Supplemental Table 1. Plasma proteins predict COVID19+ ICU patients vs. healthy controls.

Num	Assay	Unipro ID	Function
1.	TYMP	P19971	Thymidine phosphorylase also called platelet-derived endothelial cell growth factor is an intracellular protein whose major source is platelets (1). It may be involved in platelet activation and its secreted metabolites may potentiate thrombosis (1).
2.	CXCL10	P02778	Induced by IFNγ, produced by endothelial cells, monocytes, fibroblasts and keratinocytes (2). Agonist for CXCR3 which is expressed on some T, B, and NK cells (2). Promotes Th1 recruitment (3) induces T cell adherence to endothelial cells, chemoattractant for monocytes, T cells, NKs (2).
3.	C1QA	P02745	Complement C1q subunit A is one of 3 subunits making up C1q, part of the classical complement system.
4.	AGR2	O95994	Anterior gradient protein 2 homolog is a member of the protein disulfide isomerase family normally located in the endoplasmic reticulum of intestinal cells (4), as well as the lung, stomach, colon and prostate; tissues with mucus secreting or endocrine functions (5).
5.	IL-18R1	Q13478	One of the heterodimers of the IL-18 receptor complex, it is a type I transmembrane protein (2). Expressed on NKs, T cells especially activated Th1 cells; it induces IFNy in concert with IL-12 receptor (2).
6.	CDON	Q4KMG0	Cell adhesion molecule-related, down-regulated by oncogenes is a transmembrane glycoprotein that acts as a cell adhesion molecule and binds members of the hedgehog family (6). It seems to normally be involved in development and proliferating cells (6).
7.	DDX58	O95786	Retinoic acid-inducible gene 1, also called DEAD box protein 58, is a transmembrane pattern recognition receptor that recognizes viral replicative intermediates in the cytosol during RNA virus infections (7). It is expressed in endothelial cells (8) and activates the type 1 interferon response (7).
8.	CLEC6A	Q6EIG7	C-type lectin domain family 6 member A, also called dectin-2 is a transmembrane pattern-recognition receptor highly expressed on macrophages as well as monocytes, Kupffer, Langerhans and some dendritic cells (9). It binds surface polysaccharides of pathogens and ultimately causes cytokine production to direct a Th17 response (9).
9.	CLM-6	Q08708	CMRF35-like molecule 6 also called leukocyte mono- immunoglobulin-like receptor 8 (LMIR8) and CD300c

			is a transmembrane receptor expressed on almost all leukocytes and plasmacytoid dendritic cells (10) it recognizes phosphatidylethanolamine on apoptotic cells (11).
10.	PXN	P49023	Paxillin is a cytosolic scaffolding protein involved in focal adhesions and integrin-mediated signal transduction (12).
11.	LAG3	P18627	Lymphocyte activation gene 3 is a transmembrane receptor expressed on several types of T cells that regulates their function (13).
12.	APLP1	P51693	Amyloid-like protein 1 is expressed exclusively in the central nervous system and is a cytosolic protein thought to be involved in cell-cell contacts in synapses (14).
13.	LIF-R	P42702	Leukemia inhibitory factor receptor is a transmembrane protein that along with gp130 forms receptor for LIF, a member of the IL-6 family (15). LIF-R is expressed in several organs as well as monocytes and macrophages (15).
14.	B4GALT1	P15291	Beta-1,4-galactosyltransferase 1 is a trans-golgi membrane protein that transfers a sugar nucleotide to acceptors (16). When on the plasma membrane, it functions as a cell-adhesion molecule involved in cell-cell and cell-matrix interaction (16).
15.	ASGR1	P07306	1 of two subunits of the asialoglycoprotein receptor, which is mainly expressed in liver, that facilitates uptake of desialylated glycoproteins (17). It is a member of the C-type lectin family of receptors and can clear hyposialylated vonWillebrand factor from plasma (18).
16.	CRIM1	Q9NZV1	Cysteine-rich motor neuron 1 is a transmembrane receptor that regulates growth factor signaling in a number of organs during organogenesis (19).
17.	CD300E	Q496F6	Also called CLM-2, it is a transmembrane receptor expressed on the surface of monocytes and circulating myeloid dendritic cells (10). It appears to be involved in inducing cytokine release, reactive oxygen species production (10).
18.	CDKN1A	P38936	Cyclin-dependent kinase inhibitor 1 also called p21 and CIP1 is a nuclear and cytoplasmic protein which can arrest the cell cycle due to DNA damage and is antiapoptotic (20).
19.	CXCL11	O14625	A ligand for CXCR3 which is expressed on some T, B, and NK cells (2). It promotes Th1 recruitment/chemotaxis (2, 3).
20.	IL6	P05231	A key pro-inflammatory cytokine it can directly stimulate cells through its membrane-bound receptor on hepatocytes, neutrophils, monocytes, and some

lymphocytes (21). In concert with its soluble receptor, it can also stimulate a wide-variety of cells that expresses
gp130 (21).

CLM - CMRF35-like molecule

CXCR – CXC receptor

IFNγ – interferon gamma

IL – interleukin

NK – natural killer cell

Th1 – type 1 T-helper cell

References

- 1. Li W, Yue H: Thymidine phosphorylase: a potential new target for treating cardiovascular disease. *Trends Cardiovasc Med* 2018; 28:157–171
- 2. Thomson AW, Lotze MT: The cytokine handbook. Amsterdam; Boston: Academic Press; 2003.
- 3. Foti M, Locati M: Cytokine Effector Functions in Tissues [Internet]. San Diego, UNITED STATES: Elsevier Science & Technology; 2017. [cited 2020 Jun 9] Available from: http://ebookcentral.proquest.com/lib/west/detail.action?docID=4917635
- 4. Park S-W, Zhen G, Verhaeghe C, et al.: The protein disulfide isomerase AGR2 is essential for production of intestinal mucus. *PNAS* 2009; 106:6950–6955
- 5. Brychtova V, Vojtesek B, Hrstka R: Anterior gradient 2: A novel player in tumor cell biology. *Cancer Letters* 2011; 304:1–7
- 6. Sanchez-Arrones L, Cardozo M, Nieto-Lopez F, et al.: Cdon and Boc: Two transmembrane proteins implicated in cell–cell communication. *The International Journal of Biochemistry & Cell Biology* 2012; 44:698–702
- 7. Streicher F, Jouvenet N: Stimulation of Innate Immunity by Host and Viral RNAs. *Trends in Immunology* 2019; 40:1134–1148
- 8. Opitz B, Eitel J, Meixenberger K, et al.: Role of Toll-like receptors, NOD-like receptors and RIG-I-like receptors in endothelial cells and systemic infections. *Thromb Haemost* 2009; 102:1103–1109

- 9. Feinberg H, Jégouzo SAF, Rex MJ, et al.: Mechanism of pathogen recognition by human dectin-2. *J Biol Chem* 2017; 292:13402–13414
- 10. Borrego F: The CD300 molecules: an emerging family of regulators of the immune system. *Blood* 2013; 121:1951–1960
- 11. Takahashi M, Izawa K, Kashiwakura J, et al.: Human CD300C Delivers an Fc Receptor-γ-dependent Activating Signal in Mast Cells and Monocytes and Differs from CD300A in Ligand Recognition. *J Biol Chem* 2013; 288:7662–7675
- 12. The structure and functions of paxillin and its roles in neovascularization. 6
- 13. Ruffo E, Wu R, Bruno TC, et al.: Lymphocyte-Activation Gene 3 (LAG3): the Next Immune Checkpoint Receptor. *Semin Immunol* 2019; 42:101305
- 14. Ludewig S, Korte M: Novel Insights into the Physiological Function of the APP (Gene) Family and Its Proteolytic Fragments in Synaptic Plasticity [Internet]. *Front Mol Neurosci* 2017; 9[cited 2020 Jun 12] Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5247455/
- 15. Nicola NA, Babon JJ: Leukemia Inhibitory Factor (LIF). *Cytokine Growth Factor Rev* 2015; 26:533–544
- 16. Qasba PK, Ramakrishnan B, Boeggeman E: Structure and Function of β-1,4-Galactosyltransferase. *Curr Drug Targets* 2008; 9:292–309
- 17. van den Boogert MAW, Rader DJ, Holleboom AG: New insights into the role of glycosylation in lipoprotein metabolism. *Current Opinion in Lipidology* 2017; 28:502–506
- 18. O'Sullivan JM, Ward S, Lavin M, et al.: von Willebrand factor clearance biological mechanisms and clinical significance. *British Journal of Haematology* 2018; 183:185–195
- 19. Iyer S, Pennisi DJ, Piper M: Crim1-, a regulator of developmental organogenesis. *Histol Histopathol* 2016; 31:1049–1057
- 20. Ćmielová J, Řezáčová M: Protein and its function based on a subcellular localization. *Journal of Cellular Biochemistry* 2011; 112:3502–3506
- 21. Rose-John S, Scheller J, Elson G, et al.: Interleukin-6 biology is coordinated by membrane-bound and soluble receptors: role in inflammation and cancer. *Journal of Leukocyte Biology* 2006; 80:227–236