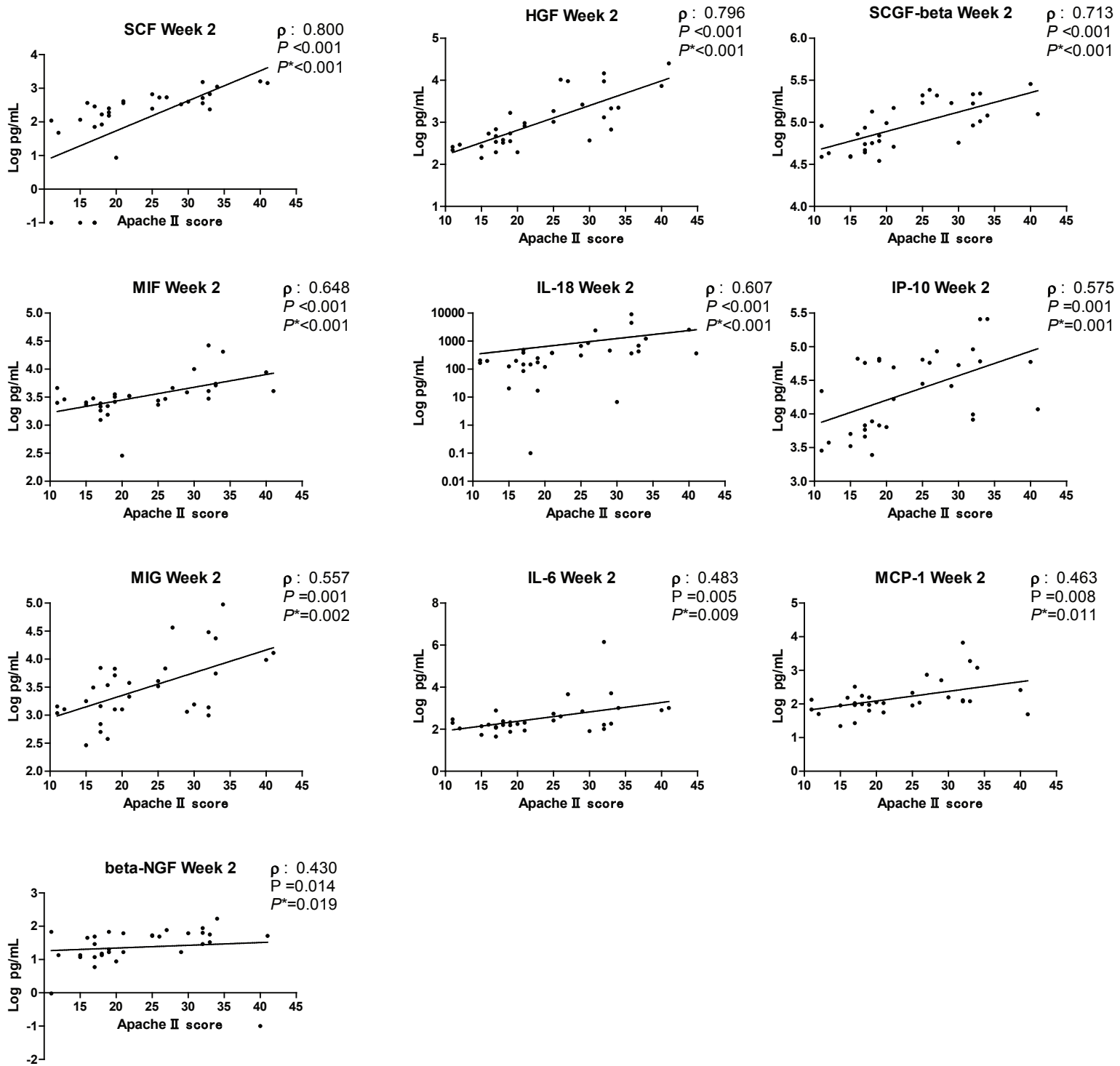
| | Control (n=6) | | H1N1 (n=21) | | | | | | | | | | H7N9 (n=46) | | | | | | | | | | | | | | | | |
|------------|---------------|----------|---------------|----------|----------------|---------------|----------|----------------|--------------|----------|----------------|----------------|----------------|----------------|-----------|----------------|----------------|----------|---------------|----------------|----------|----------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| | | | Day0-7 (n=10) | | | Day8-14 (n=7) | | | Day15- (n=4) | | | | Day0-7 (n=24) | | | Day8-14 (n=11) | | | Day15- (n=11) | | | | | | | | | | |
| | Mean | SD | Mean | SD | p ^a | Mean | SD | p ^b | Mean | SD | p ^c | p ^d | p ^e | p ^f | Mean | SD | p ^g | Mean | SD | p ^h | Mean | SD | p ⁱ | p ^j | p ^k | p ^l | p ^m | p ⁿ | p ^o |
| GM-CSF | 0.08 | 0.04 | 149.16 | 200.64 | 0.005 | 110.58 | 85.43 | 0.005 | 44.86 | 41.04 | 0.006 | 0.625 | 0.887 | 0.345 | 339.06 | 172.28 | <0.001 | 193.73 | 121.14 | <0.001 | 111.48 | 122.53 | 0.007 | 0.026 | <0.001 | 0.122 | 0.006 | 0.221 | 0.694 |
| IP-10 | 300.24 | 125.48 | 11522.70 | 13861.96 | 0.001 | 7487.00 | 5533.30 | 0.003 | 2144.25 | 1125.56 | 0.011 | 0.922 | 0.066 | 0.450 | 96542.29 | 66191.64 | <0.001 | 54232.48 | 28556.77 | <0.001 | 14333.58 | 24884.23 | 0.021 | 0.088 | <0.001 | 0.003 | <0.001 | 0.002 | 0.794 |
| IL-10 | 0.79 | 0.36 | 17.40 | 13.77 | 0.009 | 21.88 | 9.48 | 0.003 | 16.36 | 11.73 | 0.133 | 0.380 | 0.990 | 0.340 | 144.11 | 95.86 | <0.001 | 70.49 | 46.73 | <0.001 | 50.79 | 65.28 | 0.035 | 0.026 | 0.002 | 0.094 | <0.001 | 0.002 | 0.433 |
| VEGF | 2.44 | 4.43 | 297.86 | 286.67 | 0.001 | 286.67 | 155.00 | 0.002 | 142.91 | 73.83 | 0.008 | 0.626 | 0.777 | 0.089 | 292.95 | 354.14 | <0.001 | 90.04 | 61.86 | <0.001 | 237.15 | 282.28 | 0.003 | 0.014 | 0.356 | 0.250 | 0.850 | 0.016 | 0.990 |
| IL-6 | 4.10 | 1.12 | 40.32 | 41.57 | 0.001 | 20.73 | 10.86 | 0.003 | 45.91 | 45.00 | 0.011 | 0.660 | 0.671 | 0.990 | 458.11 | 842.75 | <0.001 | 114.10 | 49.48 | <0.001 | 130.63 | 178.33 | 0.035 | 0.002 | 0.006 | 0.533 | <0.001 | <0.001 | 0.514 |
| IL-5 | 1.71 | 0.47 | 0.56 | 0.83 | 0.010 | 1.26 | 1.79 | 0.111 | 7.44 | 10.04 | 0.831 | 0.585 | 0.082 | 0.322 | 133.14 | 95.03 | <0.001 | 99.01 | 39.31 | <0.001 | 66.61 | 86.23 | 0.760 | 0.434 | 0.030 | 0.209 | <0.001 | <0.001 | 0.637 |
| IL-17A | 5.53 | 4.32 | 21.46 | 12.37 | 0.013 | 23.78 | 8.51 | 0.003 | 39.47 | 41.06 | 0.019 | 0.591 | 0.777 | 0.705 | 348.40 | 250.25 | <0.001 | 159.73 | 134.74 | <0.001 | 239.82 | 382.19 | 0.263 | 0.028 | 0.024 | 0.374 | <0.001 | <0.001 | 0.598 |
| MIG | 315.66 | 109.49 | 4721.20 | 6676.86 | 0.001 | 3448.07 | 3067.92 | 0.003 | 844.69 | 246.95 | 0.011 | 0.696 | 0.034 | 0.089 | 13436.62 | 15595.19 | <0.001 | 3981.05 | 2103.34 | <0.001 | 1959.72 | 2056.38 | 0.088 | 0.241 | 0.003 | 0.033 | 0.076 | 0.342 | 0.602 |
| IL-8 | 7.02 | 3.79 | 49.41 | 38.76 | 0.001 | 42.41 | 23.01 | 0.003 | 37.72 | 19.63 | 0.011 | 0.922 | 0.990 | 0.705 | 293.28 | 128.54 | <0.001 | 217.84 | 82.97 | <0.001 | 131.89 | 129.64 | 0.007 | 0.095 | 0.002 | 0.139 | <0.001 | <0.001 | 0.296 |
| HGF | 160.94 | 34.04 | 770.27 | 704.51 | 0.001 | 823.29 | 874.19 | 0.003 | 1051.16 | 1480.78 | 0.134 | 0.845 | 0.157 | 0.186 | 5547.17 | 18788.88 | <0.001 | 793.22 | 514.05 | <0.001 | 2028.33 | 3785.47 | 0.002 | 0.915 | 0.166 | 0.158 | 0.880 | 0.751 | 0.361 |
| MCP-1 | 6.95 | 3.49 | 93.83 | 100.72 | 0.001 | 73.70 | 35.45 | 0.003 | 95.08 | 58.16 | 0.011 | 0.495 | 0.396 | 0.776 | 234.30 | 213.91 | <0.001 | 116.23 | 33.97 | <0.001 | 124.53 | 58.85 | <0.001 | 0.110 | 0.136 | 0.922 | 0.002 | 0.042 | 0.296 |
| IL-1beta | 0.81 | 0.18 | 0.31 | 0.60 | 0.007 | 0.17 | 0.13 | 0.002 | 0.92 | 1.41 | 0.194 | 0.826 | 0.869 | 0.827 | 26.96 | 25.44 | <0.001 | 17.68 | 6.19 | <0.001 | 11.68 | 15.55 | 0.362 | 0.374 | 0.009 | 0.106 | <0.001 | <0.001 | 0.130 |
| MIP-1alpha | 1.82 | 0.54 | 0.59 | 1.00 | 0.007 | 0.29 | 0.34 | 0.002 | 1.97 | 2.53 | 0.201 | 0.819 | 0.137 | 0.165 | 58.81 | 37.73 | <0.001 | 40.63 | 14.24 | <0.001 | 23.60 | 26.74 | 0.362 | 0.207 | 0.004 | 0.081 | <0.001 | <0.001 | 0.287 |
| CTACK | 383.74 | 107.84 | 704.29 | 268.40 | 0.017 | 537.18 | 356.67 | 0.775 | 361.24 | 97.06 | 0.831 | 0.143 | 0.016 | 0.705 | 10967.08 | 6259.12 | <0.001 | 10834.17 | 3393.51 | <0.001 | 3484.85 | 3969.94 | 0.482 | 0.456 | <0.001 | 0.001 | <0.001 | <0.001 | 0.433 |
| SDF-1alpha | 83.01 | 34.43 | 138.75 | 47.12 | 0.033 | 122.86 | 34.71 | 0.099 | 190.43 | 37.99 | 0.010 | 0.432 | 0.102 | 0.058 | 2357.38 | 753.90 | <0.001 | 2891.82 | 386.95 | <0.001 | 908.63 | 1246.60 | 0.960 | 0.059 | 0.003 | 0.003 | <0.001 | <0.001 | 0.432 |
| TNF-alpha | 16.48 | 2.44 | 44.52 | 49.69 | 0.193 | 35.01 | 19.78 | 0.032 | 72.81 | 62.96 | 0.019 | 0.845 | 0.203 | 0.449 | 434.82 | 290.12 | <0.001 | 325.33 | 163.85 | <0.001 | 200.05 | 269.00 | 0.362 | 0.522 | 0.009 | 0.093 | <0.001 | <0.001 | 0.598 |
| IL-13 | 2.94 | 0.57 | 21.76 | 9.85 | 0.001 | 21.27 | 8.04 | 0.004 | 22.10 | 6.58 | 0.011 | 0.922 | 0.777 | 0.990 | 75.13 | 60.61 | <0.001 | 47.50 | 17.98 | <0.001 | 34.46 | 36.68 | 0.131 | 0.241 | 0.017 | 0.107 | <0.001 | <0.001 | 0.793 |
| IL-2 | 3.85 | 1.73 | 16.13 | 12.86 | 0.001 | 11.59 | 2.31 | 0.003 | 16.93 | 10.81 | 0.011 | 0.845 | 0.524 | 0.850 | 94.34 | 77.15 | 0.002 | 54.12 | 18.13 | 0.007 | 50.64 | 74.16 | 0.363 | 0.095 | 0.031 | 0.373 | <0.001 | 0.051 | 0.990 |
| beta-NGF | 2.00 | 0.33 | 3.47 | 1.24 | 0.001 | 3.16 | 0.65 | 0.005 | 3.48 | 0.67 | 0.010 | 0.731 | 0.476 | 0.448 | 47.61 | 30.17 | <0.001 | 53.22 | 13.96 | <0.001 | 14.49 | 26.94 | 0.208 | 0.384 | <0.001 | 0.002 | <0.001 | <0.001 | 0.695 |
| basic-FGF | 14.24 | 6.07 | 42.03 | 15.47 | 0.002 | 44.80 | 6.35 | 0.003 | 53.23 | 22.44 | 0.011 | 0.380 | 0.479 | 0.925 | 229.08 | 103.46 | <0.001 | 154.90 | 71.89 | <0.001 | 108.96 | 134.51 | 0.268 | 0.036 | 0.005 | 0.100 | <0.001 | <0.001 | 0.896 |
| IFN-gamma | 66.70 | 4.69 | 277.00 | 109.63 | 0.001 | 327.71 | 96.23 | 0.003 | 402.00 | 236.77 | 0.010 | 0.205 | 0.257 | 0.705 | 1045.33 | 595.16 | <0.001 | 828.95 | 333.26 | <0.001 | 519.18 | 548.59 | 0.035 | 0.570 | 0.016 | 0.123 | <0.001 | <0.001 | 0.695 |
| G-CSF | 27.60 | 4.94 | 34.67 | 17.32 | 0.448 | 30.99 | 15.98 | 0.775 | 54.13 | 27.86 | 0.136 | 0.696 | 0.322 | 0.257 | 406.91 | 172.93 | <0.001 | 371.00 | 186.39 | <0.001 | 170.85 | 199.04 | 0.190 | 0.346 | 0.002 | 0.020 | <0.001 | <0.001 | 0.512 |
| IL-4 | 2.86 | 0.54 | 6.47 | 2.05 | 0.002 | 7.25 | 2.02 | 0.003 | 9.01 | 4.78 | 0.011 | 0.407 | 0.524 | 0.925 | 35.95 | 17.48 | <0.001 | 28.06 | 10.15 | <0.001 | 18.10 | 20.49 | 0.365 | 0.207 | 0.012 | 0.139 | <0.001 | <0.001 | 0.990 |
| IL-7 | 4.52 | 0.91 | 6.14 | 4.50 | 0.515 | 9.57 | 5.31 | 0.032 | 10.20 | 8.83 | 0.087 | 0.143 | 0.396 | 0.507 | 56.70 | 42.63 | <0.001 | 43.13 | 19.04 | <0.001 | 32.28 | 39.19 | 0.362 | 0.499 | 0.046 | 0.107 | <0.001 | <0.001 | 0.598 |
| MIF | 554.46 | 115.89 | 2746.14 | 2300.92 | 0.030 | 1088.45 | 805.83 | 0.086 | 1203.04 | 1088.92 | 0.990 | 0.205 | 0.120 | 0.705 | 6704.86 | 8785.16 | <0.001 | 3968.82 | 2085.60 | <0.001 | 1519.66 | 1243.84 | 0.227 | 0.434 | <0.001 | 0.006 | 0.041 | 0.002 | 0.601 |
| IL-9 | 7.02 | 3.79 | 68.00 | 84.89 | 0.001 | 40.53 | 18.76 | 0.003 | 51.04 | 35.78 | 0.011 | 0.732 | 0.671 | 0.924 | 80.73 | 48.26 | <0.001 | 37.70 | <0.001 | 72.79 | 33.11 | 0.007 | 0.098 | 0.070 | 0.818 | 0.070 | 0.556 | 0.990 | |
| MIP-1beta | 20.22 | 7.20 | 85.34 | 26.86 | 0.001 | 75.68 | 14.11 | 0.003 | 79.21 | 20.58 | 0.011 | 0.696 | 0.671 | 0.990 | 191.45 | 148.52 | <0.001 | 88.35 | 28.74 | <0.001 | 176.87 | 115.12 | <0.001 | 0.007 | 0.859 | 0.017 | 0.007 | 0.497 | 0.037 |
| SCF | 54.46 | 10.21 | 110.14 | 27.31 | 0.002 | 61.29 | 24.99 | 0.943 | 80.54 | 34.20 | 0.011 | 0.005 | 0.203 | 0.450 | 470.99 | 438.46 | 0.008 | 274.65 | 120.33 | <0.001 | 162.74 | 112.44 | 0.035 | 0.374 | 0.026 | 0.045 | <0.001 | <0.001 | 0.191 |
| IL-1ra | 111.83 | 19.39 | 192.57 | 100.31 | 0.065 | 182.57 | 48.78 | 0.015 | 289.50 | 210.24 | 0.033 | 0.732 | 0.571 | 0.705 | 808.00 | 508.89 | <0.001 | 404.85 | 202.62 | <0.001 | 289.18 | 358.30 | 0.688 | 0.007 | <0.001 | 0.071 | <0.001 | 0.002 | 0.695 |
| IL-18 | 69.89 | 33.36 | 202.13 | 149.90 | 0.030 | 247.41 | 118.95 | 0.004 | 81.42 | 26.57 | 0.286 | 0.425 | 0.090 | 0.014 | 500.35 | 421.82 | 0.002 | 627.91 | 1222.49 | 0.007 | 120.18 | 43.30 | 0.044 | 0.256 | <0.001 | 0.003 | 0.023 | 0.556 | 0.117 |
| PDGF-bb | 532.04 | 97.67 | 6109.80 | 2903.48 | 0.001 | 8835.57 | 2931.22 | 0.003 | 3551.25 | 700.71 | 0.011 | 0.118 | 0.090 | 0.008 | 3314.97 | 2131.40 | 0.002 | 1635.80 | 949.34 | 0.005 | 3445.35 | 4524.77 | 0.035 | 0.016 | 0.214 | 0.718 | 0.016 | <0.001 | 0.151 |
| IL-12p70 | 7.98 | 2.35 | 52.73 | 33.08 | 0.002 | 61.63 | 27.09 | 0.032 | 47.39 | 17.75 | 0.011 | 0.495 | 0.777 | 0.257 | 46.30 | 48.89 | 0.004 | 21.49 | 16.45 | 0.016 | 22.93 | 28.51 | 0.056 | 0.075 | 0.286 | 0.743 | 0.345 | 0.016 | 0.151 |
| RANTES | 798.53 | 160.94 | 7547.70 | 5505.60 | 0.001 | 8854.71 | 4907.89 | 0.003 | 5176.50 | 6619.39 | 0.011 | 0.558 | 0.120 | 0.131 | 4618.49 | 2745.17 | <0.001 | 2947.19 | 1253.42 | <0.001 | 6027.62 | 4280.65 | <0.001 | 0.055 | 0.394 | 0.020 | 0.151 | 0.010 | 0.151 |
| SCGF-beta | 45616.56 | 18076.42 | 73158.57 | 33202.14 | 0.083 | 67878.64 | 45821.33 | 0.568 | 85503.11 | 94715.44 | 0.670 | 0.696 | 0.322 | 0.705 | 111894.60 | 51239.37 | 0.001 | 80444.73 | 23216.23 | 0.016 | 90322.47 | 25575.08 | 0.005 | 0.062 | 0.214 | 0.250 | 0.019 | 0.497 | 0.151 |

- a: Compare between Control and H1N1 Day0-7 groups
- b: Compare between Control and H1N1 Day8-14 groups
- c: Compare between Control and H1N1 Day15- groups
- d: Compare between H1N1 Day0-7 and H1N1 Day8-14 groups
- e: Compare between H1N1 Day0-7 and H1N1 Day15- groups
- f: Compare between H1N1 Day8-14 and H1N1 Day15- groups
- g: Compare between Control and H7N9 Day0-7 groups
- h: Compare between Control and H7N9 Day8-14 groups
- i: Compare between Control and H7N9 Day15- groups
- j: Compare between H7N9 Day0-7 and H7N9 Day8-14 groups
- k: Compare between H7N9 Day0-7 and H7N9 Day15- groups
- l: Compare between H7N9 Day8-14 and H7N9 Day15- groups
- m: Compare between H1N1 Day0-7 and H7N9 Day0-7 groups
- n: Compare between H1N1 Day8-14 and H7N9 Day8-14 groups
- o: Compare between H1N1 Day15- and H7N9 Day15- groups

Supplementary Figure 2



Supplementary Figure 3



Supplementary Table 2. Outcomes in H7N9-infected Patients

| Cyto/Chemokines | Week1 | | | | P Value | Week2 | | | | P Value |
|-----------------|----------------------------|----------|------------|----------|---------|----------------------------|----------|------------|----------|---------|
| | Hospitalized<28 days(n=12) | | Death(n=5) | | | Hospitalized<28 days(n=16) | | Death(n=8) | | |
| | Mean | SD | Mean | SD | | Mean | SD | Mean | SD | |
| MIF | 6788.97 | 11052.77 | 8350.28 | 7592.12 | >0.05 | 2478.12 | 976.28 | 10230.90 | 8136.02 | <0.001 |
| MCP-1 | 185.02 | 119.67 | 395.86 | 373.37 | >0.05 | 104.44 | 68.94 | 1143.97 | 2113.30 | 0.001 |
| SCF | 334.60 | 296.80 | 748.49 | 608.28 | >0.05 | 144.21 | 129.21 | 762.14 | 530.10 | 0.001 |
| HGF | 2142.40 | 5417.31 | 19960.04 | 36874.91 | >0.05 | 516.96 | 384.82 | 4824.59 | 4796.72 | 0.002 |
| SCGF-beta | 106784.14 | 57776.73 | 127463.78 | 47259.38 | >0.05 | 73015.19 | 36486.71 | 151362.42 | 69428.71 | 0.004 |
| IP-10 | 81233.46 | 58401.52 | 120058.92 | 73759.23 | >0.05 | 19832.99 | 21839.53 | 70899.03 | 75499.28 | 0.008 |
| IL-18 | 335.58 | 267.76 | 653.74 | 553.92 | >0.05 | 193.28 | 142.20 | 2326.10 | 2917.72 | 0.008 |

Supplementary Table 3. ROC Curve of Cytokine/Chemokines in The Second Week H7N9-infected Illness Onset

| Cyto/Chemokines | Area under the ROC curve | P value | Std. Errora | 95% Confidence Interval | |
|-----------------|--------------------------|---------|-------------|-------------------------|-------------|
| | | | | Lower Bound | Upper Bound |
| MIF | 0.953 | <0.001 | 0.041 | 0.874 | 1.000 |
| SCF | 0.93 | 0.001 | 0.050 | 0.831 | 1.000 |
| MCP-1 | 0.906 | 0.001 | 0.060 | 0.788 | 1.000 |
| HGF | 0.891 | 0.002 | 0.073 | 0.747 | 1.000 |
| SCGF-beta | 0.867 | 0.004 | 0.075 | 0.721 | 1.000 |
| IL-18 | 0.836 | 0.008 | 0.112 | 0.617 | 1.000 |
| IP-10 | 0.836 | 0.008 | 0.082 | 0.676 | 0.996 |
| IFN-gamma | 0.777 | 0.03 | 0.111 | 0.561 | 0.994 |
| beta-NGF | 0.719 | >0.05 | 0.123 | 0.477 | 0.960 |
| IL-6 | 0.719 | >0.05 | 0.121 | 0.482 | 0.955 |
| MIG | 0.664 | >0.05 | 0.126 | 0.418 | 0.910 |
| IL-8 | 0.637 | >0.05 | 0.130 | 0.382 | 0.891 |
| MIP-1beta | 0.625 | >0.05 | 0.138 | 0.355 | 0.895 |
| SDF-1alpha | 0.586 | >0.05 | 0.131 | 0.329 | 0.843 |
| CTACK | 0.57 | >0.05 | 0.138 | 0.299 | 0.842 |
| MIP-1alpha | 0.551 | >0.05 | 0.138 | 0.281 | 0.820 |
| IL-1ra | 0.535 | >0.05 | 0.135 | 0.271 | 0.799 |
| IL-9 | 0.523 | >0.05 | 0.133 | 0.262 | 0.785 |
| IL-10 | 0.52 | >0.05 | 0.139 | 0.247 | 0.792 |
| G-CSF | 0.504 | >0.05 | 0.137 | 0.235 | 0.772 |
| IL-7 | 0.477 | >0.05 | 0.136 | 0.210 | 0.744 |
| IL-5 | 0.453 | >0.05 | 0.135 | 0.189 | 0.717 |
| GM-CSF | 0.422 | >0.05 | 0.137 | 0.153 | 0.691 |
| IL-1beta | 0.422 | >0.05 | 0.136 | 0.156 | 0.688 |
| IL-4 | 0.414 | >0.05 | 0.136 | 0.148 | 0.680 |
| VEGF | 0.406 | >0.05 | 0.138 | 0.135 | 0.677 |
| TNF-alpha | 0.402 | >0.05 | 0.136 | 0.135 | 0.670 |
| IL-13 | 0.391 | >0.05 | 0.128 | 0.141 | 0.641 |
| IL-2 | 0.391 | >0.05 | 0.129 | 0.138 | 0.644 |
| basic-FGF | 0.344 | >0.05 | 0.126 | 0.097 | 0.590 |
| IL-12p70 | 0.34 | >0.05 | 0.127 | 0.091 | 0.589 |
| PDGF-bb | 0.336 | >0.05 | 0.118 | 0.104 | 0.568 |
| IL-17A | 0.258 | >0.05 | 0.104 | 0.054 | 0.461 |
| RANTES | 0.188 | >0.05 | 0.093 | 0.006 | 0.369 |

Supplementary Figure 4

| | | | | | | | | |
|------------------|------------------|--------------|--------------|--------------|------------|------------|------------|------------------|
| IFN-gamma | 1.00 | | | | | | | |
| MCP-1 | | 1.00 | | | | | | |
| IL-18 | | | 1.00 | | | | | |
| IP-10 | 0.72 | 0.53 | 0.57 | 1.00 | | | | |
| HGF | 0.45 | 0.48 | 0.67 | 0.68 | 1.00 | | | |
| MIF | 0.60 | 0.51 | 0.46 | 0.68 | 0.64 | 1.00 | | |
| SCF | 0.49 | 0.51 | 0.62 | 0.75 | 0.77 | 0.70 | 1.00 | |
| SCGF-beta | | 0.65 | 0.62 | 0.55 | 0.69 | 0.51 | 0.64 | 1.00 |
| | IFN-gamma | MCP-1 | IL-18 | IP-10 | HGF | MIF | SCF | SCGF-beta |

Supplementary Table 4. Comparison Among H7N9, 2009 S-OIV, URTI, H5N1 and SARS Induced Plasma Chemokine and Cytokine Levels.

| | H7N9 (n=24) | p ¹ | H1N1 (n=14) | p ² | URTI(n=15) [Ref18,27] | H5N1(n=16) ³ [Ref12] |
|--------------|--------------|----------------|----------------|----------------|-----------------------|---------------------------------|
| MCP-1 | 2.3(1.8-3.0) | < 0.001 | 1.5 (-0.7-2.9) | < 0.001 | 1.6 (und-2.1) | 2.4 (1.5-4.0) |
| IP-10 | 5.0(3.8-5.4) | < 0.001 | 1.7 (0.4-4.6) | < 0.001 | 3.5 (2.3-4.2) | 5.1 (3.5-6.3) |
| IFN-γ | 3.0(2.6-3.4) | < 0.001 | 2.0 (0.4-3.0) | < 0.001 | 2.0 (und-2.4) | 2.0 (und.-4.2) |
| IL-6 | 2.3(1.7-3.6) | < 0.001 | 1.5 (0.6-1.9) | < 0.001 | 1.2 (und-1.6) | 2.1 (und.-3.7) |
| MIG | 3.7(2.6-4.8) | | | | | 4.3 (3.1-5.2) |
| IL-8 | 2.4(2.0-2.8) | < 0.001 | 1.1 (0.2-2.4) | < 0.001 | 0.7 (und-1.5) | 2.0 (0.7-3.2) |
| IL-10 | 2.1(1.1-2.5) | < 0.001 | 0.2 (0.2-2.0) | < 0.001 | und (und-1.4) | 1.5 (und.-2.8) |

Levels are given as median log pg/mL (range). URTI., upper respiratory tract infection. und., undetectable.

¹Comparison between H7N9 (0-7 d of illness onset) and 2009 swine flu (0-8 d of illness onset) patients. ²Comparison between H7N9 (0-7 d of illness) and 2009 URTI patients. ³The blood specimens of patients infected with H5N1 were obtained 4-8 d of illness onset.

| | H7N9 | | SARS [Ref28] | |
|---------------|-------------------------------|--------------------------------|--------------------------------|---------------------------------|
| | 0-7 d of illness onset (n=24) | 8-14 d of illness onset (n=11) | 0-7 d of illness onset (n=126) | 8-14 d of illness onset (n=129) |
| MCP-1 | 185.1(184.1) | 185.1(184.1) | 48.8 (26.0-94.0) | 31.6 (14.9-68.0) |
| IP-10 | 93096.4(83859.1) | 93096.0(83862.0) | 4020 (2520-6265) | 2695 (945-4760) |
| RANTES | 4361.8(3880.8) | 4361.8(3880.8) | 29 800 (18 900-33 720) | 32 500 (16 200-36 600) |
| MIG | 5418.1(20870.9) | 5418.1(20871.2) | 540 (375-918) | 612 (360-1032) |
| IL-8 | 265.0(161.2) | 265.0(161.2) | 11.7 (6.6-31.7) | 8.9 (5.4-32.8) |

Levels are given as median pg/mL (IQR).

| | H7N9(0-14 d of illness onset, n=35) | SARS(progressive stage, n=23) [Ref17] |
|---------------|-------------------------------------|---------------------------------------|
| MCP-1 | 194.2±189.1 | 475±1000 |
| IP-10 | 83245.0±61267.3 | 8100±2300 |
| IFN-γ | 977.3±544.4 | 85±35 |
| IL-6 | 350.0±726.9 | 120±160 |
| IL-8 | 270.0±123.1 | 750±1420 |
| MIP-1α | 53.1±33.8 | 1790±2880 |

Levels are given as means pg/mL ± SD.

Figure Legend

Supplementary Figure 1. Hypercytokinemia in Avian Influenza A (H7N9) Virus-Infected Patients

A total of 46 patients infected with the avian influenza A (H7N9) virus, 21 patients infected with the swine-origin influenza A (H1N1) virus and 6 healthy controls were recruited for this study. Their plasma levels of chemokines and cytokines at 0-7 days (n=24), 8-14 days (n=11) and 15 days (n=11) after the onset of the disease were measured. Detailed information is shown in supplementary table 1. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Supplementary Figure 2. The APACHE II Score was Correlated with the Plasma Levels of Chemokines and Cytokines and with Clinical Characteristics in The First Week of Disease Onset in Avian Influenza A (H7N9) Virus-Infected Patients.

Correlations between the APACHE II score and the plasma chemokine and cytokine (HGF, IL-18, SCF, MIG, IP-10, IL-6, MIF, Eotaxin, MCP-1) levels in the first week of influenza H7N9 infection for 21 patients. Spearman's rank correlation analysis (ρ), P value and the Benjamini & Hochberg multiple testing correction (P^*) to control for the false discovery rate (FDR) are shown in each graph.

Supplementary Figure 3. The APACHE II Score was Correlated with the Plasma Levels of Chemokines and Cytokines and with Clinical Characteristics in the Second Week of Disease Onset in Avian Influenza A (H7N9) Virus-Infected Patients.

Correlations between the APACHE II score and the plasma chemokine and cytokine levels (SCF, HGF, SCGF- β , MIF, IL-18, IP-10, MIG, IL-6, MCP-1, β -NGF) in the second week of influenza H7N9 infection in 32 patients. Spearman's rank correlation analysis (ρ), P value and the Benjamini & Hochberg multiple testing correction (P^*) to control for the false discovery rate (FDR) are shown in each graph.

Supplementary Figure 4. Correlation Heatmap of Plasma Cytokine/Chemokines Levels in the Second Week of H7N9-infected Illness Onsets.

Spearman's rank correlation analysis between the plasma chemokine and cytokine levels (SCF, HGF, SCGF- β , MIF, IL-18, IP-10, IFN- γ , MCP-1) in the second week of influenza H7N9 infection. The blank represents the Spearman's rank correlation analysis' P value > 0.05 .

Supplementary Table 1. Cytokine/chemokine Comparison Among 6 Healthy Controls, 21 H1N1-infected Patients and 46 H7N9-infected Patients.

Supplementary Table 2. Outcomes in H7N9-infected Patients

Supplementary Table 3. ROC Curve of Cytokine/Chemokines during the Second Week H7N9 Infection

Supplementary Table 4. Comparison among H7N9, 2009 S-OIV, URTI, H5N1 and SARS Induced Plasma Chemokine and Cytokine Levels