

**Supplemental Table 1. Biomarker Concentration by ARDS Subtype**

<b>Biomarker</b>	<b>Indirect ARDS (n=46)</b>	<b>Direct ARDS (n=52)</b>	<b>P-value<sup>a</sup></b>
Ang-1 (ng/mL)	2.2 (1.3 – 3.4)	3.2 (1.9 – 4.5)	0.02 <sup>a</sup>
Ang-2 (ng/mL)	16.6 (9.7 – 23.9)	6.9 (3.2 – 12.1)	<0.0001 <sup>a</sup>
Ang-2/Ang-1 ratio	6.8 (4.7 – 10.3)	2.6 (1.2 – 4.1)	<0.0001 <sup>a</sup>
Tie-2 (ng/mL)	1.7 (1.1 – 5.7)	1.9 (1.3 – 9.6)	0.5
E-selectin (ng/mL)	62.8 (31.0 – 141.5)	81.7 (54.4 – 146.5)	0.1
VEGF (pg/mL)	10.0 (6.0 – 36.8)	4.9 (2.3 – 12.7)	0.0002 <sup>a</sup>
sFLT (ng/mL)	2.8 (2.0 - 5.5)	2.3 (1.6 – 3.1)	0.02 <sup>a</sup>
VEGF-R2 (ng/mL)	12.6 (9.0 – 17.9)	14.0 (10.9 – 20.7)	0.06
VEGF-R3 (ng/mL)	3.8 (2.8 – 4.5)	3.7 (2.9 – 5.3)	0.8
ICAM (ng/mL)	811.0 (620.2 – 1084.1)	704.9 (548.8 – 837.5)	0.03 <sup>a</sup>
VCAM (µg/mL)	4.2 (2.1 – 6.2)	2.0 (1.0 – 2.8)	<0.0001 <sup>a</sup>
vWF (pg/mL)	298.7 (205.4 – 378.3)	231.0 (184.0 – 307.8)	0.03 <sup>a</sup>
Thrombomodulin (ng/mL)	6.5 (4.8 – 10.0)	4.7 (3.4 – 6.3)	0.001 <sup>a</sup>
Endocan (ng/mL)	3.3 (2.1 – 7.2)	1.7 (1.0 – 3.4)	0.001 <sup>a</sup>
CRP (mg/dL)	7.0 (1.8 – 12.8)	4.7 (1.2 – 11.2)	0.3
IL-6 (pg/mL)	215.8 (69.8 – 1937.2)	54.2 (15.3 – 175.0)	0.0001 <sup>a</sup>
IL-8 (pg/mL)	404.3 (70.9 – 2028.8)	54.7 (25.6 – 235.5)	<0.0001 <sup>a</sup>
IL-10 (pg/mL)	52.9 (14.7 – 315.0)	10.0 (4.8 – 18.7)	<0.0001 <sup>a</sup>
IL-17 (pg/mL)	6.5 (3.7 – 8.9)	3.2 (1.6 – 6.6)	0.008 <sup>a</sup>
IL-18 (pg/mL)	604.4 (274.2 – 1172.6)	354.7 (245.2 – 647.6)	0.02 <sup>a</sup>
IL-22 (pg/mL)	139.3 (104.2 – 196.6)	116.5 (93.9 – 161.0)	0.09
CD-14 (ng/mL)	2554.4 (1825.2 – 3261.8)	2773.4 (1989.2 – 3682.0)	0.2
CD-30 (pg/mL)	188.7 (146.8 – 252.9)	199.6 (147.6 – 297.0)	0.5
CD-163 (ng/mL)	711.6 (425.3 – 1278.9)	419.5 (244.5 – 633.5)	0.0006 <sup>a</sup>
EGF (pg/mL)	40.6 (28.3 – 53.5)	37.9 (27.2 – 49.1)	0.6
EGF-R (ng/mL)	42.0 (30.6 – 59.5)	45.1 (35.3 – 56.4)	0.5
Eotaxin (pg/mL)	44.4 (26.7 – 79.9)	30.9 (15.2 – 48.2)	0.0045 <sup>a</sup>
FGF-Basic (pg/mL)	35.4 (22.3 – 47.9)	36.9 (26.2 – 46.7)	0.98
GCSF (pg/mL)	143.8 (106.0 – 2479.7)	117.0 (72.2 – 175.6)	0.02 <sup>a</sup>
GMCSF (pg/mL)	1.6 (0.7 – 6.6)	0.63 (0.40 – 0.90)	0.0003 <sup>a</sup>
HGF (pg/mL)	759.6 (318.3 – 3303.3)	337.0 (191.7 – 601.9)	0.0004 <sup>a</sup>

IFN- $\alpha$ (pg/mL)	46.2 (31.5 – 99.8)	38.9 (31.5 – 49.3)	0.05
IFN- $\gamma$ (pg/mL)	24.0 (5.1 – 33.2)	28.1 (4.5 – 40.5)	0.7
IL-1-R $\alpha$ (ng/mL)	1.1 (0.5 – 6.1)	0.5 (0.3 – 1.4)	0.0023 <sup>a</sup>
IL-1 $\beta$ (pg/mL)	23.3 (17.1 – 37.6)	24.9 (15.1 – 38.7)	0.9
IL-1R1 (pg/mL)	372.6 (274.6 – 462.9)	378.6 (261.5 – 450.8)	0.8
IL-1R2 (ng/mL)	19.1 (10.1 – 55.3)	16.4 (11.8 – 25.5)	0.3
IL-2 (pg/mL)	6.0 (3.7 – 10.6)	7.6 (4.0 – 9.5)	0.8
IL-2R (ng/mL)	2.2 (1.0 – 3.4)	1.1 (0.8 – 2.0)	0.007 <sup>a</sup>
IL-2RA (ng/mL)	6.0 (3.2 – 11.5)	3.5 (2.2 – 5.3)	0.002 <sup>a</sup>
IL-4 (pg/mL)	8.2 (4.7 – 16.8)	10.1 (3.2 – 18.5)	0.5
IL-4R (ng/mL)	0.9 (0.5 – 1.4)	1.1 (0.5 – 1.4)	0.4
IL-5 (pg/mL)	4.2 (1.9 – 9.0)	2.4 (1.1 – 6.0)	0.02 <sup>a</sup>
IL-6R (ng/mL)	20.4 (12.5 – 30.4)	20.5 (16.3 – 29.4)	0.5
IL-12 (pg/mL)	76.6 (52.1 – 141.4)	93.6 (49.2 – 148.6)	0.7
IL-13 (pg/mL)	10.5 (5.6 – 18.0)	6.0 (4.3 – 8.2)	0.001 <sup>a</sup>
IL-15 (pg/mL)	148.1 (77.0 – 235.3)	112.7 (65.8 – 162.9)	0.09
IP-10 (pg/mL)	61.1 (28.5 – 172.9)	27.8 (17.5 – 69.6)	0.009 <sup>a</sup>
MCP-1 (ng/mL)	1.7 (0.7 – 4.3)	0.5 (0.3 – 1.1)	<0.0001 <sup>a</sup>
MIG (pg/mL)	111.7 (49.7 – 424.1)	50.8 (27.6 – 78.0)	0.0004 <sup>a</sup>
MIP-1 $\alpha$ (pg/mL)	61.8 (44.3 – 109.0)	48.3 (40.1 – 63.1)	0.01 <sup>a</sup>
MIP-1 $\beta$ (pg/mL)	110.0 (75.0 – 239.5)	66.2 (53.1 – 91.6)	0.0003 <sup>a</sup>
sRAGE (pg/mL)	213.4 (169.9 – 317.4)	212.3 (140.9 – 267.4)	0.3
RANTES (ng/mL)	0.8 (0.4 – 1.4)	1.5 (0.9 – 2.2)	0.0004 <sup>a</sup>
sgp130 (ng/mL)	188.8 (142.4 – 248.3)	182.5 (145.8 – 225.0)	0.6
TNF- $\alpha$ (pg/mL)	4.2 (3.2 – 5.9)	4.4 (2.4 – 7.2)	0.9
TNF-R1 (ng/mL)	5.1 (3.7 – 10.1)	2.9 (1.7 – 5.0)	<0.0001 <sup>a</sup>
TNF-R2 (ng/mL)	38.7 (27.8 – 50.6)	16.1 (11.9 – 23.6)	<0.0001 <sup>a</sup>

ARDS = acute respiratory distress syndrome; Ang = angiotensin; CD = cluster of differentiation; CRP = C-reactive protein; EGF = epidermal growth factor; FGF = fibroblast growth factor; G-CSF = granulocyte colony-stimulating factor; GM-CSF = granulocyte-macrophage colony-stimulating factor; HGF = hepatocyte growth factor; ICAM = intracellular adhesion molecule; IFN = interferon; IL = interleukin; MCP = monocyte chemoattractant protein; MIG = monocyte induced by interferon  $\gamma$ ; MIP = macrophage inflammatory protein; -R = receptor; RANTES = regulated on activation, normal T cell expressed and secreted; sgp = serum glycoprotein; sFLT = soluble fms-like tyrosine kinase; sRAGE = soluble receptor for advanced glycation end-products; Tie-2 = tyrosine kinase with immunoglobulin-like loop epidermal growth factor homology domain 2; TNF- = tumor necrosis factor; VCAM = vascular adhesion molecule; VEGF = vascular endothelial growth factor; vWF = von Willebrand factor

Data are presented as median (interquartile range).

<sup>a</sup> P-value for univariate analysis comparing indirect and direct ARDS by Wilcoxon rank sum test. Significance is defined as  $p < 0.05$ .