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Review Article

Dictatorial streaming of biomarkers in some diseases

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ABSTRACT:

The term 'biomarker' is used from 1980. Nowadays, diagnosis/prognosis and research in medical science are more concerned with the discovery and utilization of a number of biomarkers. The information in the library of biomarkers is rising day by day as their major concerns relate diseases, pathogenicity or pharmacology in a variety of hosts. Taking into account, we summarize a number of biomarkers in a number of diseases in human. It includes the name and their up- and/or down expressions in those situations. However, no description was plugged with the individual fact.

1. Introduction

Biological markers are known as 'biomarkers', generally refers to a measurable indicator of some biological states or conditions. Biomarkers can be of any kind, including omics data, like DNA/RNA sequences, proteins, mutations and other attributes of an organism (Dix et al., 2016).

An ideal biomarker should be like: – a finger-print, having analytical validity and the estimated parameter must accurately and clearly discern between altered/normal status and treatment response/non-response of a patient. Specific tests used to identify the biomarkers should be accurate, reliable and reproducible; – a mirror, reflecting the disease or treatment in question, thereby providing clinical validity. In other words, the ideal biomarker should document the activity or progression of the disease and assess any effect of the treatment administered. However, it should not be influenced by some other factors such as age, sex, stress, diet, exercise or genetic determinants. Otherwise, it must have feasibility and being practical to identify and measure rather than variability according to the type of sample collection, processing procedures or methods used for its identification; – non-invasiveness in samples, techniques, and pathophysiological states as well as time and cost effectiveness in treatment courses (Scotton et al., 2014).

Most often biomarkers are used as diagnostic tools, or for anticipating the severity of the disease course (diagnostic/prognostic biomarker). Diagnostic biomarkers are used to separate the healthy population from the affected, or to distinguish between different patient groups based on phenotype severity; – for defining the pharmacokinetic and pharmacodynamic action of drugs and drug response mechanisms (predictive/therapeutic biomarkers). A predictive biomarker highlights the different outcomes of a particular treatment, discriminating between patient categories based on the irresponse to it (Scotton et al., 2014).

It is noteworthy that, biomarkers are often measured and evaluated to examine normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention. Every single pharmacologic response causes up-regulation and/or down-regulation of a number of biomarkers. Direct or indirect detection of them is the ultimate detection/prediction of a particular

physiological state. Nowadays, medical sciences are more advanced with the discovery and using of biomarkers in the context of diagnosis and treatments. Notably, researches in the medical field are directly associated with the measurement of biomarkers. This revision aims at depicting some biomarkers associated with diseases. Biomarkers rather than their description or detection methods are concerned here.

Abbreviations: 15d-PGJ2: Prostaglandin 15-deoxy-PGJ2; 5HT: Serotonin; 5HTT: Serotonin transporter; 7AAD: 7-aminoactinomycin D; ABCA1/B1/G1: ATP binding cassette transporter A1/B1/G1; ACE: Angiotensin-converting enzyme; ACTH: Adrenocorticotrophic hormone; AdA: Adrenic acid; ADAMTS-13: *von Willebrand* factor-cleaving protease; ADH: Vasopressin; ADK: Adenylate kinase; AFA: Alpha-fetoprotein; AGO1: Protein argonaute 1; Akt: Gene encodes protein kinase B; ALA: α-linolenic acid; ALC: Absolute lymphocyte count; ALDOA: Aldosterone; ALK: Anaplastic lymphoma kinase; ALT: Alanine transaminase; ANCA: Anti-neutrophil cytoplasmic antibody; ANGPTL-3: Angiopoietin-like 3; ANP: Atrial natriuretic peptide; anti-AT1R: Angiotensin II type 1 receptor; anti-ETAR: Endothelin-A receptor; AOPPs: Advanced oxidation protein products; apo: Apolipoprotein; aPTT: Antithrombin; ARA: Arachidonic acid; ARHGDIB: Rho GDP dissociation inhibitor β; ARID1A/1B: DNA binding subunits 1A/1B; ASCA: Anti–*Saccharomyces cerevisiae* antibody; ASS: Argininosuccinate synthetase; AST: Aspartate transaminanse; AT1α: Adenosyltranferarse 1α; ATF3: Activating transcription factor 3; ATPIII: Adenosine tri-phosphate III; AURKA: Aurora A kinase; Aβ: Amyloid-beta; BAFF: B cell activating factor; BALF: α-1-antitrypsin, protocadherin-2 precursor, tenascin-C; BAP1: BRCA1 associated protein-1; Bcl-2: B-cell lymphoma 2; BDNF: Brain-derived neurotrophic factor; bFGF: Basic fibroblast growth factor; BHMT: Betaine–homocysteine S-methyltransferase 1; BIRC5: Baculoviral IAP repeat containing 5; BLCA-4: A member of nuclear matrix protein family; BLK: B lymphoid tyrosine kinase; BNGF: B-type neurotrophic growth factor; BNP: Brain natriuretic peptide; BP: Blood pressure; BRAF: Gene that makes a protein called B-Raf; BRCA1/A2: Breast cancer 1/2; BTA: Bladder tumor antigen; BUN: Blood urea nitrogen; C1, C2: Types I and II collagens; C1Q: Type Q collagen; C2C: Collagenase cleavage of type II collagen; C2M: Matrix metalloprotease degraded type II collagen; CA: Carbonic anhydrase; CA19-9: Carbohydrate associated antigen 19-9; CARD8: Cardinal 8; CCL: Chemokine (C-C motif) ligand; CCPs: Cyclic citrullinated proteins; CCR: Chemokine receptors; CD: Glycoprotein type; CD5L: CD5 antigen-like; CDKN2A: Cyclin-dependent kinase Inhibitor 2A; cDNA: circulatory deoxyribonucleic acid; CEA: Carcinoma embryonic antigen; CES-1: Carboxyloesterases; CHD6: Chromodomain helicase DNA binding protein 6; CHRNA3: Cloned the human alpha-3 subunit; ChT: Chitotriosidase; CI-AKI: Contrast-induced acute kidney injury; cIAP: Cellular inhibitor of apoptosis protein; CK: Creatine kinase; CK-MB: An isoenzyme of creatine kinase; CKα: Choline kinase α; CNS: Central nervous system; COMP: Cartilage oligomeric protein (COMP); COMT: Catechol-O- 139 methyltransferase; COX: Cycloxygenase; CpG: Cytosine-guanine; CPII: Propeptide of type II procollagen; CPS-1: Carbomyl phosphate synthase; CREB: cAMP response element-binding protein; CRH: Corticotrophin releasing hormone; CRHD1: Cysteine-rich hydrophobic domain 1; cRNA: circulatory ribonucleic acid; CRP: C-reactive protein; CRP1: Cysteine-rich protein 1; CTLA-4: T lymphocyte-associated 4; CTNNB1: b-catenin; CT-proAVP: Copeptin (C-terminal fragment of vasopressin precursor hormone; CTX-II: C-terminal telopeptide of collagen type II; CXCL-10/IP-10: CXC chemokine ligand-10/IP-10; CXCR4: CXC chemokine receptor type 4; CYFRA 21-1: Serum cytokeratin 19fragment; CYFRA: cytokeratin; CYP3A5: Cytochrome P3A5; D2: dopaminergic receptor-2; DC2s: Dendritic cells; DcR-3: Dacryocystorhinostomy 3; DCRT2: Dehydrocholesterol reductase-transporter 2; DGCR8: Digeorge syndrome critical region gene 8; DHA: Docosahexaenoic acid; DIC: Intravascular coagulation; DMNTB3: DNA methyltransferase 3b; DP-43: DNA-binding protein-43, DPC4: Deleted in pancreatic cancer 4; DPYS: Dihydro-pyrimidinase; EBC: Exhaled breath condensate; ECM: extracellular matrix; EGF: epidermal growth factor; EGFR: Epidermal growth factor receptor; ELAM-1: Endothelial leukocyte adhesion molecule; EMP1: Epithelial membrane protein 1; EMVs: Endothelial-derived MVs; eNOS: Endothelial NOS; EPA: Eicosapentaenoic acid; ER: Estrogen receptor; ERBB2 (HER2): Human epidermal growth factor receptor 2; ESPL1: Extra spindle pole bodies like 1; ESR: Erythrocyte sedimentation rate; ESSDAI: EULAR Sjögren's syndrome disease activity index; ET-1: Endothelin-1; FABP: Fatty acid binding protein; FAH: Fumarylacetoacetate hydrolase; FBP1: Fructose-1,6-bisphosph atase 1; FENO: Fraction of exhaled nitric oxide; FGF-21/23: Fibroblast growth factor-21/23; FGFR1/R2/R3: Fibroblast growth factor receptor 1/2/3; FHIT: Heparin-induced thrombocytopenia; Flt3/Flt3L: Fms-like tyrosine kinase 3/3L; FMD: Fibromuscular dysplasia; FOXA1: Forkhead box protein A1; FRP: Frizzled-related protein; FSITP2; Fat storage-inducing transmembrane protein 2; GABA: Gamma amino-butyric acid; GATA3: Transacting T-cell-specific transcription factor; GBP2: Guanylate binding protein 2; G-CSF: Glial cerebrospinal fluid; GDF-15: growth differentiating factor-15; GDH: Glutamate dehydrogenase; GFAP: Glial fibrillary acidic protein; GFR: Glomerular filtration rate; GNA11: Guanine nucleotide-binding protein 11; GNAQ: Guanine nucleotide-binding protein G(q); GPx: Glutathione peroxidase; GRHL2: Grainyhead-like 2; GRM4: glutamate metabotropic receptor 4; GRO-α: Spinal CXCL1; GST-A2: Glutathione S-transferase A2; GT1: Glucose transporter 1; GUSTO IV: A prognostic marker in recurrent nonfatal myocardial infarction or cardiac death; H_2O_2: Hydrogen peroxide; HA: Hyaluronan; Hb: Hemoglobin; HDAC-1/2: Histone deacetylases-1/2; HDL-C: High density lipoprotein cholesterol; HFABP: Heart type fatty acid binding protein; HGF: Hepatocyte growth factor; HIF-2α: Hypoxia-inducible factor 2α; HIP1: Huntingtin interacting protein 1; HJBS: Howell–Jolly Bodies; HLA-DRB1: Human leukocyte antigen-D related B1; HLAs: Human leukocyte alleles; HMGB: high mobility group box; HNF-α 4: Hepatocyte nuclear factor α 4; hnRNP-A2/B1: Heterogeneous

nuclear ribonucleoprotein- A2/B1; HOXB13: Homeobox protein 13; HPV: Human papillomavirus; HR: Heart rate; HRAS: Hepatorenal syndrome; HSP70: Heat shock protein 70; HSPG: Heparan sulfate proteoglycan; HYAL-1: Hyaluronoglucosaminidase 1; ICAM-1: Iintracellular adhesion molecule 1; ICAMs: Intercellular adhesion molecules; ICH: Intracerebral hemorrhage; ICOS: Inducible costimulator (T cell activation marker); IDH1: Isocitrate dehydrogenase 1; IDHs: Isocitrate dehydrogenases; IDL: Intermediate density lipoprotein; IFLCs: Immunoglobulin free light chains; IFNARs: Interferon-α/β receptor; IFNRF1: Interferon regulatory factor 1; IFN-γ: Interferon-gamma; Ig: Immunoglobulin; IGFBP7: Growth factor–binding protein 7; IKBKE: Inhibitor of kappaB kinase epsilon; IL: Interleukin; ILC2: Lymphoid type 2 cells; iNOS: Inducible nitric oxide synthase; IP-10: IFN-γ-induced protein 10 kDa; IRAK3: IL-1 receptor associated kinase 3; ISCs: Irreversibly sickled cells; KIF5B: Kinesin family member 5B; KIM-1: Kidney injury molecule 1; KL-6: Lungen-6; KLC1: Kinesin light chain 1; KLF4/6: Kruppel-like factor 4/6; KLK2/3/5/7: Kallikrein-related peptidase 2/3/5/7; KRAS: Kirstenrat sarcoma viral oncogene homolog; KRT5/6B/14/20: Human epidermolysis bullosa simplex; LBP: Lipopolysaccharide binding protein; LCK: Tyrosine kinase; LDH: Lactate dehydrogenase; LDL-C: Low density lipoprotein cholesterol; L-FABP: Liver-type fatty acid-binding protein; Lp-PLA2: lipoprotein-associated phospholipase A2; LRRN3: Leucine-rich repeat neuronal 3; LT: Leukotriene; MAP2: Microtubule associated protein 2; MBL2: Mannose-binding lectin 2; MBP: Myelin basic protein; MCP-1: Monocyte chemoattractant protein-1; MCV: Mean corpuscular volume; MeCP2: Methyl-CpG-binding protein-2; MET4: Associated protein like 4; MHC-I/II: Major histocompatibility complex I/II; MI1: Meiosis inhibitor 1; MIA: Melanoma inhibitory activity; MIF: Macrophage migration inhibitory factor; MIP: Macrophage inflammatory protein; miRNA: Micro ribonucleic acid; MLCKI: Myosin light-chain kinase I; MLL3: Mixed-lineage leukemia 3; MMPs: Matrix metalloproteinases; MOG: Myelin oligodendrocyte glycoprotein; MPO: Myeloperoxidase; MRproADM: Inflammation markers; mtDNA: Mitochondrial DNA; mTOR: Rapamycin; MUC1/5B: Mucin 1/5B; MUP2: Major urinary protein 2; NAD: Nicotinamide adenine dinucleotide; NAG: N-acetylglucosamin; NCOR1: Nuclear receptor co-repressor 1; NCR3: Natural cytotoxicity triggering receptor 3; nDNA: nuclear DNA; NF1: Neurofibromatosis-1; NFH: Neurofilaments at high level; NFL: Neurofilaments at low level; NFM: Neurofilaments at medium level; NFs: neurofilaments: ; NF-κB: Nuclear factor kappa-B; NGAL: Neutrophil gelatinase-associated lipocalin; NLR: Neutrophil-to-lymphocyte ratio; NMDA-R: N-methyl-D-aspartate receptor; NMP22: Nuclear matrix protein 22; nNOS: neuronal NOS; NO: Nitric oxide; NSE: Neuron-specific enolase; NTX: N-terminal telopeptide crosslinks; NY-ESO-1: Poly functional T cell response to the tumor antigen; OGG1: 8-Oxoguanine glycosylase 1; OmpC: Outer membrane protein C; ONECUT2: One cut homeobox 2; OSR1: Oxidative Stress Response 1; OT: Oxytocin; OTX1: Homeobox protein 1; P4P3K: Phosphatidylinositol-4-phosphate 3-kinase; PAI: plasminogen activator inhibitor-1; PBMCs: Peripheral blood monomorphonuclear cells; PCNA: Proliferating cell nuclear antigen; PCT: Procalcitonin; PCX: Podocalyxin; PD-1: Programmed death 1; PDCD1: Programmed cell death protein 1; PDGF: Platelet-derived growth factor; PDGFR-β: Beta-type platelet-derived growth factor receptor; PD-L1: Programmed death ligand 1; PFKFB4: 6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 4; PGE2: Prostaglandin E2; PGF: Placental growth factor; PI3K: Phosphatidylinositol-4,5-bisphosphate 3-kinase; PIIANP: N-propeptide of collagen II; PIIINP: N-propeptides of collagen type III; PINP: N-propeptides of collagen type I; PIT: Pitted erythrocyte; P-JNK: Phosphorylation of 49 c-jun-N terminal kinase; PLA2: Phospholipase A2; PLCL1: Phospholipase C–like 1; PlGF: Placental growth factor; PMBCs: Peripheral blood mononuclear cells; pNF: Proprioceptive neuromuscular facilitation; PNS: Peripheral nervous system; PON1: Paraoxonase-1; PP1: Protein phosphatase 1; PPARs: Peroxisome proliferator-activated receptors; PPIA: Phosphatase Inhibition A; PR: Progesterone receptor; pRB: A p53 combination molecular marker; PROVE IT-TIMI 22: Myocardial Infarction *22*; PrPC: GPI-anchored protein; PRT: Prolactin; PSA: Prostate-specific antigen; PSMB9: Proteasome subunit beta type-9; PTPN22: Protein tyrosine phosphatase non-receptor type 22; PTX3: Pentraxin 3; PUFAs: Polyunsaturated fatty acids; RAF-1: Rheumatoid Arthritis Factor 1; RAGE: receptor for advanced glycation end-products; RAN: Repeat associated non-AUG ; RANKL: Receptor activator of nuclear factor kappa B ligand; RAS: Recurrent aphthous stomatitis; RASSF1A: RAS association domain family protein 1A; RBC: Red blood cell; RBP-4: Retinol binding protein 4; REST: Repressor element 1-silencing transcription factor; RET: Rearranged in transfection; RNS: Reactive nitrogen species; ROS: Reactive oxygen species; RRM1: Ribonucleotide reductase subunit M1; RTK: Receptor tyrosine kinases; RUNX3: Runt-related transcription factor 3; S-100B: Glial protein; SAA: Serum amyloid A; SAMe: S-adenosyl-L-methionine; SAP: Serum amyloid protein; SCC-Ag: Squamous cell carcinoma antigen; SCr: Serum creatinine; SEP15s: Small intestine in sclerosing peritonitis; SERT: Platelet membrane serotonin transporter; sICAM-1: Soluble intercellular adhesion molecule 1; sIL-2R: Soluble interleukin-2 receptor; sIL-2Ra: Soluble interleukin-2 receptor a; SMAD4: SMAD family member 4; SNPs: Single nucleotide polymorphisms; SOD: Superoxide dismutase; SOX1: Ranscription factor; SP-A: Surfactant protein A; SP-D: Surfactant protein D; sPLA2: Secretory phospholipase A2; SR-B1: Scavenger receptor type B1; SSAO: semicarbazide-sensitive amine oxidase; STAT3/4: Signal transducers and activators of transcription 3/4; sTfR: A type of soluble IgA receptor; suPAR: Urokinase-type plasminogen activator receptor; sVCAM: Soluble vascular cell adhesion molecule; SVO: Small-vessel occlusion; TAFI: thrombin-activatable fibrinolysis inhibitor; TANK: A NF-kB-related gene; TEL: Telomerase; TF3I: Trefoil factor 3 intestinal; TG: Triglyceride; TGF-β1: Transforming growth factor beta 1; Th1/2: T-helper type 1/2; TILs: Tumor-infiltrating lymphocytes; TIMPs: Tissue inhibitors of metalloproteinases; TLR4: Toll-like receptor 4; TNBC: Triple-negative breast carcinoma; TNC: Tenascin-C; TNF-R: TNF receptor; TNFR1: TNF receptor 1; TNF-α/β: Tumor necrosis

factor-alpha/beta; TNM-I: TNM-immune; TRD3: Tetratricopeptide repeat domain 3; TRK: Tropomyosin-related kinase; TrKB: Transient kinase B; TRV: Tricuspid regurgitant jet velocity; TWEAK: TNF-like weak inducer of apoptosis; TZFH2: Teashirt zinc finger homeobox 2; UK1: Uridine kinase 1; UO: Urinary output; VAP-1: Vascular adhesion protein-1; VCAM-1: Vascular cell adhesion molecule 1; VGEF: Vascular endothelial growth factor; VHL: von Hippel-Lindau gene; VILIP)-1: Visininlike protein-1, VLDL: Very low density lipoprotein; VOCs: Volatile organic compounds; vWF: von Willebrand factor; WBC: White blood cell; YKL-40: Cartilage glycoprotein 39; α/πGST: Alpha/pi-glutathione S-transferase; α-sAPP: Soluble amyloid precursor protein-α; β-sAPP: Soluble amyloid precursor protein-β.

2. Biomarkers found in –

2.1 Complications in nervous system (CNS/PNS)

2.1.1 Urinary biomarkers

Up-regulation: IgA, small polypeptides, HSPG, apo-A1, α-hydroxybutyrate, oxalacetate, acetone, choline, formate, N-methylnicotinamide, serum albumin, alanine, sorbitol, uric acid, azelaic acid, β-alanine, isobutyrate, *N*-methyl-2-pyridone-5-carboxamide, *N*-methyl nicotinic acid, taurine, *N*-methyl nicotinamide, 3-(3-hydroxyphenyl)-3-hydroxypropanoic, 3,4-dihydroxybutyric acid, glycolic acid, glycine, cis-aconitic acid, oxalic acid, β-hydroxybutyric acid, ribonic acid, m-hydroxybenzoic acid, pregnanediol, valine, glucose; protein AMBP, malonate, m-hydroxyphenylacetate, hippuric acid, quinolinic acid, tyrosine, pseudouridine, 2,4-dihydroxypyrimidine, glutamate, fructose, 1,2,3-butanetriol, propylene glycol, phosphoric acid, sebacic acid, creatinine, hippurate, creatine, citrate, a-KG, TMAO (An and Gao, 2015).

2.1.2 Spinal cord injury

Up-regulation: p-Tau, NFs, NSE, GFAP, MBP, S-100β, cytokines, cysteine residues (CC, CXC and CX3X (CX3CL1)), MCP-1, chemokine (CXCL12 and its receptor CXCR4), TNF-R1, TNF-α, IL-1β, -2, -4, -5, -6, -7, -8, -10, -13, -15, -16, -17, IP-10, IFN-α, monokine induced by IFN-γ (MIG or CXCL9), MIP (Cruz et al., 2015).

2.1.3 Alzheimer's disease

Up-regulation: Aβ-1-40, -42 in apo-E, p-tau/t-tau, DP-43, VILIP-1, YKL-40, HFABP (Mattsson et al., 2015; Blennow et al., 2015); Micro-RNAs (miR-486-5p, hsa-miR-4299, let-7a-5p, let-7d-5p, let-7e-5p, let-7f-5p, let-7g-5p, miR-1, miR-103, miR-122-5p, miR-125b, miR-126-3p, miR-1274a, miR-1294, miR-1306-5p, miR-133a, miR-137, miR138-5p, miR-139-5p, miR-142-3p, miR-143, miR-144-5p, miR-145, miR-146a, miR-148a-3p, miR-15a-5p, miR-17-3p, miR-17-5p, miR-181b, miR-181c, miR-191-5p, miR-19a, miR-19b, miR-20a-5p, miR-210-3p, miR-21-5p, miR-219, miR-22p, miR-23a, miR-24-3p, miR-26b, miR-29a, miR-29b, miR-29b-3p, miR-29c, miR-301a-3p, miR-30e-5p, miR-31, miR-3200-3p, miR-335, miR-342-3p, miR-36, miR-365, miR-375, miR-449, miR-4674, miR-483-3p, miR-485-5p, miR-486-5p, miR-5001-3p, miR-502-3p, miR-545-3p, miR-548at-5p, miR-659-5p, miR-660-5p, miR-708, miR-885-5p, miR-9, miR-93, miR-98-5p); Down-regulation: Micro-RNAs (let-7b, let-7d-5p, miR- 20a-5b, miR- 221-3p, miR-100, miR-100-5p, miR-101-3p, miR-103, miR-106a-5p, miR-106b-5p, miR-107, miR-125a-3p, miR-125b, miR-126, miR-1274a, miR-137, miR-140-3p, miR-141-3p, miR-142-3p, miR-143-3p, miR-145-5p, miR-1468, miR-146a, miR-146b-5p, miR-148a, miR-148b-5p, miR-151a-3p, miR-151b, miR-155, miR-15a, miR-15a-5p, miR-15b, miR-15b-5p, miR-16-2-3p, miR-181b, miR-181c, miR-182-5p, miR-185-5p, miR-186, miR-186-5p, miR-18a, miR-18b-5p, miR-191, miR-191-5p, miR-193a-5p, miR-196b, miR-1975, miR-206, miR-20a-5p, miR-210-3p, miR-21-5p, miR-23b-3p, miR-24, miR-26a-2-3p, miR-26b, miR-26b-3p, miR-27a-3p, miR-28-3p, miR-296, miR-29a/c, miR-301a-3p, miR-3065-5p, miR-30a, miR-30c-5p, miR-30d-5p, miR-30e-5p, miR-3158-3p, miR-320, miR-320a, miR-323b-5p, miR-331-5p, miR-335-5p, miR-338-3p, miR-342-3p, miR-342-5p, miR-34a, miR-3613-3p, miR-361-5p, miR-3622b-3p, miR-375, miR-378, miR-425, miR-425-5p, miR-4467, miR-451, miR-454, miR-4649-5p, miR-4781-3p, miR-483-3p, miR-483-5p, miR-5001-3p, miR-505, miR-545-3p, miR-550a-5p, miR-563, miR-582-5p, miR-596, miR-600, miR-6513-3p, miR-766, miR-885-5p, miR-9, miR-93, miR-93-5p, miR-98-5p) (Kumar and Reddy, 2016).

2.1.4 Schizophrenia

Up-regulation: BDNF, plasma pro-inflammatory cytokines, pro-inflammatory mediators (PGE2, COX-2, NFκB), 15d-PGJ2, IL-1, -4, -6, -10, -12, -17, TNF, CB1, -2, D2 (Penadés et al., 2015; Goff et al., 2016).

2.1.5 Rare neuromuscular diseases

Up-regulation: TNC, CK (Scotton et al., 2014).

2.1.6 Cognition and cognitive disorders

Up-regulation: Aβ amyloid, Aβ42/Tau (McConathy and Sheline, 2015); Micro-RNAs (miR-132/212, miR-134, miR-34a, miR-128b, miR- 182, miR-183, miR-34, miR- 124, miR-210, miR-278, miR-928, miR-932, miR-641, miR-7a, miR-26a, miR-124, miR-384-5p, miR-188, miR-191, miR-135a/b, miR-146b, miR-92, miR-125b, miR-34c, miR-181b, miR-1274a, miR-137, miR-195, miR-30e, miR-449a, miR-564, miR-548d, miR-572,

miR-652, miR-34c-5p, miR-770-5p, Meso-miR-1, miR-16); Down-regulation: Micro-RNAs (miR-219, miR-132-3p, miR-34c, miR- 137, miR-181c, miR-9, miR-29a/b, miR-34a, miR-146a, miR-125b, miR-432, miR-1271, miR-664, miR-18a, miR-22-3p, miR-106b, miR-107) (Woldemichael and Mansuy, 2016).

2.1.7 Amyotrophic lateral sclerosis (ALS)

Up-regulation: Proinflammatory monocyte, phenotype, microglia or cytokine expression, increased expression of CD4+ T cells, neurofilament in blood/CSF, T2 weighted MRI structural changes, alterations in RAN dipeptide proteins; Down-regulation: Tregs expression, complement activation, SOD1 in the CSF (Bakkar et al., 2015).

2.1.8 Oxidative stress in neonatal brain injury

Up-regulation: F2-isoprostanes (IsoPs), isofurans (IsoFs), F4-neuroprostane, neurofurans, NO, isoforms of NOS (nNOS, eNOS), iNOS, superoxide, H_2O_2 (Tataranno et al., 2015).

2.1.9 Psychiatric disorders

Up-regulation: OT and ADH (Grazia et al., 2016).

2.1.10 Cerebral ischemia

Up-regulation: NR2 peptide, NMDA-R antibody, glutamate, S100b, sRAGE, GFAP, vWF, VCAM-1, ICAM-1, VAP-1, MMP-9, MCP-1, fibronectins, CRP, ESR, TNF-α, IL-6, APC, Lp-PLA2, BNGF, BNP, D-dimer, ICH, SSAO, SVO, fibrinogen, PAI, TAFI, a2-antiplasmin, homocysteine, HDL, VLDL, apo-C-III, apoC-I, glycemia, copeptin, ferritin, NSE, p-Tau protein, albumin, GABA (Maestrini et al., 2016).

2.1.11 Depression

Up-regulation: DMNTB3, B-cell lymphoma 2), 5HT, 5HTT, 5-HT1A receptor, GRM4, polymorphisms in DGCR8 and AGO1, differences in lncRNA-mRNA expression, mtDNA, TEL) FKBP5, OGG1, IL-6, NF-κB, pro-inflammatory heterodimer (RelA:p50), apo-E2, CD8+, CD20+, CD4+ cells, STMN1 and P16INK4A, leukocytes, lymphocytes, platelets, PMBCs, BDNF; Micro-RNAs (pre-miR-30e, pre-miR-182, miR-429, miR-642, miR-589, miR-579, miR-941, miR-133a, miR-494, miR-107, miR-148a, miR-652, miR-425-3p , miR-20b-3p, miR-433, miR-409-3p, miR-410, miR-485-3p, miR-133a, miR-145 , miR-130b, miR-505, miR-29b-2, miR-26b, miR-22, miR-26a, miR-664, miR-494, let-7d, let-7g, let-7e, let-7f, miR-629, miR-106b, miR-103, miR-191, miR-128, miR-502-3p, miR-374b, miR-132, miR-30d, miR-500, miR-589, miR-183, miR-574-3p, miR-140-3p, miR-335, miR-361-5p , miR-132, miR-182 , miR-1972, miR26b, miR-4485, miR-4498, miR-4743, miR-511, miR-320a); Down-regulation: Micro-RNAs (miR-142-3p, miR-517b, miR-636, miR-1243, miR-381, miR-200c, miR-331-5p, miR-34c-5p, miR-770-5p, miR-135 , miR-1202, miR-144-5p, miR-451a, miR-17-5p, miR-223-3p) (Gururajan et al., 2016).

2.1.12 Epilepsy

Up-regulation: Glutamate receptors, nicotinic acetylcholine receptors, CDK5, CK2, TrKB, ADK, m-TOR, CRP, IL-1β, -6, COX-2, TGF-βR, CREB, MeCP2, REST, reelin, myoinositol, glutathione, *N*-acetyl aspartate, hemovanilic acid, hydroxyindolacetic acid; Micro-RNAs (miR-132, miR-34a, miR-146a) (Dixit et al., 2015).

2.1.13 Brain injury

Up-regulation: S100β, enolase, GFAP, p-Tau (Kawata et al., 2016).

2.1.14 Glial tumors

Up-regulation: IDH (IDH1) mutations, promoter methylation of MGMT, chromosomal deletion of 1p/19q, TP53, mutations of *EGFR* and *ATRX* genes, and *BRAF* fusion *via* RAS/RAF/MEK/MAPK signaling pathway (Siegal, 2015).

2.1.15 Oxidative stress and neurological disorders (AdA, ALA, EPA and DHA)

Up-regulation: PUFAs (ARA, AdA, ALA, EPA, DHA) (Galano et al., 2015); sIgA, IgA, IgE, salivary 8-epi-PGF2α, myoglobin, salivary α-amylase, IL-8 (Wang et al., 2015).

2.1.16 Psychogenic nonepileptic seizures

Up-regulation: PRL, ACTH, CRH, CK, NSE, ghrelin and nesfatin-1, GABA, BDNF, WBC count, SERT (Sundararajan et al., 2016).

2.1.17 Neurodegenerative and vascular dementias

Up-regulation: Aβ40, Aβ42, Aβ42/40, Tau, p-Tau, PSEN mutations, Aβ42/p-Tau, α-sAPP, β-sAPP, YKL-40, YKL-40/Aβ42, IL-8, MCP-1, synaptic proteins neurogranin and SNAP-25, APOE-E4; Micro-RNAs (miR-29, miR-146a-5p, miR-27a-3p, miR-29a); Down-regulation: Micro-RNAs (miR-27a-3p, miR-34a, miR-125b, miR-146a, miR-146a) (Llorens et al., 2016).

2.1.18 Systemic sclerosis

Up-regulation: sICAM-1, anti-annexin V antibodies (IgG), endostatin, b-FGF, endostatin, IL-8, -13, -33, sE-

selectin, tissue kallikrein, AECA, soluble endoglin, PBMCs production of TWEAK and VEGF, activated-platelets release of VEGF, PDGF, PDGF-BB, TGF-β1, Ang-1 and Ang-2, ET-1, sVEGF receptor-2, CCL-2, -3, -5 and -13, soluble CD36, CXCL5, 8, 9, 10 and 16, PDGF-BB, G-CSF, sPECAM-1, leptin, HGF, folistatin, anti-AT1R and anti-ETAR, sVCAM, PlGF, MMP-12, galectin-1/3, DcR-3, apelin, Tie-2, endostatin, endoglin, ratio soluble CD163/soluble, TWEAK, sJAM-A and sJAM-C, VEGF165b, sTie-1, RBP-4, ANGPTL-3 (Chora et al., 2015).

2.1.19 Multiple sclerosis

Up-regulation: IgG, MBP, myelin-associated glycoprotein, proteolipid protein, myelin autoantigens, MOG, anti-KIR4.1 antibodies, anti-MOG antibodies, anti-EBNA-1 antibodies, anti-HHV-6 antibodies, anti-MBP antibodies, anti-glycan antibodies, TOB1, vitamin D, BBB damage biomarkers (S100β, sCAMS, zonuline), proinflammatory cytokines (PTX3, OPN, s-4-1BBL, PD-1/PD-L1, MMP-9/TIMP-1, Fas/FasL mRNA, sTRAIL, survivin, K2P5.1, anti-EBNA-1 IgG), EMVs, miRNA in PBMC and plasma, NFL, NFM, NFH, pNF-H, anti-NF-L-IgG, anti-tubulin IgG, MAP2, p-Tau, anti-glycopeptide antibodies, Hsp, sTNF-RII, lactate, Nabs, MxA, sTRAIL mRNA, CXCL-10/IP-10, CCL-2/MCP-1, IFNARs, genome wide expression profiles of PBMC, miRNA expression in PBMC, IL-4, -10, -12, -16, -17, -17F, , PD-1/PD-L1 or PD-1/PD-L2, anti-JCV antibody; Micro-RNAs (miR-21, miR-146a, miR-146b, miR-150, miR-155, miR-326, miR-let-7a, miR-92a, miR-648a, miR-17-5p, miR-92, miR-193a, miR-497, miR-106, miR-25, miR-19a, miR-19b), PTX3, pro-apoptotic gene BCL2L11 (BIM), TGF-β (D'Ambrosio et al., 2015).

2.2 Cancers

2.2.1 Head and neck carcinoma

Up-regulation: Micro-RNAs (miR-425-5p, miR-93-5p) (Bedreag et al., 2015).

2.2.2 Esophageal cancer

Up-regulation: Micro-RNAs (miR-1246, miR-31, miR-1322) (Bedreag et al., 2015).

2.2.3 Nasopharyngeal cancer

Up-regulation: Micro-RNAs (miR-17, miR-20a, miR-29c, miR-223) (Bedreag et al., 2015).

2.2.4 Biliary tract cancers

Up-regulation: ErbB-1/EGFR, ErbB-2/HER-2, ErbB-3/HER-3, VEGF, MAPK, P38MAPKs, ERKs, PIK/PTEN/AKT/mTOR, CA19-9, MMPs, CYFRA 21-1, SMAD4/DPC4, IDHs; Micro-RNAs (miR-135a, miR-26a, miR-21, miR-192) (Hu and Yin, 2016).

2.2.5 Pancreatic cancer

Up-regulation: CA19-9 (Silva, 2015).

2.2.6 Thyroid cancer

Up-regulation: Thyroglobulin, calcitonin (Silva, 2015).

2.2.7 Urothelial carcinoma

Mutations in *UTX*, *MLL3*, *CREBBP-EP300*, *NCOR1*, *ARID1A*, *CHD6*, *STAG2*, *ESPL1*, *RAS* oncogenes (*KRAS*, *HRAS*, *NRAS)*, *FGFR1/R3*, *ERBB2 (HER2*), *MET*, *NF1*, *TSC1*; Up-regulation: expression of orp53/Rb, RTK/RAS/PI3K/Akt/mTOR, histone-modifying genes (acetyl-transferases, methyl-transferases de-methylases) SWI/SNF nucleosome remodeling complex, such as ARID1A/1B, SMARCA2-A4/C1-C2, FGFR3, CD24/44, KRT5/6B/14/20, HER2, FOXA1, GATA3, TRIM24, XBP1, PPAR, BLCA-4, CYFRA 21-1, survivin, DD23, VEGF; CTLA-4, PD-1, CD279, PD-L1 (B7-H1); Micro-RNAs (miR-187, miR-18a, miR-25, miR-142-3p, miR-140-5p, miR-204) (Grivas et al., 2015).

2.2.8 Genitourinary malignancies

Up-regulation: Sipuleucel-T, the check point inhibitors, anti-cytotoxic T-lymphocyte-associated protein 4 (anti-CTLA-4), anti-PD-L1, anti-PD-1, prostate stem cell antigen, MUC1/2, Globo-H, GM2, EGFR, orerbB2, gene markers included KLK2/3, HOXB13, GRHL2, and FOXA1, CD33+, CD11b+, CD15+, CD14+, CD8+ cells, TILs, IL-2, -4, -5, -10, -17, -26, 22RA1, -1RAPL1, -1F5, -17RB, -17RE, -20, -21, -28A, TRAF2; TGF-β , CTLA-4, lymph node, PD-L1/L2, mutation in PDCD1 gene, ALC, CA9, IgG1, fractalkine (CX3CL1), Th1, STAT3 signaling, lymphocyte populations (CD3/CD45RO, CD3/CD8 or CD8/CD45RO), HER-2/neu (p185erbB-2), EGFR, Bcl-2, p53, *BRAF* mutation, TNM-I (Slovin et al., 2016).

2.2.9 Colon cancer

Carcinoembryonic antigen (Silva, 2015); KRAS (Buchbinder and Flaherty, 2016).

2.2.10 Colorectal cancer

Mutations in *KRAS*, *RAS NRAS*, *EGFR* (Waring et al., 2015); Up-regulation: VEGF (VEGFR1, VEGFR2), t/rCECs (CD45+, CD146+, CD34+, CD106+), APO-CECs (CD45-, CD146+, CD34+, CD133-), annexin V+ cells, Tie-2, or CXCR4, 7AAD- (Manzoni et al., 2015); Micro-RNAs (miR-29a, miR-92a, miR-378, miR-21,

miR-18a) (Bedreag et al., 2015); Down-regulation: Vitamin D and calcium (Bostick, 2015).

2.2.11 Bladder cancer

Up-regulation: NMP22, FGFR3, BTA, ImmunoCyt/uCyt1, SOX1, a specific LINE-1 element, IL-1, IRAK3, OTX1, ONECUT2, OSR1, HDAC-1/2 overexpression, KLF4, survivin (BIRC5 or EPR-1), AURKA, NLR, pRB, p21, -27, HRAS, PI3K, CD44v6, VEGFR1/2, HYAL-1, CA-IX, PFKFB4; Micro-RNAs (miR-96, miR-138, miR-126, miR-182, miR-143, miR-222, miR-21, miR-133b, miR-518c-5p, miR-452, miR-129, miR-99a, miR-100, miR-141, miR-639); Down-regulation: Micro-RNAs (miR-200c, miR-99a, miR-100, miR-29c) (Bedreag et al., 2015; Lucca et al., 2015).

2.2.12 Testicular cancer

Up-regulation: Human chorionic gonadotropin-β (Silva, 2015).

2.2.13 Cervical cancer

Up-regulation: HPV DNA, SCC-Ag, CYFRA, CEA, COX-2, sCD44, matrix, MMPs (MMP-2, -9, TIMPs (Dasari et al., 2015).

2.2.14 Prostate cancer

Micro-RNAs (Up-regulation: miR-16, miR-92a, miR-103, miR-107, miR-197, miR-34b, miR-328, miR-485-3p, miR-92b, miR-636, miR-640, miR-766, miR-885-5p) (Bedreag et al., 2015); PSA (Buchbinder and Flaherty, 2016).

2.2.15 Overian cancer

CA125; Micro-RNAs (Up-regulation: miR-21, miR-92, miR-93, miR-126, miR-92a) (Bedreag et al., 2015).

2.2.16 Breast cancer

Up-regulation: Micro-RNAs (miR-10b, miR-341, miR-195) (Bedreag et al., 2015); ER, PR, CA15-3, HER2 (Silva, 2015); EGFR, TNBC, HER1/ErbB1, HER2/new/ErbB2, HER3/ ErbB3, and HER4/ErbB4, TNCs, Bcl-2, adhesion molecule (CD44/CD24), BRCA1/A2, p53, p63, p53siRNA gene, p16INK4a, cytokeratins 5, 14, and 17 (Kallel et al., 2015).

2.2.17 T-cell lymphoma

Mutations in *GATA3*, *TBX21*, *STAT3* genes, Up-regulation: IL-4,-5, -6, -10, -13, -18, -21, Bcl-6, CXCL13, PD-1, VEGF, JAK1/2 expression (Tse and Kwong, 2015).

2.2.18 Melanoma

Lymphocyte count, lymphocytic infiltrates; Up-regulation: LDH; mutations in viral oncogene homolog B1 (BRAF; especially V600 E/K and non- V600 E/K), RAS, NF1, KIT, GNA11/GNAQ, TP53/CDKN2A, IDH1, BAP1; melanoma biomarkers- MIA, S-100B, and TYRP2; IL-2, CTLA-4, PD-1 and PD-L1 antibodies, VGEF expression, ICOS, NY-ESO-1, IFN-γ, pre-existing CD8+ T cells, LCK protein expression; Down-regulation: CTNNB1 (b-catenin) score (Buchbinder and Flaherty, 2016).

2.3 Complications related to kidney

2.3.1 IgA nephropathy

Up-regulation: IL-1β, 2, -6, 2R, TNF-α, IgAN/A1–C3/A1–G/A1–M, sIL-2Ra, PCX, MCP-1, BAFF, EGF, NAG, sTfR, CD89–IgA complexes, AOPPs; Micro-RNAs (miR-146a, miR-155, miR-21, miR-29, miR-29b, miR-29c, miR-93, miR-223) (Moresco et al., 2015).

2.3.2 Renal cancer

Up-regulation: Micro-RNA (miR-1233) (Bedreag et al., 2015).

2.3.3 Kidney injury

Up-regulation: L-FABP, NGAL, αGST, πGST, TLR4, NF-κB, cytokines, FENα, albumin, kidney injury molecule-1 (Belcher, 2015); FGF-23 (Wasung et al., 2015); TIMP-2, IGFBP7, IL-18, CI-AKI, KIM-1 and Cystatin-C (McMahon and Koyner, 2016).

2.3.4 Renal cell carcinoma

Up-regulation: VEGF (VEGF-A, -C, -1, -2, -3), PDGFR-β, Flt-3, RAF-1, c-KIT, IL-6, -8, NLR, CRP, LDH, HIF-2α, PDGF, CA-IX, VHL gene, FGFR2, NR1/2/3, CYP3A5, ABCB1 (Winer et al., 2016)

2.4 Complications related to lungs

2.4.1 Lung disease

Up-regulation: CRP, TGF-β, elastin, fibronectin, collagen, IL-8, *Pseudomoas aeruginosa*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Aspergillus sp* and *Streptococcus pneumoniae*, IgG1, -G4, IP-10 (Ramsey et al., 2015); Proteins: Neuroendocrine markers, p53, HER2, CEA, CYFRA 21-1, CA 15-3, 19-9, 125, TPA, NSE, TAG-72.3, SCC, hnRNP-A2/B1, PCNA, CD34, c-erbB2, FHIT, CTNNB1, MUC1, cyclin D1; Genes: FHIT, p19ras, CHRNA3 SNP, telomere related genes, miRs, Bcl-2, K-ras, methylation of p16INK4a, cdc25B, KLF6, caspase 7, survivin, p16, KLK5, -7, RRM1, RASSF1A, RUNX3, SEPP1, -15, hGPX1, cDNA and cRNA (Altintas and Tothill, 2013).

2.4.2 Interstitial lung diseases

Up-regulation: MMP7, SP-A, -D, KL-6, CCL-18, YKL-40, MUC5B (Nathan et al., 2015).

2.4.3 Lung cancer

Mutations in *EGFR*, *MET*, EML4, *TRK*, *HIPI*, *TRP*, *KIF5B*, *KLC1*, *KRAS*, *I1171T*, protein tyrosine phosphatase, non-receptor type 3, acquired mutations in *L1196M*, *S1206Y*, *C1156Y*, *G1202R*, *1151Tins*, *L1152R*, *c-KIT*, *ROS1*, *RET*, *BRAF*, *and HER2*, *HER2/erbB2* (Kumar et al., 2015); Micro-RNAs (Up-regulation: miR-7i, miR-146b, miR-206, miR-21, miR-10b, miR-15b, miR-19b, miR-182, miR-197, miR-222, miR-320, miR-375, miR-574-5p, miR-660, miR-1254) (Bedreag et al., 2015); Up-regulation: ALK (Buchbinder and Flaherty, 2016); PD-1)/PD-L1, cytotoxic T-lymphocyte antigen-4 protein (Chae et al., 2016).

2.4.4 Childhood asthma

Up-regulation: FENO, LTB4, -C4, -D4, -E4, Cys-LT, IL-4, -5, NO, 8-isoprostane, IFN-γ, Th2/Th1 cytokine, VOCs (Moschino et al., 2015).

2.4.5 Community-acquired pneumonia

Up-regulation: Procalcitonin, MRproADM/ANP, copeptin, cortisol, CRP (Viasus et al., 2016).

2.5 Complications related to liver

2.5.1 Liver cancer

AFP (Buchbinder and Flaherty, 2016).

2.5.2 Hepatocellular carcinoma

Up-regulation: Micro-RNAs (miR-9-3p, miR-9, miR-10a, miR-10b, miR-15a, miR-18a, miR-21, miR-27a, miR-92, miR-96) (Bedreag et al., 2015).

2.5.3 Hepatotoxicity

Up-regulation: GDH, GSH, P-JNK, cytokeratin-18, miR-122, HMBG-1, nDNA, ASS fragments, AST, ALT, BHMT, DPYS, FAH, FBP1, SAMe, COMT, CPS1, mtDNA, nDNA, keratins 8, 18, caspase-3, -7, -9, CES-1, HMGB-1, IL-6, -8 **(**Siemionow et al., 2016**).**

2.5.4 Non-alcoholic fatty liver disease

Altered genes encoding chromatin-remodeling enzymes, including jumonji C-domain-containing histone demethylases; Up-regulation: Micro-RNAs (miR-122, miR-21, miR-34a, miR-451, miR-29, miR-200b, miR-155, miR-200a, miR-200b and miR-429), TLR-4 (i.e.-Asp299Gly and Thr399IleTLR4); Genes: *CYP2A12*, *CYP2C38*, *CYP4A10*, *CYP4A14*, IL-1R-related molecule, aldo-keto reductase family 1 member B10, keratin, type I cytoskeletal 23, FGF-21, GST-A2, AR, NR subfamily 2 group F member 1, HNF-α4, retinoic acid receptor-related orphan receptor 1 α, lymphocyte antigen 6D, fat-specific protein 27, aquaporin 4, UK1, tearoyl-CoA desaturase-1, CD36, CKα, P4P3K, catalytic subunit type 2 γ, insulin induced gene 2, PP1, regulatory subunit 3C, PGD2 synthase 21 kDa, decorin, EMP1, IjB kinase b interacting protein, PPARγ; Protein: FABP, 17β-HSD13, apo-A1, E, protein disulfide isomerase, CYFRA-8, -18, vimentin, MUP2, methylenetetrahydrofolate dehydrogenase 1, LDH-A, annexin A5, DCRT2, cadherin 2, guanosinetriphosphate-binding protein SAR1b; Metabonomic: 1,3-dihydroxyacetone, 12-hydroxyeicosatetraenoic acid, adenosine, butyrylcarnitine, carnitine, cholesterol esters, choline, di-homo-c-linolenic acid, free cholesterol, fructose, glucose, glutamate, glutamyl dipeptides, glutamyl leucin, glutamyl phenylalanine, glutamyl tyrosine, glutamyl valine, glycero pc, glycerylphosphorylethanolamine, glycine conjugates, histidine, inosine, isoleucine, lactate, leucine, linoleic acid, lipids, lysine, methionine sulfoxide, methionine, non-esterified fatty acid, oleic acid, oxidized glutathione, phenylalanine, sarcosine, sorbitol, taurine, taurochendeoxycholate, taurocholate, taurocholic acid, taurodeoxycholic acid, tauro-β-muricholate, tg, tyrosin, tyrosine, uridine, valine, α-hydroxybutyrate; Down-regulation: Genes: glucose-6-phosphatase, PP2, regulatory subunit B, δ, flavin containing monooxygenase 3, CYP7B1, TF3I, synaptotagmin 1, 3-ketosteroid reductase; Proteins: HSP70, senescence marker, p30, chaperonin GroEL, S-adenosylhomocysteine hydrolase, GPx1, GT1, methylthioadenosine, phosphorylase, methionine, AT1α, EGFR, six-transmembrane epithelial antigen of prostate 4, translocation protein SEC62; Metabonomic: 10-undecenoate, 3-phospoglycerate, adenosine triphosphate, arachidonic acid, caprate, carnitine, cholesterol, cholic acid, cis-aconiate, citrate, creatine, cysteine, cysteine-glutathione disulfide, docosahexaenoic acid, eicosapentaenoic acid, ethanolamine, fumarate, glutamate, glutathione, glycine, glycochendeoxycholate, glycocholate, glycodeoxycholic acid, glycogen, gsh, homocysteine, hypotaurine, insulin, lactate, leptin, leucine, malate, methionine, nicotinamide adenine dinucleotide, oleoyllyso pc, oxidized and reduced glutathione, palmitoyllyso pc, pc, phosphate, phosphatidylcholine, phosphoenolpyruvate, phosphoethanolamine, serine, stearoyllyso pc, succinylcarnitine, tgs, tryptophan (Willebrords et al., 2015).

2.5.5 Liver cirrhosis

Up-regulation: Cystatin C, BUN, Beta-2 microglobulin (β2M), GFR, UO, SCr, NGAL, IL-18,

KIM-1, L-FABP, type-1 HRS, CKD, HBV/HCV-associated glomerulonephritis; Micro-RNAs (miR-21, miR-192, miR-433, miR-29, miR-200, miR-223), TGF-β1, IgA, suPAR (Francoz et al., 2016).

2.6 Complications related to heart

2.6.1 Pediatric pulmonary arterial hypertension

Up-regulation: BNP, N-terminal pro-BNP fragments, ANP, CRP, NO, VOCs, endothelin-1, 6-keto PGF, CD11b+, CD62e+, CD31+ CD61+, vascular cell adhesion molecule-1, monocyte chemo attractant protein-1-CRP, CD105+, ILs; MicroRNAs (miR-21, miR-204) (Lohani et al., 2015).

2.6.2 Heart failure with preserved ejection fraction

Up-regulation: ECM, MMPs (TIMP-1, -4, MMP-2, -8, PIIINP, NT-proBNP); galectin-3, ST2 (IL-1) levels; GDF-15, CRP, SAP, pentraxin-3 (Kanagala et al., 2015); IL-33, natriuretic peptides, high-sensitivity troponin, procalcitonin (Wettersten and Maisel, 2016).

2.6.3 Acute coronary syndrome

Up-regulation: CK, CK-MB, LDH, AST, cardiac troponins (cTn: cTnC, cTnI, and cTnT), cystatin C, CRP, GUSTO IV, PROVE IT-TIMI 22, CT-proAVP, GDF-15 (Martin et al., 2015).

2.6.4 Cardiovascular risk

Up-regulation: LDL-C, IDL, VLDL, NO, apo-A-I, -B, ABCA1, -G1, SR-B1 proteins, PLA1, PON1, MPO, ICAMs, VCAM-1, NF-κB expression, endothelial adhesion molecules (including ICAM1/VCAM1) (Hafiane and Genest, 2015), cardiac troponins and/or NT-proBNP (Witteles et al., 2016), TnI, TnT, Hs-CRP, CRP, proBNP, copeptin, CK-MB (Patelis et al., 2016); Down-regulation: HDL-C, HDL (HDL2, HDL3, α-HDL, β-HDL), GPx (Hafiane and Genest, 2015).

2.6.5 Heart failure

Up-regulation: Levels of plasma renin, angiotensin 2, aldosterone, and catecholamines, CRP, IL-1,-6, -18, Fas (APO-1), TNFα, renal challenge (creatinine, BUN, cystatin C), cardiac matrix derangement and fibrosis (procollagens, MMPs, tissue inhibitors of MMPs), ROS status (ROS/RNS, MPO), GDF15, BNPs (BNP1–BNP32, NT-proBNP1–NTproBNP76, pro-BNP), ANP, N-terminal proANP, mid region pro-ANP, norepinephrine, epinephrine, dopamine, arginine vasopressin, copeptin, endothelin 1, big endothelin, adrenomedullin, pentosidine, propeptide procollagen I, procollagen III, MLCKI, HFABP, CK, CK-MB, ST2, osteoprotegerin, adiponectin, galectin 3, coenzyme Q10, multiple amino acids, phosphatidylcholine moieties, serum albumin, urine albumin, Hb, HbA1c, red cell distribution in width (Richards, 2015).

2.7 Complications involving inflammation

2.7.1 Inflammation and inflammatory diseases

Up-regulation: TNF, IL-1, -1β, -2, -4, -6, -10, -13, CRP, COX, LDL-C, HIF-1a, IFN-γ, HLAs, CCPs, ROS, HLA-DRB1, PTPN22, GSH, (Jutley and Young, 2015); IgE, IgG4, IL-2, -C2, -5, -17, -15R, -33, CRTh2+, CD25, CD25+, CD127−, CD161+, CD49d+, CD27−, CD45RB−, PD-L1, Foxp3, TGF-β, FOXP3+ cells (Odegard et al., 2015); MMPs (MMP-2, -9, -2/-9), cathepsins (primary members of the cysteine protease), CD34+ cells, FR-β (Wang et al., 2016); leukocyte antigen (*HLA*)-*DQ* and *HLA-DR* gene, *CpG*, *HLA- DQB1* gene, IgE (Martino et al., 2016).

2.7.2 Idiopathic inflammatory myopathy

Up-regulation: IL-1, 4, -6, -8, -17, -23, -33, sST2, CXCL10, CX3CL1, TNF-α, IFN-α, -β, -ω, -ε, -κ, -λ-1, -λ-2, -λ-3, KL-6, BAFF, MBL2, PTPN22, PLCL1, BLK, CCL21, TYK2; Micro-RNAs (miR-1, miR-133, miR-206); Down-regulation: MHC-I,/II, TLR2, 3, 4, 7 and 9; Micro-RNA (miR-7) (Lu et al., 2015).

2.7.3 Osteoarthritis

Up-regulation: Serum COMP, C2M, urinary CTX-I, -II, urinary α-CTX, serum CD163, plasma CD14,CD163, CRP, PINP, PIIANP, PIINP, serum aggrecan, cIAP, urinary NTx, plasma leptin, adiponectin, resistin, HA, hsCRP, KS, serum TGF-β1, serum VCAM, VCAM-1, ICAM, ICAM-1, adiponectin, leptin, osteocalcin, RANKL, osteoprotegerin, E-selectin, P-selectin, β-CrossLaps, serum FRP, DKK-1, serum C1, C2, C2C, CPII, NTX, CS846, serum MMP-1, -3, -9, YKL-40, serum TIMP-1, FRP, DKK-1 (Hosnijeh et al., 2015).

2.7.4 Allergen immunotherapy

Up-regulation: Th2, Th1/regulatory T-cell profile, Th2/Th1, Th2/Th17, or even Th1/Th17 immune responses, IL-4, -5, -9, -10, -12, -13, -17, -22, IgE, CD4+ T cells, IFN-γ, PBMCs, IgG4, IgAs, IgGs, IgG4s, C1Q, stabilin, proallergic DC2s (i.e.- DCs supporting the differentiation of Th2 cells), PD-L1; Micro-RNAs (miR-21, miR-146, miR-223, miR-126, miR-145, let-7b, miR-132,), ILC1s, -2, -3 (Moingeon, 2016).

2.7.5 Sarcoidosis

Up-regulation: ACE, sIL-2R, SAA, chitotriosidase, BALF (α-1-antitrypsin, protocadherin-2 precursor,

tenascin-C), IL-17RC, TGF-β1, TNF-α, -β, lysozyme, T-bet mRNA, Th1-type immune responses (STAT1, CCL5, IL-7, -15), MMP12, ADAM (decysin 1(ADAMDEC1), ADAMDEC1) gene/protein expression, PBMCs, SNPs, heparin-binding EGF-*like* growth factor, sin3A-associated protein 30 kDa, ATF3, carcinoembryonic antigen-related cell adhesion molecule 1, dehydrogenase/reductase member 9, GBP2, interferon-inducible, IFNRF1, syntaxin 11, transporter 1, ATP-binding cassette, subfamily B (MDR/TAP); Down-regulation: apo-B mRNA editing enzyme, catalytic polypeptide-like 3D, CRP1 (intestinal), chemokine (C-X3-C motif) receptor 1, FSITP2, FK506 binding protein 1A 12 kDa, KIAA1147, killer cell lectin-like receptor subfamily B member 1, hypothetical protein LOC100132356, cytokine receptor CRL2, MI1, noggin, RNA binding motif protein 12B, SERTA domain containing 1, sestrin 3, TZFH2, ZFP 512, 540, 614, 662, 671, 709, CD27 and CD3g molecule, g (CD3-TCR complex), CRHD1, GTPase, IMAP family member 5, IL-7 receptor, potassium voltage-gated channel, shaker-related subfamily member 3, LRRN3, Progestin and adipo Q receptor family member VIII, TRD3, exportin 4 (Casanova et al., 2015).

2.7.6 Sepsis (systemic inflammatory response syndrome; SIRS)

Up-regulation: Plasma ChT, presepsin (a 13-kDa protein), IL-6, -27, hepcidin, MIF, CRP or PCT (Limongi et al., 2016); IL-1, -8, -10, PCT (21, 32, 57, 141 AK), iNOs, TNF-α, LBP (58 kD), IgG, CD 14, 64, 73, IFN-γ, G-CSF, DIC, sCD14-ST (presepsin), TREM-1 (sTREM-1, mTREM-1) (Prucha et al., 2015); IL-2, CD11b/CD18 (Delanghe and Speeckaert, 2015); lactate, procalcitonin, IL-4; GRO alpha, MIP-1, 2; CD-10, 11c, 14, CCR2, 3; TLR2, 4, aPTT, fibrin, thrombomodulin, ADAMTS-13, ELAM-1 (cellular and soluble), adrenomedullin, proadrenomedullin, copeptin, ANP, BNP, CPS-1, SAA, cerulospasmin, ferritin, hepcidin, alpha2 macroglobulin, dipeptidylpeptidase (Kumar et al., 2015); Down-regulation: Micro-RNAs (miR-15a, miR-16, miR-182, miR-199a-5p, miR-203, miR-211, miR-222, miR-29b) (Bedreag et al., 2015); Down-regulation: Micro-RNAs (miR-122, miR-146a, miR-223, miR-483-5p, miR-499-5p, miR-574-5p, miR-150, miR-193b, miR-233, miRNA-146, miR-150, miR-342-5p, miR-466I) (Bedreag et al., 2015).

2.8 Complications related to autoimmune diseases

2.8.1 Primary Sjögren's syndrome

Up-regulation: Type II cryoglobulins, CD4 lymphopenia, B cell lymphomas, anti-Ro/SSA and anti-La/SSB antibodies, lymphotoxins, specific chemokines (CXCL12, CXCL13, CCL11, CCL19 and CCL21), IL-4, -5, -12, -17α, -18; Micro-RNAs (miR-765, miR-181a, miR-766, miR-335, miR-16, miR-671, miR-663, miR-340, hsa-miR-155, miR-5100), BAFF (variants: rs1224141, rs12583006, rs9514828, rs1041569 and rs9514827), NF-kB1/2 (genes: *TANK*, *IKBKE*, *CARD8*), ESSDAI score, Flt3/Flt3L, genes (*GRB2*, *ARHGDIB*, *CD40*, *PSMB9*, *ALDOA*, *PRDX5*, *PARC*, *PPIA*), NCR3/NKp30, STAT4 SNPs (rs7574865 and rs7582694), TNF-α, ICA1, PKN1 (Goules and Tzioufas, 2016).

2.8.2 Kawasaki disease

Up-regulation: ESR, WBC/leukocyte count, platelet count, CRP, NT-proBNP, fibrinogen-related plasma protein (fibrinogen, alpha-1-antitrypsin, clusterin and CD5L), serum cTnI, CK-MB, CD69+/CD8T cell proportion in CD8T cell count, apo-B, haptoglobin, iNOS expression in neutrophils, monocytes, CXCL10 (IP-10), CXCR3, HLA class I gene polymorphisms, MICA alleles, ITPKC gene (SNP itpkcα3, SNP rs7251246); Down-regulation: IFLCs, apo-A–I levels, plasma clusterin (apo-J), PI3K signaling (in B cells and T cell receptor signaling pathway) (Parthasarathy et al., 2015).

2.9 Other Complications

2.9.1 HIV (Human immunodeficiency virus)/neuroAIDS (Acquired immunodeficiency syndromes)

Up-regulation: Beta-2-microglobulin, neopterin, quinolinic acid, and MCP-1, sCD163, sCD14, sCD16, sCD69, Aβ42, IL-1β, -6, -10, TNF-α, sAPPα/β, PrPC, PrPSc, sPrPC, $CD4^+$ count, p-Tau, t-Tau, S100B, GFAP, YKL-40, IFN-γ, $CD163^+$ monocytes and macrophages, MCP-1, CXCL10; Micro-RNAs (miR-495, miR-744, miR-19, miR-16, miR-92, miR-139) (Rahimian and He, 2015).

2.9.2 Human tears

Up-regulation: MMP-9, IgE and lactoferrin (Azkargorta et al., 2016).

2.9.3 Problems in germ cell production

Up-regulation: LDH, α-Fetoprotein (Silva, 2015).

2.9.4 Posttraumatic stress disorder

Up-regulation: Corticotropin-releasing hormone, arginine vasopressin, CRP, HR, IL-1β, -2, -6, norepinephrine, glucocorticoid negative feedback, pituitary adenylate cyclase-activating polypeptide,

dehydroepiandrosterone, dehydroepiandrosterone sulfate, ghrelin, insulin, serotonin 1A receptor, NF-κB, TNF-α, immune cell sensitivity to glucocorticoids, amygdale reactivity; Down-regulation: Allopregnanolone, estradiol, HR variability, serotonin transporter; NF-κB, neuropeptide Y, testosterone, cortisol, endocannabinoids, hippocampus activity (Michopoulos et al., 2015).

2.9.5 Sickle cell disease

Up-regulation: HbS, HbF, HbSF, MCV, HbA2, ISCs, CD36 (glycoprotein IV), integrin a4b1 (very late activation antigen-4) to VCAM-1 and fibronectin, integrin α4β1, leukocyte adhesion molecules (L-selectin and αMβ2), CRP, ESR, sPLA2, IL-2, -3, -6, -8, -10, urinary cysteinyl LTE4, PGE2, CA 15-3, sCD40 ligand, HSP-70, ferritin, angiopoietin 1/2, stromal derived factor 1, TNF-α, TNFR-1, LDH-1, haptoglobin, Hb, reticulocyte count, RBC survival, blood coagulation, GSH/GSSG, stroke, BP, renal disease, TG, LDH, FMD, VEGF, PGF, ET-1, vitamin D, ALP, TRV, NT-proBNP, cTnI, PIT, HJBs, pitted RBCs (Damanhouri et al., 2015).

2.9.6 Metabolic syndrome

Up-regulation: BP, LDL-C, insulin, glucose, TG; Micro-RNAs (miR-17, miR-197, miR-509-5p, miR-92a, miR-320a) (O'Neill et al., 2016).

2.9.8 Acute graft-versus-host disease

Up-regulation: ST2, TNFR1, IL-7, sBAFF, REG3a, S100, TIM-3, CK-18, HGF, elafin; Micro-RNAs (miR-155, miR-586, miR-423, miR-199a-3p, miR-93, miR-377) (Ali et al., 2016).

2.9.9 Non-communicable diseases

Up-regulation: IL-1R1, -8, -4, -5, -10, -12, -13, -17A, -17F, -17AF, -18, -31, -9, -17E, -25, -21, -22, -23R, -26, LPS, CD4+ CD25+ T cells, TNF-α, TLR4, sICAM-1, LL-37, CCL17, 22, 27, 28; Micro-RNA (miR-203, miR-483-5p, miR-146a, miR-21, miR-638, miR-125-5p, miR-342-3p, miR-365-3p), carnitine, lactic acid, CD5L, apo-E, IgA, -G, -E, calprotectin, sFasL, polyubiquitin C, filaggrin, calmodulin-like protein 5, FoxP3, FENO/eosinophils/periostin, VOCs, ANCA, ASCA, anti-OmpC, anti-glycoprotein 2, adiponectin, EPCs, EMPs, CRP, insulin, bradykinin, naringenin, L-thyronine, citrate, succinate, creatinine, glutaric acid, 3-aminoisobutyric acid, p-Hydroxyphenyllactate (Skevaki et al., 2016).

3 Conclusion

Information of this article may be helpful for the researchers those are working in medical sciences, especially pharmaceutical sciences - in drug discovery and development.

Conflict of interest

We have no conflict of interest from any point of view.

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