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Supplementary Material



Bibliometric and Semantic Analysis of the Global Research on Biomarkers in Personalized Medicine

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Table S1. The most frequently cited personalized medicine and biomarkers research articles in Science Citation Index Expanded.

	Rank	(TC ₂₀₂₁)		Rank	(C ₂₀₂₀)	Year
	PC	(%)	AC	Article title	Authors	
6 (17)	2011	8,76	17,64	Predictive biomarkers: a paradigm shift towards personalized cancer medicine	La Thangue et al.	2 (178)
3 (22)	2013	12,36	19,78	Pitfalls and limitations in translation from biomarker discovery to clinical utility in predictive and personalised medicine	Drucker et al.	3 (172)
33 (5)	2013	2,91	19,11	Personalized Cancer Medicine: Molecular Diagnostics, Predictive Biomarkers, and Drug Resistance	de Castro et al.	4 (122)
17 (9)	2013	7,38	13,56	Digital PCR strategies in the development and analysis of molecular biomarkers for personalized medicine	Day et al.	5 (115)
2 (29)	2016	25,22	19,17	Tear fluid biomarkers in ocular and systemic disease: potential use for predictive, preventive and personalised medicine	Hagan et al.	6 (104)
22 (7)	2012	6,73	10,4	Personalized medicine using DNA biomarkers: a review	Ziegler et al.	7 (64)
18 (9)	2011	14,06	5,82	The potential use of the neurotensin high affinity receptor 1 as a biomarker for cancer progression and as a component of personalized medicine in selective cancers	Dupouy et al.	8 (63)
1 (33)	2019	52,38	21	Biomarkers for Acute Respiratory Distress syndrome and prospects for personalised medicine	Spadaro et al.	9 (60)
4 (19)	2016	31,67	10	High microsatellite instability (MSI-H) colorectal carcinoma: a brief review of predictive biomarkers in the era of personalized medicine	Gatalica et al.	10 (60)
8(15)	2016	25,00	10	Personalized medicine: an update of salivary biomarkers for periodontal diseases	Korte, Kinney	11 (58)
53 (2)	2011	3,45	5,27	Biomarkers in solid organ transplantation: establishing personalized transplantation medicine	Roedder et al.	12 (56)
21 (8)	2014	14,29	7	miRNAs as biomarkers of myocardial infarction: a step forward towards personalized medicine?	Goretti et al.	13 (54)
54 (2)	2012	3,70	5,4	Personalized medicine and pharmacogenetic biomarkers: progress in molecular oncology testing	Ong et al.	14 (53)
23 (7)	2015	13,21	7,57	Biomarker-guided personalised emergency medicine for all - hope for another hype?	Schuetz et al.	14 (52)
34 (5)	2015	9,62	7,43	Immune biomarkers: the promises and pitfalls of personalized medicine	Willis et al.	16 (51)
13 (11)	2015	21,57	7,29	Personalized Medicine: Review and Perspectives of Promising Baseline EEG Biomarkers in Major Depressive Disorder and Attention Deficit Hyperactivity Disorder	Olbrich et al.	17 (51)
71 (1)	2012	1,96	5,1	Making Personalized Cancer Medicine a Reality: Challenges and Opportunities in the Development of Biomarkers and Companion Diagnostics	Parkinson et al.	18 (43)
55 (2)	2013	4,65	4,78	Proteomic Approaches to the Discovery of Cancer Biomarkers for Early Detection and Personalized Medicine	Honda et al.	19 (42)
5 (19)	2019	45,24	14	Identification of clinical trait-related lncRNA and mRNA biomarkers with weighted gene co-expression network analysis as useful tool for personalized medicine in ovarian cancer	Li, Zhan	20 (42)

(Table S1) contd.....

15 (10)	2018	23,81	10,5	Understanding the microbiome: Emerging biomarkers for exploiting the microbiota for personalized medicine against cancer	Rajpoot et al.	21 (40)
35 (5)	2013	12,50	4,44	Prognostic and Putative Predictive Biomarkers of Gastric Cancer for Personalized Medicine	Warneke et al.	22 (40)
72 (1)	2008	2,50	2,86	Targeted imaging: an important biomarker for understanding disease progression in the era of personalized medicine	Eckelman et al.	23 (40)
73 (1)	2006	2,50	2,5	Methods and biomarkers for the diagnosis and prognosis of cancer and other diseases: Towards personalized medicine	Anderson et al.	24 (39)
11 (13)	2016	33,33	6,5	Personalized medicine in diabetes: the role of 'omics' and biomarkers	Pearson	24 (37)
24 (7)	2016	18,92	6,17	Biomarkers, the control panel and personalized COPD medicine	Agusti et al.	26 (35)
14 (11)	2017	31,43	7	Exploitation of Gene Expression and Cancer Biomarkers in Paving the Path to Era of Personalized Medicine	Kamel et al.	31,43

TC_{2021} : number of citations from Web of Science Core Collection from its publication to the September of 2021; C_{2021} : number of citations in 2021; PC : percentage of C_{2020} in total

C_{2021} in personalized medicine and biomarkers research field; AC : average citation per year.

Table S2. Parameters of selected articles for keyword analysis.

Nº	$PC_{2016-2021}$	$C_{2016-2021}$	TC_{2021}	Authors	Title	DOI
1	79,21	141	178	Drucker et al. [20]	Pitfalls and limitations in translation from biomarker discovery to clinical utility in predictive and personalised medicine	10.1186/1878-5085-4-7
2	100,00	115	115	Hagan et al. [19]	Tear fluid biomarkers in ocular and systemic disease: potential use for predictive, preventive and personalised medicine	10.1186/s13167-016-0065-3
3	73,77	90	122	Day et al. [21]	Digital PCR strategies in the development and analysis of molecular biomarkers for personalized medicine	10.1016/j.ymeth.2012.08.001
4	100,00	63	63	Spadaro et al. [18]	Biomarkers for Acute Respiratory Distress syndrome and prospects for personalised medicine	10.1186/s12950-018-0202-y
5	100,00	60	60	Gatalica et al. [22]	High microsatellite instability (MSI-H) colorectal carcinoma: a brief review of predictive biomarkers in the era of personalized medicine	10.1007/s10689-016-9884-6
6	100,00	60	60	Korte, Kinney [23]	Personalized medicine: an update of salivary biomarkers for periodontal diseases	10.1111/prd.12103
7	92,86	52	56	Goretti et al. [24]	miRNAs as biomarkers of myocardial infarction: a step forward towards personalized medicine?	10.1016/j.molmed.2014.10.006
8	98,04	50	51	Olbrich et al. [25]	Personalized Medicine: Review and Perspectives of Promising Baseline EEG Biomarkers in Major Depressive Disorder and Attention Deficit Hyperactivity Disorder	10.1159/000437435
9	94,23	49	52	Willis et al. [26]	Immune biomarkers: the promises and pitfalls of personalized medicine	10.1038/nri3820
10	86,79	46	53	Schuetz et al. [27]	Biomarker-guided personalised emergency medicine for all - hope for another hype?	10.4414/smw.2015.14079
11	100,00	42	42	Li, Zhan [28]	Identification of clinical trait-related lncRNA and mRNA biomarkers with weighted gene co-expression network analysis as useful tool for personalized medicine in ovarian cancer	10.1007/s13167-019-00175-0
12	100,00	42	42	Rajpoot et al. [29]	Understanding the microbiome: Emerging biomarkers for exploiting the microbiota for personalized medicine against cancer	10.1016/j.semcancer.2018.02.003

TC_{2021} : number of citations from Web of Science Core Collection from its publication to the september of 2021; $C_{2016-2021}$: number of citations from 2016 to 2021; $PC_{2016-2021}$: percentage of $C_{2016-2021}$ in total TC_{2021} : average citation per year.

Table S3. Keywords from the most cited in recent years articles in Science Citation Index Expanded.

Reference	Keywords from Title	Keywords from Abstract	Author Keywords	Semantic core of the text of the article (in decreasing order of frequency)
Drucker et al. (2013) [18]	Biomarker, Discovery, clinical utility, predictive and personalised medicine	Biomarker, Issue, clinically approved test, identify, opportunity, patients, potential, potential biomarkers, test	Predictive medicine, Targeted prevention, Validation strategies, Regulatory overview, Biomarker perspectives, Tailored therapy	Biomarker, clinical, Patient, sample, disease, study, different, drug, protein, Diagnostic, numb, trial, Test, development, Process, sensitivity, clinical trials, phase, analysis, discovery, improve, result, specificity, marker, potential, selection, treatment, validation, datum, lack, age

(Table S3) contd.....

Reference	Keywords from Title	Keywords from Abstract	Author Keywords	Semantic core of the text of the article (in decreasing order of frequency)
Hagan et al. (2016) [19]	Tear fluid, Biomarkers, Ocular, systemic disease, predictive, preventive and personalised medicine	Disease, biomarker, Field, identify, ocular, tear fluid, body fluid, ocular surface disease, personalized, predictive, putative tear fluid, sensitivity	Biomarkers, Tear fluid, Proteome, Metabolome, Predictive preventive personalised medicine (PPPM), Dry eye, Glaucoma, Diabetic retinopathy, Cancer, Neurological disorders	Tear, patient, level, Study, fluid, disease, Protein, tear fluid, DED, biomarker, Control, increase, Ocular, significantly, Cytokine, group, Analysis, healthy, subject, clinical, Compare, molecule, TNF- α , eye, IL-6, identify
Day et al. (2013) [20]	Digital PCR, Development, Analysis, molecular biomarkers, personalized medicine	PCR, Digital, Advantage, Biomarker, Delivery, Development, Goal, Medicine, personalize, personalized medicine	Digital PCR, Single molecule, Biomarkers	PCR, digital, digital PCR, Analysis, platform, mutation, biomarker, Aliquot, clinical, numb, Sample, specific, DNA, Potential, detect, variant, Locus, allele, application, Cell, molecule, rare, analyse, positive, system, Mutant, protocol, single, tumour
Spadaro et al. (2019) [21]	Biomarkers, Acute Respiratory Distress syndrome, Prospects, personalised medicine	ARDS, biomarker, care, blood, clinical, Critical, expression, Gene, potential, Acute, application, critical care, diagnosis, gene expression, inflammatory	Acute respiratory distress syndrome, Biomarkers, Inflammatory	ARDS, patient, lung, injury, Biomarker, mortality, factor, study, clinical, alveolar, level, therapy, endothelial, risk, severe, Acute, cell, early, respiratory, epithelial, gene, phase, sepsis, ventilation, diagnosis, inflammatory, marker, protein
Gatalica et al. (2016) [22]	High microsatellite instability (MSI-H), colorectal carcinoma, predictive biomarkers, era of personalized medicine	MSI-H, Characteristic, colorectal carcinomas, CRC, Gene, Instability, level microsatellite	Colorectal cancer, Microsatellite instability, Lynch syndrome, Biomarkers, Conventional chemotherapy, Targeted therapy	MSI-H, CRC, tumor, cell, mutation, CRCs, gene, cancer, expression, MGMT, patient, protein, sporadic, colorectal, immune, lynch syndrome, subtype, syndrome, tumor cells, cause, MLH1, clinical, status, study, base, chemotherapy, colorectal cancers, microsatellite, molecular, PD-L1, treatment, various, carcinoma, checkpoint, cohort, DNA, hereditary, metastatic, pathway, PD-1, response
Korte, Kinney (2016) [23]	Personalized medicine, salivary biomarkers, periodontal diseases	Clinical, diagnosis, periodontal diseases, risk, assessment, inflammatory, pathogen, provide	-	Disease, periodontal, periodontal disease, salivary, level, biomarker, matrix, inflammatory, tissue, saliva, marker, protein, bone, periodontitis, progression, metalloproteinase, study, collagen, macrophage, increase, matrix metalloproteinase, oral, subject, clinical, degradation, identify, type, cell, fluid, osteoprotegerin, response, activity, cytokine, monitor, patient, treatment, demonstrate, diagnostic, necrosis, process, tumor, aminotransferase, health, inhibitor, role
Goretti et al. (2014) [24]	miRNAs, biomarkers, myocardial infarction, personalized medicine	miRNA, biomarker, potential, regulate	biomarker; miRNAs; myocardial infarction; personalized medicine; therapeutic targets.	miRNA, patient, level, circulating, study, risk, biomarker, value, acute, prognostic, factor, protein, blood, cardiac, medicine, heart, MIR-1, increase, assay, cardiovascular, cell, target
Olbrich et al. (2015) [25]	Personalized Medicine, Promising Baseline EEG Biomarkers, Major Depressive Disorder, Attention Deficit Hyperactivity Disorder	EEG, Marker, Potential, attention deficit hyperactivity disorder, biomarker, condition, disorder, ERP, personalize, personalized medicine, psychiatric, research, sleep, treatment outcome	Quantitative electroencephalography, Depression, Attention deficit hyperactivity disorder, Event-related potentials, Personalized medicine, Biomarker, Research domain criteria	Treatment, EEG, Study, Activity, MDD, ADHD, Sleep, Patient, Biomarker, Increase, Marker, Response, Measure, Connectivity, Value, Reported, Vigilance, Disorder, Frontal, outcome, clinical, Antidepressant, Suggest, treatment outcome, association, parameter, power
Willis et al. (2015) [26]	Immune biomarkers, personalized medicine	Field, Progress, research	-	Biomarker, Treatment, Patient, Immune, Clinical, Datum, Disease, Approach, immune biomarkers, cell, research, example, response, medicine, process, therapeutic, analysis, stratify, molecular, potential, sample, trial

(Table S3) contd.....

Reference	Keywords from Title	Keywords from Abstract	Author Keywords	Semantic core of the text of the article (in decreasing order of frequency)
Schuetz et al. (2015) [27]	Biomarker-guided, personalised emergency medicine, hope	Clinical, Patient, Diagnostic, Biomarker, Emergency, laboratory test, medical, result, triage, algorithm, care, decision, hospital, improve, intervention, study, therapeutic	Troponin, proadrenomedullin, procalcitonin, emergency medicine, biomarker, personalized medicine, adrenomedullin, natriuretic peptides, comprehensive effectiveness research, d-dimer	Patient, Clinical, Test, Infection, Biomarker, Antibiotic, Care, PCT, Disease, Risk, Therapy, d-dimer, level, diagnosis, result, physician, sepsis, study, bacterial, setting, acute,
Li, Zhan (2019) [28]	Identification, Clinical trait-related, lncRNA, mRNA, biomarkers, gene co-expression, network analysis, personalized medicine, ovarian cancer	lncRNA, mRNA, network, co-expression, patient, identify, invasion, module, OCs, RNA, Tissue, Biomarker, Cancer, co-expression gene, co-expression module	Ovarian cancer, Co-expression module, lncRNA, mRNA, WGCNA, Diagnosis, Prognostic assessment, Predictive preventive personalized medicine (PPPM)	Module, lncRNA, mRNA, co-expression, gene, cancer, clinical, cell, network, analysis, datum, RNA, identify, trait, OCs, expression, patient, invasion, biomarker, correlation, diagnosis, study, WGCNA, value, base, ovarian, clinical traits, sample, molecular, tissue, cluster, score
Rajpoot et al. (2018) [29]	Microbiome, Emerging biomarkers, Microbiota, personalized medicine, cancer	Microbiome, Microbe, Disease, Individual, Human, Microbial, Cancer, Commensal, Genome, Healthy, Microbiota, Pathological, study	Biomarker; Cancer; Flora; Microbiome; Personalized medicine.	Microbiome, Microbiota, Disease, Cancer, Body, Human, Microbial, Oral, Gut, Host, Personalize, Bacterial, Community, Health, Treatment, Individual, Study, Microbe, Complex, gut microbiome, help, intestinal, lead, patient, present, condition, gene, healthy, species

Table S4. The keywords by subject groups from the title, annotations, author keywords and the full text of the article (in brackets is the number of articles in the semantic core of which this term occurs).

	Subject Group	Keywords from titles	Keywords from abstracts	Author keywords	Keywords from texts
1	biomolecules and medical materials, drugs	Biomarker(s) (7), Molecular biomarkers, Predictive biomarkers, miRNAs, salivary biomarkers, Emerging biomarkers, Promising Baseline EEG, Immune biomarkers, lncRNA, mRNA	Biomarker (8), potential biomarkers, miRNA, marker, lncRNA, mRNA, RNA, Gene	Biomarker(s) 8, miRNAs; Troponin, proadrenomedullin, procalcitonin, mRNA, d-dimer, lncRNA, adrenomedullin, natriuretic peptides, Biomarker perspectives	Biomarker (10), Protein (6), gene (4), cytokine (2), DNA (2), PD- (2), Allele, Aminotransferase, Antidepressant, circulating miRNAs, collagen, d-dimer, hub-mRNA, IL-6, immune biomarkers, lncRNA, macrophage, metalloproteinase, MGMT, miR-, miRNA, MLH1, mRNA, osteoprotegerin, PCT, RNA, TNF- α , antibiotic
2	the field of medicine and health care	personalized medicine (8), predictive and personalised medicine, personalised medicine, predictive, preventive and personalised medicine, personalised emergency medicine	personalize (2), personalized medicine (2), Personalized, Predictive, Medicine, psychiatric, therapeutic	Personalized medicine (4), Predictive preventive personalised medicine (PPPM) (2), Predictive medicine, Tailored therapy, Conventional hemotherapy, Targeted therapy, emergency medicine	therapy (2), Chemotherapy, therapeutic, personalize, prognostic
3	diseases	Acute Respiratory Distress syndrome, ovarian cancer, cancer, colorectal carcinoma, myocardial infarction, Major Depressive Disorder, Attention Deficit Hyperactivity Disorder periodontal diseases	cancer (2), ARDS, attention deficit hyperactivity disorder, colorectal carcinomas, CRC, ocular surface disease, periodontal diseases, OCs	Ovarian cancer (2), Cancer (2), Glaucoma, Diabetic retinopathy, Neurological disorders, Depression, Acute respiratory distress syndrome, Colorectal cancer, Lynch syndrome, myocardial infarction; Attention deficit hyperactivity disorder	cancer (4), Periodontitis, lynch syndrome, CRC, carcinoma, colorectal cancers, CRCs, ADHD, ARDS, DED, dry eye, MDD, periodontal disease, OCs
4	medical technology	Digital PCR	PCR, EEG, ERP	Digital PCR, Quantitative electroencephalography, Event-related potentials, WGCNA	digital PCR, EEG, WGCNA, PCR
5	medical and biological processes	microsatellite instability, gene co-expression	gene expression, co-expression, MSI-H	Microsatellite instability, Co-expression module,	Mutation (2), expression (2), invasion, degradation, co-expression, necrosis, MSI-H

(Table S4) contd.....

	Subject Group	Keywords from titles	Keywords from abstracts	Author keywords	Keywords from texts
6	biological body components	Microbiome, Microbiota, Tear fluid	tear fluid, body fluid, blood, microbiome, microbe, microbial, microbiota, genome	Tear fluid, Single molecule, Flora; Microbiome;	Microbe, microbial, microbiome, microbiota, blood, gut microbiome, tear fluid
7	medical vocabulary	clinical utility, ocular, systemic disease, clinical trait	patient(s) (3), clinical (3), care (2), diagnosis (2), disease (2), clinically approved test, commensal, diagnostic, disorder, emergency, hospital, inflammatory, laboratory test, medical, ocular, pathogen, pathological, and others	Proteome, Metabolome, Inflammatory, Diagnosis, Targeted prevention, Validation strategies, therapeutic targets.	Patient (12), clinical (10), cell (7), disease (5), health(y) (4), diagnosis (3), Diagnostic (3), inflammatory (3), acute (3), assay (2), bacterial (2), clinical traits (2), immune (2), medicine (2), numb (2), oral (2), saliva(ry) (2), sepsis (2), tissue (2), tumor (2), -and others
8	general scientific vocabulary	prospects (6), Discovery, development, analysis, Identification, network analysis	potential (3), identify (3), field (2), research (2), study (2), advantage, algorithm, application, assessment, characteristic, condition, critical, decision, delivery, development, digital, goal, improve, individual, intervention, invasion, and others	Prognostic assessment (4), Regulatory overview, Research domain criteria, comprehensive effectiveness research	Study (10), analyse (6), molecule(ar) (5), level (5), response (5), sample (4), increase (4), identify (3), datum (3), potential (3), process (3), specific(ity) (3), risk (3), value (3), Activity (2), base (2), compare (2), factor (2), fluid (2), detect(ion) (2), improve (2), phase (2), subject (2), system(ic) (2), test (2), and others
9	other vocabulary	hope	Sleep, human, healthy		Help, eye, early, large, age, sleep, human, vigilance
	Total	53	116	64	352