

# BQC19 Core Analyses February 16, 2021

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### Overview of the core analyses

Table 1 summarizes the core analyses to be undertaken. The data generated by these analyses will be shared widely with the scientific community via the BQC19 data access process. The assays selected are either industry-standard analyses or, in the case of serology-based testing, best-in-class given present methods. When academic laboratories were selected to carry out some of these core analyses, no privileged access to the data generated will be granted to these laboratories.

Table 1: Overview of the core analyses

| Type of analysis                          | Objective   |
|---|---|
| Proteomics-1<br>SomaScan®                 | Simultaneous measurement of 5000 proteins provide data to improve risk prediction for COVID-19, while allowing for more exploratory and hypothesis-generating findings. This technology was chosen because of the large number of proteins measured in a single sample. <a href="https://somalogic.com">https://somalogic.com</a>   |
| Proteomics-2<br>Circulating markers       | This approach is complementary to SomaScan® and enables the measurement of established markers of inflammation/disease activity using a very specific and sensitive technique developed by nplex. These data will validate findings from SomaScan® and could lead to a better understanding of the biology of patient responses to disease and help guide future treatment. <a href="https://www.nplexbio.com">https://www.nplexbio.com</a> |
| Roche Laboratory analysis for outpatients | These analyses, to be performed on clinical-grade Roche platform, are carried out on samples collected from non-hospitalized patients. They include evaluations of liver, heart, and kidney damage, as well as measurements of standard inflammatory markers.   |
| Metabolomics                              | Defining the plasma metabolomic profile complements the proteomic data and further increases the capacity to identify/predict individuals at risk of developing severe disease. It also enables a deeper understanding of the molecular pathways underlying various clinical outcomes. https://www.metabolon.com  |
| Immuno-serology                           | These analyses provide detailed quantitative measurements of specific antibodies against the SARS-CoV-2 virus in affected patients, well beyond standard serological tests, as well as the ability of these antibodies to neutralize the virus. This helps guide research on the immune response to COVID-19, a key element in the patient management.  |
| Transcriptomics                           | Transcriptomic signatures have been associated in other viral diseases with cellular and immune responses, disease pathogenesis and infection outcomes. Transcriptomic analyses performed on RNA extracted from whole blood will generate important data in this area of COVID-19 research.   |
| Genome-wide genotyping (GWS) and          | Identification of all genetic variants in the host genome and genetic variations such as changes in the copy number of certain genes (genome-wide sequencing) as well as common genetic variations across the genome  |



| Type of analysis               | Objective  |
|--------------------------------|--|
| Whole genome sequencing (GWAS) | (genome-wide genotyping) associated with COVID-19 enables studies on the susceptibility and risk of developing a severe form of the disease and complications. |

In addition to these core analyses, it is anticipated that the genomes of the viral samples collected from part of the BQC19 participants affected by the disease will be sequenced by the *Laboratoire de santé publique du Québec* (LSPQ). Since the participants of BQC19 have consented to access to all data related to their care, including that held by any provincial government authority, linkage of the viral genome sequencing data with the host genome sequencing data will be undertaken. This data linkage will help understand the trajectory of infection, the source of viral strains/variants from other parts of the world, thus enabling better preparation for future waves of the pandemic. In addition, this data can be correlated with clinical severity and humoral response.

#### Patient population

We are performing core assays on three cohorts of BQC-19 participants:

- Patients hospitalized or presenting to hospital for acute COVID-19 (positive qRT-PCR for SARS-CoV-2: Analyses of clinical samples collected during the active phase of the infection and at follow-up time points (convalescent time points);
- 2. Patients hospitalized for another acute illness (negative qRT-PCR for SARS-CoV-2), i.e., controls;
- 3. Patients with asymptomatic or mild COVID disease consented and followed-up as an outpatient, with emphasis on longitudinal follow-up.

Depth of investigation (assays performed) will be adjusted to the expected relevance and yield for the respective cohorts. For example, systematic assessment of convalescent outpatients following mild disease will include screening for end-organ damage and inflammatory profiling, but in that group of patients in-depth transcriptomic, metabolomic and proteomic profiling will be considered in a second step if the first set of assays shows abnormalities.

#### Sample selection

#### 1- SARS-CoV-2 positive patients with severe disease

For the purpose of these analyses, we define severe disease as:

- · Death, or
- Intensive care unit, or
- Using any oxygen support, or
- Respiratory rate > 24, or
- O2 saturation <90%, or</li>
- Age <=45.</li>

#### 2- SARS-CoV-2 positive patients with mild disease

For the purpose of these analyses, we define mild disease as:

• Absence of the first 5 criteria above.



#### 3- Controls

SARS-CoV-2 negative participants.

#### Detailed assay description

#### 1- Proteomics-1: SomaScan®

Simultaneous measurement of 5,000 proteins is performed using a world-leading proteomics assay, developed by SomaLogic. The SomaScan® technology uses aptamers to accurately measure proteins, which have been used to precisely predict several important clinical outcomes, such as cardiovascular risk. Since plasma samples have been obtained at multiple time points, these measurements provide data on the evolution of protein levels for the duration of the infection. The SomaScan® technology was selected due to the breadth of protein measurement. This prevents the use and re-use of samples to measure few proteins, thus preventing needless freeze and thaw cycles that can greatly influence protein levels. Some protein levels vary by time since blood draw, diurnal cycle, as well as time since last meal, and this will be partially controlled since the exact time of sample draw and processing has been recorded and can be included as a covariate in analyses. Large-scale processing of fresh SARS-CoV-2 PCR positive plasma samples is logistically impossible, given biohazard safety concerns.

#### 2- Proteomics-2: Core plasma biomarkers

This approach is complementary to SomaScan® and enables the measurement of established markers of inflammation/disease activity using a very specific and sensitive technique developed by nplex. These data will validate findings from SomaScan® and could lead to a better understanding of the biology of patient responses to disease and help guide future treatment (200 proteins, Appendix 1) (https://www.nplexbio.com). analyte panel from nplex.

#### 3- Laboratory analyses for outpatients

For most visits from non hospitalized patients, no clinical lab tests were performed. An optimal set of clinical grade analyses will be performed on these samples, in collaboration with the *Institut universitaire* de cardiologie et pneumologie (IUCPQ) and Roche, using a panel of 25 biomarkers (Appendix 2) to assess basic tissue function and damage. Serology measurements will also be carried out on the samples.

#### 4- Whole blood transcriptomics

A standard short-read RNA sequencing on poly-A RNAs will be performed on a fraction of the RNA extracted. Initial quality control will be performed at the sequencing facility. Daniel Kaufmann's laboratory will coordinate first-level sequence alignment and gene mapping at the CRCHUM. RNA-seq data will be normalized to the transcript's length, resulting in fragments per kilobase transcript per million reads (FPKM).

#### 5- Immuno-serology: Measurement of the SARS-CoV-2 specific antibody responses

The generation and maintenance of virus-specific antibody and cellular responses are likely key for protective immunity against SARS-CoV-2. Andrés Finzi (CRCHUM) will carry out the following two serological tests on BQC19 plasma samples:



- ELISA (receptor binding domain, RBD): total antibodies, IgM, IgA, IgG;
- Cell-based ELISA (CBE) measuring antibody binding to the full length S glycoproteic assays for BQC-19 plasma samples.

These assays have been validated by the Finzi laboratory in terms of sensitivity, specificity and functionality on cohorts of patients at different time points post-infection, in collaboration with the LSPQ and Héma-Québec through a project supported by the MEIQ/FRQS.

In addition to these two sets of assays, neutralization against the WT and D614G SARS-CoV-2 S glycoprotein variant (circulating in the US and Canada) will be tested at the National Microbiology Laboratory (NML – Guillaume Poliquin) with actual virus.

#### 6- Metabolomics

Metabolomics is the assaying of extensive panel of small molecules. A large-scale metabolomics analysis is undertaken using the Metabolon platform which uses ultra-high-performance liquid chromatography/tandem mass spectrometry (UHPLC/MS/MS) methods. The latest platform, Metabolon Global Untargeted Platform, allows for the assay of 12,000 metabolites using Metabolon's extensive chemical library. This breadth of data will enable multiple groups to have access to extensive small molecule phenotyping, thereby helping to understand the pathways that are activated by COVID-19 disease and identify pathways that influence COVID-19 outcome.

### 7- Genome-wide genotyping

Genome-wide genotyping is the industry-standard assay used to detect common genetic variations across the human genome. The Axiom Precision Array was selected because this is a well-validated array providing a breadth of ethnicity coverage, which is important, given the higher proportion of COVID-19 affected individuals who are not of European ancestry. Genome-wide genotyping is performed by the McGill University Genome Centre which has recently completed the same assay for the Canadian Longitudinal Study of Aging (CLSA). QC is performed free of charge by Brent Richards' laboratory, which has done such QC for the CLSA and for multiple UK-based cohorts. These assays are funded by Brent Richards' research funds.

#### 8- Whole genome sequencing

Whole genome sequencing involves the assay of all genetic variants in an individual human genome, not just the common variants assayed by genome-wide genotyping. This technology also allows for the identification of structural genetic variations, such as copy number changes. Whole genome sequencing of BQC19 samples are done in collaboration with CanCOGeN, Canada's sequencing consortium that has received funding of \$20M from the federal government to generate whole genome sequence data from COVID-19 patients in the country. Sequencing is being done using Illumina technologies and genotype calling is performed at the McGill University Genome Centre.



#### Access to data from core analyses of BQC19 samples

Data-release computational support for the large data files generated by these core analyses is being put in place in collaboration with Michaël Chassé's bio-informatics team (CRCHUM) and Guillaume Bourque's team at the Genome Centre.

All data generated by the core analyses on BQC19 samples (provincial samples) will be made rapidly available to the scientific community via the BQC19 data access process <a href="https://www.bqc19.ca/en/access-data-samples">www.bqc19.ca/en/access-data-samples</a>).

In all cases, whether these data were generated from BQC19 samples in academic laboratories or by a private company, no privileged access to the data will be granted to the academic researcher or to the company that generated them. The samples and, if relevant, the associated phenotypic data will be sent only for core analysis purposes and will not permit data analysis. Access to the data for research purposes will have to follow the BQC19 data access process.



## Appendix 1

## nplex

| Activin A | Inhibin beta A chain (Activin beta-A chain) (Erythroid differentiation protein) (EDF)        |
|-----------|--|
|           |  |
| AITRL     | Tumor necrosis factor ligand superfamily member 18 (Activation-inducible TNF-related         |
| (GITR     | ligand) (AITRL) (Glucocorticoid-induced TNF-related ligand) (hGITRL)                         |
| Ligand)   |  |
| alpha-    | Alpha-synuclein (Non-A beta component of AD amyloid) (Non-A4 component of amyloid            |
| Synuclei  | precursor) (NACP)  |
| n         |  |
| Amphire   | Amphiregulin (AR) (Colorectum cell-derived growth factor) (CRDGF)                            |
| gulin     |  |
| Amyloid   | Amyloid-beta precursor protein (APP) (ABPP) (APPI) (Alzheimer disease amyloid protein)       |
| beta      | (Amyloid precursor protein) (Amyloid-beta A4 protein) (Cerebral vascular amyloid             |
|           | peptide) (CVAP) (PreA4) (Protease nexin-II) (PN-II) [Cleaved into: N-APP; Soluble APP-alpha  |
|           | (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99 (Beta-secretase C-terminal fragment)       |
|           | (Beta-CTF); Amyloid-beta protein 42 (Abeta42) (Beta-APP42); Amyloid-beta protein 40          |
|           | (Abeta40) (Beta-APP40); C83 (Alpha-secretase C-terminal fragment) (Alpha-CTF); P3(42);       |
|           | P3(40); C80; Gamma-secretase C-terminal fragment 59 (Amyloid intracellular domain 59)        |
|           | (AICD-59) (AID(59)) (Gamma-CTF(59)); Gamma-secretase C-terminal fragment 57 (Amyloid         |
|           | intracellular domain 57) (AICD-57) (AID(57)) (Gamma-CTF(57)); Gamma-secretase C-             |
|           | terminal fragment 50 (Amyloid intracellular domain 50) (AICD-50) (AID(50)) (Gamma-           |
|           | CTF(50)); C31]   |
| APRIL     | Tumor necrosis factor ligand superfamily member 13 (A proliferation-inducing ligand)         |
|           | (APRIL) (TNF- and APOL-related leukocyte expressed ligand 2) (TALL-2) (TNF-related death     |
|           | ligand 1) (TRDL-1) (CD antigen CD256)  |
| BAFF      | Tumor necrosis factor ligand superfamily member 13B (B lymphocyte stimulator) (BLyS)         |
|           | (B-cell-activating factor) (BAFF) (Dendritic cell-derived TNF-like molecule) (TNF- and APOL- |
|           | related leukocyte expressed ligand 1) (TALL-1) (CD antigen CD257) [Cleaved into: Tumor       |
|           | necrosis factor ligand superfamily member 13b, membrane form; Tumor necrosis factor          |
|           | ligand superfamily member 13b, soluble form]   |
| BCMA      | Tumor necrosis factor receptor superfamily member 17 (B-cell maturation protein) (CD         |
| (TNFRSF   | antigen CD269)   |
| 17)       |  |
| BDNF      | Brain-derived neurotrophic factor (BDNF) (Abrineurin) [Cleaved into: BDNF precursor form     |
|           | (ProBDNF)]   |
| BMP2      | Bone morphogenetic protein 2 (BMP-2) (Bone morphogenetic protein 2A) (BMP-2A)                |
| BMP3      | Bone morphogenetic protein 3 (BMP-3) (Bone morphogenetic protein 3A) (BMP-3A)                |
|           | (Osteogenin)   |
| BMP4      | Bone morphogenetic protein 4 (BMP-4) (Bone morphogenetic protein 2B) (BMP-2B)                |
| BMP6      | Bone morphogenetic protein 6 (BMP-6) (VG-1-related protein) (VG-1-R) (VGR-1)                 |
|           |  |



| BMP7          | Bone morphogenetic protein 7 (BMP-7) (Osteogenic protein 1) (OP-1) (Eptotermin alfa)  |
|---------------|---|
| ВМР9          | Growth/differentiation factor 2 (GDF-2) (Bone morphogenetic protein 9) (BMP-9)  |
| C5/C5a        | Complement C5 (C3 and PZP-like alpha-2-macroglobulin domain-containing protein 4) [Cleaved into: Complement C5 beta chain; Complement C5 alpha chain; C5a anaphylatoxin; Complement C5 alpha' chain]  |
| Calbindi<br>n | Calbindin (Calbindin D28) (D-28K) (Vitamin D-dependent calcium-binding protein, aviantype)  |
| CCL1          | C-C motif chemokine 1 (Small-inducible cytokine A1) (T lymphocyte-secreted protein I-309)   |
| CCL11         | Eotaxin (C-C motif chemokine 11) (Eosinophil chemotactic protein) (Small-inducible cytokine A11)  |
| CCL13         | C-C motif chemokine 13 (CK-beta-10) (Monocyte chemoattractant protein 4) (Monocyte chemotactic protein 4) (MCP-4) (NCC-1) (Small-inducible cytokine A13) [Cleaved into: C-C motif chemokine 13, long chain; C-C motif chemokine 13, medium chain; C-C motif chemokine 13, short chain]  |
| CCL14         | C-C motif chemokine 14 (Chemokine CC-1/CC-3) (HCC-1/HCC-3) (HCC-1(1-74)) (NCC-2) (Small-inducible cytokine A14) [Cleaved into: HCC-1(3-74); HCC-1(4-74); HCC-1(9-74)]   |
| CCL15         | C-C motif chemokine 15 (Chemokine CC-2) (HCC-2) (Leukotactin-1) (LKN-1) (MIP-1 delta) (Macrophage inflammatory protein 5) (MIP-5) (Mrp-2b) (NCC-3) (Small-inducible cytokine A15) [Cleaved into: CCL15(22-92); CCL15(25-92); CCL15(29-92)]  |
| CCL16         | C-C motif chemokine 16 (Chemokine CC-4) (HCC-4) (Chemokine LEC) (IL-10-inducible chemokine) (LCC-1) (Liver-expressed chemokine) (Lymphocyte and monocyte chemoattractant) (LMC) (Monotactin-1) (MTN-1) (NCC-4) (Small-inducible cytokine A16)   |
| CCL17         | C-C motif chemokine 17 (CC chemokine TARC) (Small-inducible cytokine A17) (Thymus and activation-regulated chemokine)   |
| CCL18         | C-C motif chemokine 18 (Alternative macrophage activation-associated CC chemokine 1) (AMAC-1) (CC chemokine PARC) (Dendritic cell chemokine 1) (DC-CK1) (Macrophage inflammatory protein 4) (MIP-4) (Pulmonary and activation-regulated chemokine) (Small-inducible cytokine A18) [Cleaved into: CCL18(1-68); CCL18(3-69); CCL18(4-69)] |
| CCL19         | C-C motif chemokine 19 (Beta-chemokine exodus-3) (CK beta-11) (Epstein-Barr virus-induced molecule 1 ligand chemokine) (EBI1 ligand chemokine) (ELC) (Macrophage inflammatory protein 3 beta) (MIP-3-beta) (Small-inducible cytokine A19)   |
| CCL2          | C-C motif chemokine 2 (HC11) (Monocyte chemoattractant protein 1) (Monocyte chemotactic and activating factor) (MCAF) (Monocyte chemotactic protein 1) (MCP-1) (Monocyte secretory protein JE) (Small-inducible cytokine A2)  |
| CCL20         | C-C motif chemokine 20 (Beta-chemokine exodus-1) (CC chemokine LARC) (Liver and activation-regulated chemokine) (Macrophage inflammatory protein 3 alpha) (MIP-3-alpha) (Small-inducible cytokine A20) [Cleaved into: CCL20(1-67); CCL20(1-64); CCL20(2-70)]  |
| CCL21         | C-C motif chemokine 21 (6Ckine) (Beta-chemokine exodus-2) (Secondary lymphoid-tissue chemokine) (SLC) (Small-inducible cytokine A21)  |
| CCL22         | C-C motif chemokine 22 (CC chemokine STCP-1) (MDC(1-69)) (Macrophage-derived chemokine) (Small-inducible cytokine A22) (Stimulated T-cell chemotactic protein 1) [Cleaved into: MDC(3-69); MDC(5-69); MDC(7-69)]  |



| CCL23   | C-C motif chemokine 23 (CK-beta-8) (CKB-8) (Macrophage inflammatory protein 3) (MIP-3)     |
|---------|--|
|         | (Myeloid progenitor inhibitory factor 1) (MPIF-1) (Small-inducible cytokine A23) [Cleaved  |
|         | into: CCL23(19-99); CCL23(22-99); CCL23(27-99); CCL23(30-99)]                              |
| CCL24   | C-C motif chemokine 24 (CK-beta-6) (Eosinophil chemotactic protein 2) (Eotaxin-2)          |
|         | (Myeloid progenitor inhibitory factor 2) (MPIF-2) (Small-inducible cytokine A24)           |
| CCL25   | C-C motif chemokine 25 (Chemokine TECK) (Small-inducible cytokine A25) (Thymus-            |
|         | expressed chemokine)   |
| CCL26   | C-C motif chemokine 26 (CC chemokine IMAC) (Eotaxin-3) (Macrophage inflammatory            |
|         | protein 4-alpha) (MIP-4-alpha) (Small-inducible cytokine A26) (Thymic stroma chemokine-    |
|         | 1) (TSC-1)   |
| CCL27   | C-C motif chemokine 27 (CC chemokine ILC) (Cutaneous T-cell-attracting chemokine)          |
|         | (CTACK) (ESkine) (IL-11 R-alpha-locus chemokine) (Skinkine) (Small-inducible cytokine A27) |
| CCL28   | C-C motif chemokine 28 (Mucosae-associated epithelial chemokine) (MEC) (Protein CCK1)      |
|         | (Small-inducible cytokine A28)   |
| CCL3    | C-C motif chemokine 3 (G0/G1 switch regulatory protein 19-1) (Macrophage inflammatory      |
|         | protein 1-alpha) (MIP-1-alpha) (PAT 464.1) (SIS-beta) (Small-inducible cytokine A3)        |
|         | (Tonsillar lymphocyte LD78 alpha protein) [Cleaved into: MIP-1-alpha(4-69) (LD78-alpha(4-  |
|         | 69))]  |
| CCL4    | C-C motif chemokine 4 (G-26 T-lymphocyte-secreted protein) (HC21) (Lymphocyte              |
|         | activation gene 1 protein) (LAG-1) (MIP-1-beta(1-69)) (Macrophage inflammatory protein     |
|         | 1-beta) (MIP-1-beta) (PAT 744) (Protein H400) (SIS-gamma) (Small-inducible cytokine A4)    |
|         | (T-cell activation protein 2) (ACT-2) [Cleaved into: MIP-1-beta(3-69)]                     |
| CCL5    | C-C motif chemokine 5 (EoCP) (Eosinophil chemotactic cytokine) (SIS-delta) (Small-         |
|         | inducible cytokine A5) (T cell-specific protein P228) (TCP228) (T-cell-specific protein    |
|         | RANTES) [Cleaved into: RANTES(3-68); RANTES(4-68)]   |
| CCL7    | C-C motif chemokine 7 (Monocyte chemoattractant protein 3) (Monocyte chemotactic           |
|         | protein 3) (MCP-3) (NC28) (Small-inducible cytokine A7)                                    |
| CCL8    | C-C motif chemokine 8 (HC14) (Monocyte chemoattractant protein 2) (Monocyte                |
|         | chemotactic protein 2) (MCP-2) (Small-inducible cytokine A8) [Cleaved into: MCP-2(6-76)]   |
| CD14    | Monocyte differentiation antigen CD14 (Myeloid cell-specific leucine-rich glycoprotein)    |
|         | (CD antigen CD14) [Cleaved into: Monocyte differentiation antigen CD14, urinary form;      |
|         | Monocyte differentiation antigen CD14, membrane-bound form]                                |
| CD163   | Scavenger receptor cysteine-rich type 1 protein M130 (Hemoglobin scavenger receptor)       |
|         | (CD antigen CD163) [Cleaved into: Soluble CD163 (sCD163)]                                  |
| CD276   | CD276 antigen (4lg-B7-H3) (B7 homolog 3) (B7-H3) (Costimulatory molecule) (CD antigen      |
| (B7-H3) | CD276)   |
| CD27L   | CD70 antigen (CD27 ligand) (CD27-L) (Tumor necrosis factor ligand superfamily member 7)    |
|         | (CD antigen CD70)  |
| CD30    | Tumor necrosis factor receptor superfamily member 8 (CD30L receptor) (Ki-1 antigen)        |
|         | (Lymphocyte activation antigen CD30) (CD antigen CD30)                                     |
| CD40    | Tumor necrosis factor receptor superfamily member 5 (B-cell surface antigen CD40)          |
| (TNFRSF | (Bp50) (CD40L receptor) (CDw40) (CD antigen CD40)  |
|         |  |



| CD40L    | CD40 ligand (CD40-L) (T-cell antigen Gp39) (TNF-related activation protein) (TRAP) (Tumor necrosis factor ligand superfamily member 5) (CD antigen CD154) [Cleaved into: CD40 ligand, membrane form; CD40 ligand, soluble form (sCD40L)] |
|----------|--|
| CNTF     | Ciliary neurotrophic factor (CNTF)   |
| CRP      | C-reactive protein [Cleaved into: C-reactive protein(1-205)]   |
| CX3CL1   | Fractalkine (C-X3-C motif chemokine 1) (CX3C membrane-anchored chemokine)  |
| 07.0022  | (Neurotactin) (Small-inducible cytokine D1) [Cleaved into: Processed fractalkine]  |
| CXCL1    | Growth-regulated alpha protein (C-X-C motif chemokine 1) (GRO-alpha(1-73)) (Melanoma   |
|          | growth stimulatory activity) (MGSA) (Neutrophil-activating protein 3) (NAP-3) [Cleaved   |
|          | into: GRO-alpha(4-73); GRO-alpha(5-73); GRO-alpha(6-73)]   |
| CXCL10   | C-X-C motif chemokine 10 (10 kDa interferon gamma-induced protein) (Gamma-IP10) (IP-   |
|          | 10) (Small-inducible cytokine B10) [Cleaved into: CXCL10(1-73)]  |
| CXCL11   | C-X-C motif chemokine 11 (Beta-R1) (H174) (Interferon gamma-inducible protein 9) (IP-9)  |
| 01/01/40 | (Interferon-inducible T-cell alpha chemoattractant) (I-TAC) (Small-inducible cytokine B11)   |
| CXCL12   | Stromal cell-derived factor 1 (SDF-1) (hSDF-1) (C-X-C motif chemokine 12) (Intercrine  |
| (alpha)  | reduced in hepatomas) (IRH) (hIRH) (Pre-B cell growth-stimulating factor) (PBSF) [Cleaved into: SDF-1-beta(3-72); SDF-1-alpha(3-67)]   |
| CXCL12   | Stromal cell-derived factor 1 (SDF-1) (hSDF-1) (C-X-C motif chemokine 12) (Intercrine  |
| (beta)   | reduced in hepatomas) (IRH) (hIRH) (Pre-B cell growth-stimulating factor) (PBSF) [Cleaved  |
| (Seta)   | into: SDF-1-beta(3-72); SDF-1-alpha(3-67)]   |
| CXCL13   | C-X-C motif chemokine 13 (Angie) (B cell-attracting chemokine 1) (BCA-1) (B lymphocyte   |
|          | chemoattractant) (CXC chemokine BLC) (Small-inducible cytokine B13)  |
| CXCL14   | C-X-C motif chemokine 14 (Chemokine BRAK) (MIP-2G) (Small-inducible cytokine B14)  |
| CXCL16   | C-X-C motif chemokine 16 (Scavenger receptor for phosphatidylserine and oxidized low density lipoprotein) (SR-PSOX) (Small-inducible cytokine B16) (Transmembrane chemokine CXCL16)  |
| CXCL17   | C-X-C motif chemokine 17 (6-Cys CXCL17) (Dendritic cell and monocyte chemokine-like  |
|          | protein) (DMC) (VEGF coregulated chemokine 1) [Cleaved into: 4-Cys CXCL17]   |
| CXCL2    | C-X-C motif chemokine 2 (Growth-regulated protein beta) (Gro-beta) (Macrophage   |
|          | inflammatory protein 2-alpha) (MIP2-alpha) [Cleaved into: GRO-beta(5-73) (GRO-beta-T)  |
| 01/01/0  | (Hematopoietic synergistic factor) (HSF) (SB-251353)]  |
| CXCL3    | C-X-C motif chemokine 3 (GRO-gamma(1-73)) (Growth-regulated protein gamma) (GRO-gamma) (Managama) (Managama) (Glosved into GRO-gamma)  |
|          | gamma) (Macrophage inflammatory protein 2-beta) (MIP2-beta) [Cleaved into: GRO-gamma(5-73)]  |
| CXCL4    | Platelet factor 4 (PF-4) (C-X-C motif chemokine 4) (Iroplact) (Oncostatin-A) [Cleaved into:  |
| CACL     | Platelet factor 4, short form (Endothelial cell growth inhibitor)]   |
| CXCL5    | C-X-C motif chemokine 5 (ENA-78(1-78)) (Epithelial-derived neutrophil-activating protein   |
|          | 78) (Neutrophil-activating peptide ENA-78) (Small-inducible cytokine B5) [Cleaved into:  |
|          | ENA-78(8-78); ENA-78(9-78)]  |
| CXCL6    | C-X-C motif chemokine 6 (Chemokine alpha 3) (CKA-3) (Granulocyte chemotactic protein   |
|          | 2) (GCP-2) (Small-inducible cytokine B6) [Cleaved into: Small-inducible cytokine B6, N-  |
|          | processed variant 1; Small-inducible cytokine B6, N-processed variant 2; Small-inducible   |
|          | cytokine B6, N-processed variant 3]  |



| CVCL 7                      | Plantather and the (PPP) (C.V. C. and C. day, 11, 12, 13, 14, 14, 14, 14, 14, 14, 14, 14, 14, 14  |
|-----------------------------|---|
| CXCL7                       | Platelet basic protein (PBP) (C-X-C motif chemokine 7) (Leukocyte-derived growth factor) (LDGF) (Macrophage-derived growth factor) (MDGF) (Small-inducible cytokine B7) [Cleaved into: Connective tissue-activating peptide III (CTAP-III) (LA-PF4) (Low-affinity platelet factor IV); TC-2; Connective tissue-activating peptide III(1-81) (CTAP-III(1-81)); Beta-thromboglobulin (Beta-TG); Neutrophil-activating peptide 2(74) (NAP-2(74));  |
|                             | Neutrophil-activating peptide 2(73) (NAP-2(73)); Neutrophil-activating peptide 2 (NAP-2); TC-1; Neutrophil-activating peptide 2(1-66) (NAP-2(1-66)); Neutrophil-activating peptide 2(1-63) (NAP-2(1-63))]   |
| CXCL9                       | C-X-C motif chemokine 9 (Gamma-interferon-induced monokine) (Monokine induced by interferon-gamma) (HuMIG) (MIG) (Small-inducible cytokine B9)  |
| Cytochro<br>me C            | Cytochrome c  |
| EGF                         | Pro-epidermal growth factor (EGF) [Cleaved into: Epidermal growth factor (Urogastrone)]   |
| EGFR                        | Epidermal growth factor receptor (EC 2.7.10.1) (Proto-oncogene c-ErbB-1) (Receptor tyrosine-protein kinase erbB-1)  |
| EMMPRI<br>N                 | Basigin (5F7) (Collagenase stimulatory factor) (Extracellular matrix metalloproteinase inducer) (EMMPRIN) (Leukocyte activation antigen M6) (OK blood group antigen) (Tumor cell-derived collagenase stimulatory factor) (TCSF) (CD antigen CD147)  |
| Erythrop<br>oietin<br>(EPO) | Erythropoietin (Epoetin)  |
| FAS-L                       | Tumor necrosis factor ligand superfamily member 6 (Apoptosis antigen ligand) (APTL) (CD95 ligand) (CD95-L) (Fas antigen ligand) (Fas ligand) (FasL) (CD antigen CD178) [Cleaved into: Tumor necrosis factor ligand superfamily member 6, membrane form; Tumor necrosis factor ligand superfamily member 6, soluble form (Receptor-binding FasL ectodomain) (Soluble Fas ligand) (sFasL); ADAM10-processed FasL form (APL); FasL intracellular domain (FasL ICD) (SPPL2A-processed FasL form) (SPA)] |
| FGF-1                       | Fibroblast growth factor 1 (FGF-1) (Acidic fibroblast growth factor) (aFGF) (Endothelial cell growth factor) (ECGF) (Heparin-binding growth factor 1) (HBGF-1)  |
| FGF-19                      | Fibroblast growth factor 19 (FGF-19)  |
| FGF-2                       | Fibroblast growth factor 2 (FGF-2) (Basic fibroblast growth factor) (bFGF) (Heparin-binding growth factor 2) (HBGF-2)   |
| FGF-21                      | Fibroblast growth factor 21 (FGF-21)  |
| FGF-4                       | Fibroblast growth factor 4 (FGF-4) (Heparin secretory-transforming protein 1) (HST) (HST-1) (HSTF-1) (Heparin-binding growth factor 4) (HBGF-4) (Transforming protein KS3)  |
| FGF-6                       | Fibroblast growth factor 6 (FGF-6) (Heparin secretory-transforming protein 2) (HST-2) (HSTF-2) (Heparin-binding growth factor 6) (HBGF-6)   |
| FGF-7                       | Fibroblast growth factor 7 (FGF-7) (Heparin-binding growth factor 7) (HBGF-7)   |
| (KGF)                       | (Keratinocyte growth factor)  |
| FGF-9                       | Fibroblast growth factor 9 (FGF-9) (Glia-activating factor) (GAF) (Heparin-binding growth factor 9) (HBGF-9)  |
| FGFR3<br>(IIIc)             | Fibroblast growth factor receptor 3 (FGFR-3) (EC 2.7.10.1) (CD antigen CD333)   |



| FLRG<br>(FSTL3)       | Follistatin-related protein 3 (Follistatin-like protein 3) (Follistatin-related gene protein)  |
|-----------------------|--|
| Flt-3                 | Fms-related tyrosine kinase 3 ligand (Flt3 ligand) (Flt3L) (SL cytokine)   |
| Ligand<br>G-CSF       | Granulocyte colony-stimulating factor (G-CSF) (Pluripoietin) (Filgrastim) (Lenograstim)  |
|                       |  |
| GDF-11                | Growth/differentiation factor 11 (GDF-11) (Bone morphogenetic protein 11) (BMP-11)   |
| (BMP-<br>11)          |  |
| GDF-15                | Growth/differentiation factor 15 (GDF-15) (Macrophage inhibitory cytokine 1) (MIC-1)   |
| (MIC-1)               | (NSAID-activated gene 1 protein) (NAG-1) (NSAID-regulated gene 1 protein) (NRG-1)  |
| (IVIIC 1)             | (Placental TGF-beta) (Placental bone morphogenetic protein) (Prostate differentiation  |
|                       | factor)  |
| GDNF                  | Glial cell line-derived neurotrophic factor (hGDNF) (Astrocyte-derived trophic factor) (ATF)   |
| GFAP                  | Glial fibrillary acidic protein (GFAP)   |
| GM-CSF                | Granulocyte-macrophage colony-stimulating factor (GM-CSF) (Colony-stimulating factor) (CSF) (Molgramostin) (Sargramostim)  |
| Granzym               | Granzyme B (EC 3.4.21.79) (C11) (CTLA-1) (Cathepsin G-like 1) (CTSGL1) (Cytotoxic T-   |
| е В                   | lymphocyte proteinase 2) (Lymphocyte protease) (Fragmentin-2) (Granzyme-2) (Human  |
|                       | lymphocyte protein) (HLP) (SECT) (T-cell serine protease 1-3E)   |
| Growth                | Somatotropin (Growth hormone) (GH) (GH-N) (Growth hormone 1) (Pituitary growth   |
| Hormon                | hormone)   |
| e                     |  |
| (Somatot ropin)       |  |
| HGF                   | Hepatocyte growth factor (Hepatopoietin-A) (Scatter factor) (SF) [Cleaved into:  |
| 1101                  | Hepatocyte growth factor alpha chain; Hepatocyte growth factor beta chain]   |
| HVEM                  | Tumor necrosis factor receptor superfamily member 14 (Herpes virus entry mediator A)   |
|                       | (Herpesvirus entry mediator A) (HveA) (Tumor necrosis factor receptor-like 2) (TR2) (CD  |
|                       | antigen CD270)   |
| ICAM-1                | Intercellular adhesion molecule 1 (ICAM-1) (Major group rhinovirus receptor) (CD antigen   |
|                       | CD54)  |
| ICAM-2                | Intercellular adhesion molecule 2 (ICAM-2) (CD antigen CD102)  |
| IFN                   | Interferon alpha-1/13 (IFN-alpha-1/13) (Interferon alpha-D) (LeIF D)   |
| alpha                 |  |
| IFN                   | Interferon alpha-2 (IFN-alpha-2) (Interferon alpha-A) (LeIF A)   |
| alpha 2               |  |
| (alpha A)<br>IFN beta | Interferon beta (IFN-beta) (Fibroblast interferon)   |
|                       | , , , ,  |
| IFN                   | Interferon gamma (IFN-gamma) (Immune interferon)   |
| gamma<br>IFN-         | Interferon epsilon (IFN-epsilon) (Interferon epsilon-1)  |
| epsilon               | interior epsilon (in Wepsilon) (interior epsilon-1)  |
| IGF-1                 | Insulin-like growth factor I (IGF-I) (Mechano growth factor) (MGF) (Somatomedin-C)   |
|                       | The state of the s |



| IGF-2     | Insulin-like growth factor II (IGF-II) (Somatomedin-A) (T3M-11-derived growth factor)                        |
|-----------|--|
| IGF-Z     | [Cleaved into: Insulin-like growth factor II; Insulin-like growth factor II Ala-25 Del; Preptin]             |
| IL-1      | Interleukin-1 alpha (IL-1 alpha) (Hematopoietin-1)   |
| alpha     | interreakin 1 dipila (il 1 dipila) (riematopoletin 1)  |
| IL-1 beta | Interleukin-1 beta (IL-1 beta) (Catabolin)   |
| IL-1 R1   | Interleukin-1 receptor type 1 (IL-1R-1) (IL-1RT-1) (IL-1RT1) (EC 3.2.2.6) (CD121 antigen-like                |
|           | family member A) (Interleukin-1 receptor alpha) (IL-1R-alpha) (Interleukin-1 receptor type                   |
|           | I) (p80) (CD antigen CD121a) [Cleaved into: Interleukin-1 receptor type 1, membrane form                     |
|           | (mIL-1R1) (mIL-1RI); Interleukin-1 receptor type 1, soluble form (sIL-1R1) (sIL-1RI)]                        |
| IL-1      | Interleukin-1 receptor antagonist protein (IL-1RN) (IL-1ra) (IRAP) (ICIL-1RA) (IL1 inhibitor)                |
| RA/RN     | (Anakinra)   |
| IL-10     | Interleukin-10 (IL-10) (Cytokine synthesis inhibitory factor) (CSIF)   |
| IL-11     | Interleukin-11 (IL-11) (Adipogenesis inhibitory factor) (AGIF) (Oprelvekin)                                  |
| IL-12 p35 | Interleukin-12 subunit alpha (IL-12A) (Cytotoxic lymphocyte maturation factor 35 kDa                         |
|           | subunit) (CLMF p35) (IL-12 subunit p35) (NK cell stimulatory factor chain 1) (NKSF1)                         |
| IL-12 p40 | Interleukin-12 subunit beta (IL-12B) (Cytotoxic lymphocyte maturation factor 40 kDa                          |
|           | subunit) (CLMF p40) (IL-12 subunit p40) (NK cell stimulatory factor chain 2) (NKSF2)                         |
| IL-12 p70 | Interleukin-12 subunit alpha (IL-12A) (Cytotoxic lymphocyte maturation factor 35 kDa                         |
|           | subunit) (CLMF p35) (IL-12 subunit p35) (NK cell stimulatory factor chain 1) (NKSF1)                         |
| IL-13     | Interleukin-13 (IL-13)   |
| IL-15     | Interleukin-15 (IL-15)   |
| II-15/IL- | Interleukin-15 (IL-15)   |
| 15R       | 8  |
| alpha .   | Interleukin-15 receptor subunit alpha (IL-15 receptor subunit alpha) (IL-15R-alpha) (IL-                     |
| complex   | 15RA) (CD antigen CD215) [Cleaved into: Soluble interleukin-15 receptor subunit alpha                        |
| II 1C     | (sIL-15 receptor subunit alpha) (sIL-15R-alpha) (sIL-15RA)]  |
| IL-16     | Pro-interleukin-16 [Cleaved into: Interleukin-16 (IL-16) (Lymphocyte chemoattractant factor) (LCF)]          |
| IL-17A    | Interleukin-17A (IL-17) (IL-17A) (Cytotoxic T-lymphocyte-associated antigen 8) (CTLA-8)                      |
| IL-17B    |  |
| IL-1/B    | Interleukin-17B (IL-17B) (Cytokine Zcyto7) (Interleukin-20) (IL-20) (Neuronal interleukin-17-related factor) |
| IL-17C    | Interleukin-17C (IL-17C) (Cytokine CX2)  |
| IL-17D    | Interleukin-17D (IL-17D) (Interleukin-27) (IL-27)  |
| IL-17E    | Interleukin-25 (IL-25) (Interleukin-17E) (IL-17E)  |
| (IL-25)   |  |
| IL-17F    | Interleukin-17F (IL-17F) (Cytokine ML-1)   |
| IL-18     | Interleukin-18 (IL-18) (Iboctadekin) (Interferon gamma-inducing factor) (IFN-gamma-                          |
|           | inducing factor) (Interleukin-1 gamma) (IL-1 gamma)  |
| IL-2      | Interleukin-2 (IL-2) (T-cell growth factor) (TCGF) (Aldesleukin)   |
| IL-2 RA   | Interleukin-2 receptor subunit alpha (IL-2 receptor subunit alpha) (IL-2-RA) (IL-2R subunit                  |
|           | alpha) (IL2-RA) (TAC antigen) (p55) (CD antigen CD25)  |
| IL-20     | Interleukin-20 (IL-20) (Cytokine Zcyto10)  |
|           |  |



| IL-21    | Interleukin-21 (IL-21) (Za11)   |
|----------|---|
| IL-22    | Interleukin-22 (IL-22) (Cytokine Zcyto18) (IL-10-related T-cell-derived-inducible factor) (IL-                              |
|          | TIF)  |
| IL-22 BP | Interleukin-22 receptor subunit alpha-2 (IL-22 receptor subunit alpha-2) (IL-22R-alpha-2)                                   |
|          | (IL-22RA2) (Cytokine receptor class-II member 10) (Cytokine receptor family 2 member 10)                                    |
|          | (CRF2-10) (Cytokine receptor family type 2, soluble 1) (CRF2-S1) (Interleukin-22-binding                                    |
|          | protein) (IL-22BP) (IL22BP) (ZcytoR16)  |
| IL-23    | Interleukin-23 subunit alpha (IL-23 subunit alpha) (IL-23-A) (Interleukin-23 subunit p19)                                   |
|          | (IL-23p19)  |
| IL-24    | Interleukin-24 (IL-24) (Melanoma differentiation-associated gene 7 protein) (MDA-7)   |
|          | (Suppression of tumorigenicity 16 protein)  |
| IL-27    | Interleukin-27 subunit alpha (IL-27 subunit alpha) (IL-27-A) (IL27-A) (Interleukin-30) (p28)                                |
| IL-28A   | Interferon lambda-2 (IFN-lambda-2) (Cytokine Zcyto20) (Interleukin-28A) (IL-28A)  |
| IL-29    | Interferon lambda-1 (IFN-lambda-1) (Cytokine Zcyto21) (Interleukin-29) (IL-29)  |
| IL-3     | Interleukin-3 (IL-3) (Hematopoietic growth factor) (Mast cell growth factor) (MCGF)   |
|          | (Multipotential colony-stimulating factor) (P-cell-stimulating factor)  |
| IL-31    | Interleukin-31 (IL-31)  |
| IL-32    | Interleukin-32 (IL-32) (Natural killer cells protein 4) (Tumor necrosis factor alpha-inducing                               |
| (alpha)  | factor)   |
| IL-32    | Interleukin-32 (IL-32) (Natural killer cells protein 4) (Tumor necrosis factor alpha-inducing                               |
| (gamma)  | factor)   |
| IL-33    | Interleukin-33 (IL-33) (Interleukin-1 family member 11) (IL-1F11) (Nuclear factor from high                                 |
|          | endothelial venules) (NF-HEV) [Cleaved into: Interleukin-33 (95-270); Interleukin-33 (99-                                   |
| u 25     | 270); Interleukin-33 (109-270)]   |
| IL-35    | Interleukin-27 subunit beta (IL-27 subunit beta) (IL-27B) (Epstein-Barr virus-induced gene                                  |
| IL-4     | 3 protein) (EBV-induced gene 3 protein) Interleukin-4 (IL-4) (B-cell stimulatory factor 1) (BSF-1) (Binetrakin) (Lymphocyte |
| 1L-4     | stimulatory factor 1) (Pitrakinra)  |
| IL-5     | Interleukin-5 (IL-5) (B-cell differentiation factor I) (Eosinophil differentiation factor) (T-cell                          |
| "- "     | replacing factor) (TRF)   |
| IL-6     | Interleukin-6 (IL-6) (B-cell stimulatory factor 2) (BSF-2) (CTL differentiation factor) (CDF)                               |
|          | (Hybridoma growth factor) (Interferon beta-2) (IFN-beta-2)  |
| IL-6 R   | Interleukin-6 receptor subunit alpha (IL-6 receptor subunit alpha) (IL-6R subunit alpha) (IL-                               |
| alpha    | 6R-alpha) (IL-6RA) (IL-6R 1) (Membrane glycoprotein 80) (gp80) (CD antigen CD126)   |
| IL-7     | Interleukin-7 (IL-7)  |
| IL-8     | Interleukin-8 (IL-8) (C-X-C motif chemokine 8) (Chemokine (C-X-C motif) ligand 8)   |
|          | (Emoctakin) (Granulocyte chemotactic protein 1) (GCP-1) (Monocyte-derived neutrophil  |
|          | chemotactic factor) (MDNCF) (Monocyte-derived neutrophil-activating peptide) (MONAP)  |
|          | (Neutrophil-activating protein 1) (NAP-1) (Protein 3-10C) (T-cell chemotactic factor)                                       |
|          | [Cleaved into: MDNCF-a (GCP/IL-8 protein IV) (IL8/NAP1 form I); Interleukin-8 ((Ala-IL-                                     |
|          | 8)77) (GCP/IL-8 protein II) (IL-8(1-77)) (IL8/NAP1 form II) (MDNCF-b); IL-8(5-77); IL-8(6-77)                               |
|          | ((Ser-IL-8)72) (GCP/IL-8 protein I) (IL8/NAP1 form III) (Lymphocyte-derived neutrophil-                                     |
|          | activating factor) (LYNAP) (MDNCF-c) (Neutrophil-activating factor) (NAF); IL-8(7-77)                                       |



|                 | (GCP/IL-8 protein V) (IL8/NAP1 form IV); IL-8(8-77) (GCP/IL-8 protein VI) (IL8/NAP1 form                                  |
|-----------------|---|
| IL-9            | V); IL-8(9-77) (GCP/IL-8 protein III) (IL8/NAP1 form VI)]   |
|                 | Interleukin-9 (IL-9) (Cytokine P40) (T-cell growth factor P40)  |
| Leptin          | Leptin (Obese protein) (Obesity factor)   |
| LIF             | Leukemia inhibitory factor (LIF) (Differentiation-stimulating factor) (D factor) (Melanoma-                               |
|                 | derived LPL inhibitor) (MLPLI) (Emfilermin)   |
| Liver-          | Fatty acid-binding protein, liver (Fatty acid-binding protein 1) (Liver-type fatty acid-binding                           |
| FABP<br>(FABP1) | protein) (L-FABP)   |
| LOX1            | Oxidized low-density lipoprotein receptor 1 (Ox-LDL receptor 1) (C-type lectin domain                                     |
| (OLR1)          | family 8 member A) (Lectin-like oxidized LDL receptor 1) (LOX-1) (Lectin-like oxLDL                                       |
| (02.1.2)        | receptor 1) (hLOX-1) (Lectin-type oxidized LDL receptor 1) [Cleaved into: Oxidized low-                                   |
|                 | density lipoprotein receptor 1, soluble form]   |
| M-CSF           | Macrophage colony-stimulating factor 1 (CSF-1) (M-CSF) (MCSF) (Lanimostim) [Cleaved                                       |
|                 | into: Processed macrophage colony-stimulating factor 1]   |
| M-CSF R         | Macrophage colony-stimulating factor 1 receptor (CSF-1 receptor) (CSF-1-R) (CSF-1R) (M-                                   |
| (CD115)         | CSF-R) (EC 2.7.10.1) (Proto-oncogene c-Fms) (CD antigen CD115)  |
| Mesothe         | Mesothelin (CAK1 antigen) (Pre-pro-megakaryocyte-potentiating factor) [Cleaved into:                                      |
| lin             | Megakaryocyte-potentiating factor (MPF); Mesothelin, cleaved form]  |
| MIF             | Macrophage migration inhibitory factor (MIF) (EC 5.3.2.1) (Glycosylation-inhibiting factor)                               |
|                 | (GIF) (L-dopachrome isomerase) (L-dopachrome tautomerase) (EC 5.3.3.12)   |
| MMP-1           | (Phenylpyruvate tautomerase) Interstitial collagenase (EC 3.4.24.7) (Fibroblast collagenase) (Matrix metalloproteinase-1) |
| IVIIVIP-1       | (MMP-1) [Cleaved into: 22 kDa interstitial collagenase; 27 kDa interstitial collagenase]                                  |
| MMP-10          | Stromelysin-2 (SL-2) (EC 3.4.24.22) (Matrix metalloproteinase-10) (MMP-10) (Transin-2)                                    |
| MMP-12          | Macrophage metalloelastase (MME) (EC 3.4.24.65) (Macrophage elastase) (ME) (hME)  |
| IVIIVII 12      | (Matrix metalloproteinase-12) (MMP-12)  |
| MMP-2           | 72 kDa type IV collagenase (EC 3.4.24.24) (72 kDa gelatinase) (Gelatinase A) (Matrix                                      |
|                 | metalloproteinase-2) (MMP-2) (TBE-1) [Cleaved into: PEX]  |
| MMP-3           | Stromelysin-1 (SL-1) (EC 3.4.24.17) (Matrix metalloproteinase-3) (MMP-3) (Transin-1)                                      |
| MMP-7           | Matrilysin (EC 3.4.24.23) (Matrin) (Matrix metalloproteinase-7) (MMP-7) (Pump-1   |
|                 | protease) (Uterine metalloproteinase)   |
| MMP-9           | Matrix metalloproteinase-9 (MMP-9) (EC 3.4.24.35) (92 kDa gelatinase) (92 kDa type IV                                     |
|                 | collagenase) (Gelatinase B) (GELB) [Cleaved into: 67 kDa matrix metalloproteinase-9; 82                                   |
| NE I            | kDa matrix metalloproteinase-9]   |
| NF-L            | Neurofilament light polypeptide (NF-L) (68 kDa neurofilament protein) (Neurofilament triplet L protein)                   |
| NGF             | Beta-nerve growth factor (Beta-NGF)   |
| beta            | beta herve growth factor (beta fior)  |
| NRG1            | Pro-neuregulin-1, membrane-bound isoform (Pro-NRG1) [Cleaved into: Neuregulin-1   |
| beta 1          | (Acetylcholine receptor-inducing activity) (ARIA) (Breast cancer cell differentiation factor                              |
|                 | p45) (Glial growth factor) (Heregulin) (HRG) (Neu differentiation factor) (Sensory and                                    |
|                 | motor neuron-derived factor)]   |
|                 |   |



| Oncostat         | Oncostatin-M (OSM)   |
|------------------|--|
| in M             | onostatiii iii (osiii)   |
| (OSM)            |  |
| Osteopo          | Osteopontin (Bone sialoprotein 1) (Nephropontin) (Secreted phosphoprotein 1) (SPP-1)   |
| ntin             | (Urinary stone protein) (Uropontin)  |
| (OPN)            | ( ) production of the control of the |
| PCSK9            | Proprotein convertase subtilisin/kexin type 9 (EC 3.4.21) (Neural apoptosis-regulated  |
|                  | convertase 1) (NARC-1) (Proprotein convertase 9) (PC9) (Subtilisin/kexin-like protease PC9)  |
| PDGF-BB          | Platelet-derived growth factor subunit B (PDGF subunit B) (PDGF-2) (Platelet-derived   |
|                  | growth factor B chain) (Platelet-derived growth factor beta polypeptide) (Proto-oncogene c-Sis) (Becaplermin)  |
| PLGF             | Placenta growth factor (PIGF)  |
| Procalcit        | Calcitonin [Cleaved into: Calcitonin; Katacalcin (Calcitonin carboxyl-terminal peptide)  |
| onin             | (CCP) (PDN-21)]  |
| PTX3             | Pentraxin-related protein PTX3 (Pentaxin-related protein PTX3) (Tumor necrosis factor  |
| (Pentraxi        | alpha-induced protein 5) (TNF alpha-induced protein 5) (Tumor necrosis factor-inducible  |
| n 3)             | gene 14 protein) (TSG-14)  |
| Resistin         | Resistin (Adipose tissue-specific secretory factor) (ADSF) (C/EBP-epsilon-regulated  |
|                  | myeloid-specific secreted cysteine-rich protein) (Cysteine-rich secreted protein A12-alpha-  |
|                  | like 2) (Cysteine-rich secreted protein FIZZ3)   |
| S100A8           | Protein S100-A8 (Calgranulin-A) (Calprotectin L1L subunit) (Cystic fibrosis antigen) (CFAG)  |
|                  | (Leukocyte L1 complex light chain) (Migration inhibitory factor-related protein 8) (MRP-8)   |
|                  | (p8) (S100 calcium-binding protein A8) (Urinary stone protein band A)  |
| S100A8-          | Protein S100-A8 (Calgranulin-A) (Calprotectin L1L subunit) (Cystic fibrosis antigen) (CFAG)  |
| A9               | (Leukocyte L1 complex light chain) (Migration inhibitory factor-related protein 8) (MRP-8)   |
| Heterodi         | (p8) (S100 calcium-binding protein A8) (Urinary stone protein band A)  |
| mer              | &  |
|                  | Protein S100-A9 (Calgranulin-B) (Calprotectin L1H subunit) (Leukocyte L1 complex heavy   |
|                  | chain) (Migration inhibitory factor-related protein 14) (MRP-14) (p14) (S100 calcium-  |
|                  | binding protein A9)  |
| S100A9           | Protein S100-A9 (Calgranulin-B) (Calprotectin L1H subunit) (Leukocyte L1 complex heavy   |
|                  | chain) (Migration inhibitory factor-related protein 14) (MRP-14) (p14) (S100 calcium-  |
|                  | binding protein A9)  |
| SAA              | Serum amyloid A-1 protein (SAA) [Cleaved into: Amyloid protein A (Amyloid fibril protein   |
|                  | AA); Serum amyloid protein A(2-104); Serum amyloid protein A(3-104); Serum amyloid   |
|                  | protein A(2-103); Serum amyloid protein A(2-102); Serum amyloid protein A(4-101)]  |
| SCF              | Kit ligand (Mast cell growth factor) (MGF) (Stem cell factor) (SCF) (c-Kit ligand) [Cleaved  |
|                  | into: Soluble KIT ligand (sKITLG)]   |
| ST2 (IL-<br>33R) | Interleukin-1 receptor-like 1 (EC 3.2.2.6) (Protein ST2)   |
| Tau              | Microtubule-associated protein tau (Neurofibrillary tangle protein) (Paired helical  |
| (MAPT)           | filament-tau) (PHF-tau)  |
| TDP-43           | TAR DNA-binding protein 43 (TDP-43)  |
|                  | ואות בותר בווומווק אוסנכווו דב ווכר דבן  |



| TGF-beta  | Transforming growth factor beta-1 proprotein [Cleaved into: Latency-associated peptide     |
|-----------|--|
| 1 (LAP &  | (LAP); Transforming growth factor beta-1 (TGF-beta-1)]                                     |
| Latent)   |  |
| TGF-beta  | Transforming growth factor beta-1 proprotein [Cleaved into: Latency-associated peptide     |
| 1 (total) | (LAP); Transforming growth factor beta-1 (TGF-beta-1)]                                     |
| TGF-beta  | Transforming growth factor beta-2 proprotein (Cetermin) (Glioblastoma-derived T-cell       |
| 2         | suppressor factor) (G-TSF) [Cleaved into: Latency-associated peptide (LAP); Transforming   |
|           | growth factor beta-2 (TGF-beta-2)]   |
| TGF-beta  | Transforming growth factor beta-3 proprotein [Cleaved into: Latency-associated peptide     |
| 3         | (LAP); Transforming growth factor beta-3 (TGF-beta-3)]                                     |
| Tie-2     | Angiopoietin-1 receptor (EC 2.7.10.1) (Endothelial tyrosine kinase) (Tunica interna        |
|           | endothelial cell kinase) (Tyrosine kinase with Ig and EGF homology domains-2) (Tyrosine-   |
|           | protein kinase receptor TEK) (Tyrosine-protein kinase receptor TIE-2) (hTIE2) (p140 TEK)   |
|           | (CD antigen CD202b)  |
| TIMP1     | Metalloproteinase inhibitor 1 (Erythroid-potentiating activity) (EPA) (Fibroblast          |
|           | collagenase inhibitor) (Collagenase inhibitor) (Tissue inhibitor of metalloproteinases 1)  |
|           | (TIMP-1)   |
| Tissue    | Tissue factor (TF) (Coagulation factor III) (Thromboplastin) (CD antigen CD142)            |
| Factor    |  |
| (TF)      |  |
| TNF       | Tumor necrosis factor (Cachectin) (TNF-alpha) (Tumor necrosis factor ligand superfamily    |
| alpha     | member 2) (TNF-a) [Cleaved into: Tumor necrosis factor, membrane form (N-terminal          |
|           | fragment) (NTF); Intracellular domain 1 (ICD1); Intracellular domain 2 (ICD2); C-domain 1; |
|           | C-domain 2; Tumor necrosis factor, soluble form]   |
| TNF beta  | Lymphotoxin-alpha (LT-alpha) (TNF-beta) (Tumor necrosis factor ligand superfamily          |
|           | member 1)  |
| TNF RI    | Tumor necrosis factor receptor superfamily member 1A (Tumor necrosis factor receptor       |
|           | 1) (TNF-R1) (Tumor necrosis factor receptor type I) (TNF-RI) (TNFR-I) (p55) (p60) (CD      |
|           | antigen CD120a) [Cleaved into: Tumor necrosis factor receptor superfamily member 1A,       |
|           | membrane form; Tumor necrosis factor-binding protein 1 (TBPI)]                             |
| TNF RII   | Tumor necrosis factor receptor superfamily member 1B (Tumor necrosis factor receptor       |
|           | 2) (TNF-R2) (Tumor necrosis factor receptor type II) (TNF-RII) (TNFR-II) (p75) (p80 TNF-   |
|           | alpha receptor) (CD antigen CD120b) (Etanercept) [Cleaved into: Tumor necrosis factor      |
|           | receptor superfamily member 1b, membrane form; Tumor necrosis factor-binding protein       |
|           | 2 (TBP-2) (TBPII)]   |
| TNF RIII  | Tumor necrosis factor receptor superfamily member 3 (Lymphotoxin-beta receptor)            |
| (Lympho   | (Tumor necrosis factor C receptor) (Tumor necrosis factor receptor 2-related protein)      |
| toxin     | (Tumor necrosis factor receptor type III) (TNF-RIII) (TNFR-III)                            |
| Beta R)   |  |
| TPO       | Thrombopoietin (C-mpl ligand) (ML) (Megakaryocyte colony-stimulating factor)               |
| (Thromb   | (Megakaryocyte growth and development factor) (MGDF) (Myeloproliferative leukemia          |
| opoietin) | virus oncogene ligand)   |
| TRAIL     | Tumor necrosis factor ligand superfamily member 10 (Apo-2 ligand) (Apo-2L) (TNF-related    |
|           | apoptosis-inducing ligand) (Protein TRAIL) (CD antigen CD253)                              |
|           |  |



| TREM2                         | Triggering receptor expressed on myeloid cells 2 (TREM-2) (Triggering receptor expressed on monocytes 2)  |
|-------------------------------|---|
| TSLP                          | Thymic stromal lymphopoietin  |
| TWEAK                         | Tumor necrosis factor ligand superfamily member 12 (APO3 ligand) (TNF-related weak inducer of apoptosis) (TWEAK) [Cleaved into: Tumor necrosis factor ligand superfamily member 12, membrane form; Tumor necrosis factor ligand superfamily member 12, secreted form] |
| uPA                           | Urokinase-type plasminogen activator (U-plasminogen activator) (uPA) (EC 3.4.21.73) [Cleaved into: Urokinase-type plasminogen activator long chain A; Urokinase-type plasminogen activator short chain A; Urokinase-type plasminogen activator chain B]               |
| VCAM-1                        | Vascular cell adhesion protein 1 (V-CAM 1) (VCAM-1) (INCAM-100) (CD antigen CD106)  |
| VEGF<br>Receptor<br>2 (Flk-1) | Vascular endothelial growth factor receptor 2 (VEGFR-2) (EC 2.7.10.1) (Fetal liver kinase 1) (FLK-1) (Kinase insert domain receptor) (KDR) (Protein-tyrosine kinase receptor flk-1) (CD antigen CD309)  |
| VEGF-A<br>(165)               | Vascular endothelial growth factor A (VEGF-A) (Vascular permeability factor) (VPF)  |
| VEGF-C                        | Vascular endothelial growth factor C (VEGF-C) (Flt4 ligand) (Flt4-L) (Vascular endothelial growth factor-related protein) (VRP)   |
| VEGF-D                        | Vascular endothelial growth factor D (VEGF-D) (c-Fos-induced growth factor) (FIGF)  |
| VEGFR-1                       | Vascular endothelial growth factor receptor 1 (VEGFR-1) (EC 2.7.10.1) (Fms-like tyrosine kinase 1) (FLT-1) (Tyrosine-protein kinase FRT) (Tyrosine-protein kinase receptor FLT) (FLT) (Vascular permeability factor receptor)   |
| WISP-1<br>(CCN4)              | CCN family member 4 (WNT1-inducible-signaling pathway protein 1) (WISP-1) (Wnt-1-induced secreted protein)  |
| XCL1<br>(Lympho<br>tactin)    | Lymphotactin (ATAC) (C motif chemokine 1) (Cytokine SCM-1) (Lymphotaxin) (SCM-1-alpha) (Small-inducible cytokine C1) (XC chemokine ligand 1)  |



## Appendix 2

## Clinical grade analyses for non hospitalized patients

- CA125 (TO BE CONFIRMED)
- CKMB
- FERRITIN
- HE4
- IL6 (TO BE CONFIRMED)
- sFlt-1 (TO BE CONFIRMED)
- TROPONIN
- NT-PRO-BNP
- GDF-15
- PCT
- VIT D
- LIPID PROFILE
- TSH
- CYSC2
- LDH
- ALP
- ALT
- CRE
- UREA
- ELECTROLYTES
- CK
- D-DIMER
- CRPHS
- FIBRINOGEN
- Ca2, PHOS
- VIT B12
- FREE T4

## Serology

- COVID Atc-N
- COVID Atc-S