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Supplementary Table 1: The potential biomarkers for schizophrenia

Biomarker	Method	Tested population	Number of schizophrenias	Number of controls	Note	Differentiation diagnosis
Genetic markers						
deletion at 22q11.2 [1-2]	The largest genome-wide analysis (GWAS) of CNVs for any psychiatric disorder	Data sets assembled by the Schizophrenia Working Group of the Psychiatric Genomics Consortium	21094	20227	Previously known as DiGeorge syndrome or velocardiofacial syndrome, OR=67	Also related to other psychiatric conditions, including bipolar disorder and autism spectrum disorder
duplications at 16p11.2 [3, 4]					OR=9.4	
deletions at 15q11.2 [3, 4]					Angelman or Prader-Willi syndrome, OR=1.8	

						Candidate genes for further research
3p21.31, 6q21, 6q27, 7q31.1 [6]	GWAS	Chinese	7699	18327	Novel GWS loci in Chinese people	
HNF4G [5]	Genetic studies	Caucasian	127	136	Associated with attention/vigilance	
NDUFS4 [5]		Caucasian	127	136	Associated with verbal memory	
HDAC9 [5]		Caucasian	127	136	Associated with reasoning/problem solving	
ANK3 [7]		Caucasian	116	359	Associated with working/verbal memory, attention; and white matter integrity, brain structure, widespread cortical thinning; and regional activation during executive tasks	
NRGN [7]		Caucasian, Asian	99	645	Associated with episodic memory, working memory; and grey-matter volume, brain volumes; and regional activation during executive tasks pathways involved in brain development, memory and cognition	

NRG1 [8]		Asian	135	119	Associated with cognitive deficits	
GRM5 [9]		Australian	249	261	Associated with cognitive impairments; and reduction of right hippocampal volume	
DTNBP1 [10, 11]		Asian, Caucasian	360	166	Associated with attention, vigilance, memory and speed of processing	
5-HT2A [12, 30]		Caucasian	53	46 (siblings)	Associated with sustained attentional impairment	
DβH [13]		Chinese	200	0	Associated with cognitive deficits	
CACNA1C [14]		Caucasian	177	2448	Associated with grey-matter volume; and regional activation/functional connectivity during executive tasks	
TCF4 [7, 16]		Caucasian	106	212	Associated with grey-matter volume; and pathways involved in brain development, memory and cognition	

ZNF804A [7, 15]		Caucasian, Chinese	825	3212	Associated with grey-matter volume, white matter integrity; and regional activation/functional connectivity during executive tasks	
DGKH [7]		Caucasian	81	75	Associated with regional activation during executive tasks	
COMT [15]		Caucasian	175	219 (siblings) + 55 controls	Associated with prefrontal dopamine catabolism	
Hypermethylation of RELN Promoter [17]	Sequencing	Caucasian	5 (post-mortem brain samples)	5	Responsible for gene silencing in the frontal lobe of schizophrenic patients	
Hypermethylation of GAD1 Promoter [17]		Caucasian	14	14	Responsible for gene silencing in the prefrontal cortex of schizophrenic patients	

Hypermethylation of HTR1A Promoter [17]		Caucasian	40 (blood samples)	67	Responsible for gene silencing of 5HTR1A gene	Both schizophrenia and bipolar disorder were similarly affected, indicating the partial overlap model of these two psychotic disorders.
DNA methylation of C17orf63, THAP1, KCNQ4 [18]		Chinese	499 first-episode patients (blood samples)	497	Specific epigenetic markers for Chinese population	

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miR-328, miR-17-5p, miR-134, miR-652, miR-382, and miR-107 [19]	Microarray analysis	Australian	37 (post-mortem dorsolateral prefrontal cortex)	37	Elevated miRNA expression in schizophrenia	
miR-181b-5p, miR-21-5p, miR-195-5p, miR-137, miR-346 and miR-341-5p [20]	Meta-analysis	Chinese	330 (peripheral blood mononuclear cells)	202	Pooled sensitivity (0.81), specificity (0.81), diagnostic odds ratio (18), positive and negative likelihood ratio was 4.3 and 0.24. ROC was 0.87.	
Inflammatory markers						
CRP [21-23]	ELISA	Caucasian, Arabic, Indian,	4392	3039	Positive correlation with disease severity and cognitive function. Threshold: > 5mg/L	

		Japanese, Chinese				
IL-6 [24, 25, 26]	ELISA	Caucasian	164 (serum samples), 230 (CSF samples)	164 (serum samples)	Increased in both serum and CSF samples; higher baseline IL-6 predicts prognosis; associated with kynurenine pathway; could be normalized by antipsychotic treatment	
IL-8 [24, 25]	ELISA	Caucasian	119 (serum samples), 95 (CSF samples)	119 (serum samples)	Increased in both serum and CSF samples	
KYN [27]	Mass Spectrometry	Caucasian	28	30	Plasma level was positively correlated with IL-1β and PANSS	
TNF-α [28, 29]	ELISA	Caucasian	171	171	Increased in schizophrenia, associated with kynurenine pathway; increased in acute exacerbations were not reversible following anti-psychotic treatment	

IL-1β [27, 29]	ELISA	Caucasian, Asian	127	127	Increased in schizophrenia, which could be normalized by antipsychotic treatment	
TGF-β [29]	ELISA	Caucasian, Asian	78	262	Increased in schizophrenia, which could be normalized by antipsychotic treatment	
IL-12 [29]	ELISA	Caucasian	78	113	Increased in acute exacerbations were not reversible following anti-psychotic treatment	
IFN-ɣ [24, 29]	ELISA	Caucasian	57	202	Increased in acute exacerbations were not reversible following anti-psychotic treatment	
sIL-2R [29]	ELISA	Caucasian	32	94	Increased in acute exacerbations were not reversible following anti-psychotic treatment	
Neurotransmitter markers						
5-HIAA [31]	mass fragmentography	Caucasian	515 (CSF samples)	68	Negatively associated with delusions and sadness but not with suicidal attempt	
HVA [32]	mass fragmentography	Caucasian	515 (CSF samples)	68	Decreased in schizophrenia	

Glutathione (GSH) [33, 34]	Modifications of Tietze method	American	46 (plasma samples)	50	Decreased in schizophrenia	
Norepinephrine [35]	ELISA	Turkish	33	31	Decreased in schizophrenia. Sensitivity: 76.6% Specificity: 78.8% positive predictive value: 76.6% negative predictive value: 76.4% Threshold: 4666 (cut-off of renalase-norepinephrine ratio)	
Peripheral proteins						
NGF [36-38].	ELISA	Chinese	30	0	Decreased in schizophrenia	
BDNF [39-43]	ELISA	Chinese, Caucasian, Australian	380	144	Decreased in schizophrenia; correlated with memory; lower in patients with depression than those without; changes continuously from preclinical to clinical stages, higher in female patients	

Hcy [44-48]	Enzyme cycle method / latex enhanced immunoturbidimetric assay	Chinese, Caucasian	1219	231	Prevalence of hyperhomocysteinemia in Han Chinese schizophrenia patients and healthy controls was 55.05% and 26.98%, respectively; negatively associated with cognitive performance, positively correlated with CDSS; homocysteine-related SNPs were associated with schizophrenia. Threshold: >15μmol/L	
VitB6 [49-52]	LC-MS	Australian, Chinese	195	168	Decreased in schizophrenia	
G72 [53-55]	ELISA	Japanese, Turkish	134	87	Increased serum level, no significant change of CSF level. Sensitivity: 0.991 Specificity: 0.821 Threshold: 141.51pg/mL	
Gut Microbiota						

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Ruminococcacea e [56]	16S rRNA sequencing	American	25	25	negatively correlated with severity of negative symptoms	
Bacteroides [56]	16S rRNA sequencing	American	25	25	positively correlated with depressive symptoms	
IgA level in response to Pseudomonas [57]	ELISA	Thailand	80	38	elevated IgA level in response to Pseudomonas, elevated IgM level in response to Gram negative bacteria are highly predictive for deficit schizophrenia	Deficit schizophrenia
Candida [58]	ELISA	American	440	0	increased seropositivity, correlated with positive psychiatric symptoms	
Pharmacogenomic markers						
CYP2D6 & CYP2C19 polymorphism [59]	Genotyping / Sequencing	African, African American, Caucasian, Near Eastern,	For Chinese population: CYP2D6 (n=5795);	0	Test when making individualized therapeutic strategies. Frequencies of poor metabolizer of CYP2D6 and CYP2C19 is 0.9% and 13% in East Asian population	

		East Asian, South/Central Asian, Americas, Latino, Oceanian	CYP2C19 (n=13475)			
HLA-A & HLA-B polymorphism [59]			For Chinese population: n=39048	0	Test when carbamazepine is administrated. Frequencies of poor metabolizer of HLA-A and HLA-B is 3.5% and 4.6% in East Asian population. Threshold: HLA-A*31:01; HLA-B*15:02	
HLA-B polymorphism [59]			For Chinese population: n=39048	0	Test when oxcarbazepine is provided. Frequency of poor metabolizer is 4.6% in East Asian population. Threshold: HLA-B*15:02	
CYP2C9 & HLA-B polymorphism [59]			For Chinese population: CYP2C9 (n=14167)	0	Test when phenytoin is administrated. Frequencies of poor metabolizer of CYP2C9 is 0.6% in East Asian population	

Dopamine transporter gene [60]	DNA sequencing	Chinese	160 patients treated with clozapine only, 160 treated with chlorpromazine only.	0	Test polymorphism of dopamine transporter gene (rs2975226) when using clozapine.	Clozapine responders and non-responders
Serotonergic receptor type 2A, T102C, type 2C and type 6 [61, 62]	DNA sequencing	Caucasian	200 patients treated with clozapine	0	Test polymorphism when using clozapine. Sensitivity: 95% prediction of clozapine response: 76.7%	Clozapine responders and non-responders
HTR2C [63]	Taqman Assay	American	171	0	Test polymorphism when using HTR2C antagonists	Responders and non-responders

N/A: not applicable; UNK: unknown

Supplementary Table 1: Evidence linking genetics, inflammation, neurotransmitter, peripheral protein, gut microbiota and pharmacogenetics to schizophrenia.

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Abbreviations: CNV: copy number variants; SNP: single-nucleotide polymorphism; GWAS: genome-wide association study; MHC: major histocompatibility complex; ZNF804A: zinc-finger protein 804A; NRGN: neurogranin; TCF4: transcription factor 4; HNF4G: hepatocyte nuclear factor 4γ; HDAC9: NADH dehydrogenase [ubiquinone] iron-sulfur protein 4; HDAC9: histone deacetylase 9; ANK3: ankyrin-3; NRG1: neuregulin 1; DTNBP1: dystrobrevin-binding protein 1; 5-HT2A: serotonin receptor 2A; DβH: dopamine β-hydroxylase; DGKH: diacylglycerol kinase eta; COMT: catechol-O-methyltransferase; RELN: reelin; GAD1: glutamic acid decarboxylase; HTR1A: serotonin receptor type-1; THAP1: THAP domain-containing protein 1; KCNQ4: potassium voltage-gated channel subfamily KQT member 4; CRP: C-reactive protein; GM-CSF: granulocyte macrophage colony-stimulating factor; MCP-1: monocyte chemoattractant protein 1; PDGF-B: platelet-derived growth factor subunit B; MIP: monocyte inflammatory protein; VEGF-A: vascular endothelial growth factor A; RANTES: regulated on activation, normal T cell expressed and secreted; TGF-β: transforming growth factor-β; TNF-α: tumor necrosis factor-α; $GABA_AR\alpha1$: gamma-aminobutyric acid A receptor; DPYD: dihydropyrimidine dehydrogenase; MAD1L1: mitotic arrest deficient-like 1; DRD2: dopamine receptor D2; TRANK1: tetratricopeptide repeat and ankyrin repeat containing 1; MMP16: matrix metalloproteinase-16; HVA: homovanillic acid; NGF: Nerve Growth Factor; BDNF: Brain Derived Neurotrophic Factor; Hcy: homocysteine; CDSS: Calgary Depression Scale for Schizophrenia; HLA: human leukocyte antigen

Supplementary Table 1 References

1. Murphy KC. Schizophrenia and velo-cardio-facial syndrome. Lancet. 2002; 359(9304): 426-30.
2. Sporn A, Addington A, Reiss AL, et al. 22q11 deletion syndrome in childhood onset schizophrenia: an update. Mol Psychiatry. 2004; 9(3):

225-6.

3. Marshall CR, Howrigan DP, Merico D, et al. Contribution of copy number variants to schizophrenia from a genome-wide study of 41,321 subjects. Nature Genetics. 2017; 49(1): 27-35.

4. Lowther C, Costain G, Baribeau DA, et al. Genomic Disorders in Psychiatry-What Does the Clinician Need to Know? Curr Psychiatry Rep. 2017; 19(11): 82.

5. Nakahara S, Medland S, Turner JA, et al. Polygenic risk score, genome-wide association, and gene set analyses of cognitive domain deficits in schizophrenia. Schizophrenia Research. 2018; 201: 393-399.

6. Li Z, Chen J, Yu H, et al. Genome-wide association analysis identifies 30 new susceptibility loci for schizophrenia. Nat Genet. 2017; 49(11): 1576-1583.

7. Gurung R and Prata DP. What is the impact of genome-wide supported risk variants for schizophrenia and bipolar disorder on brain structure and function? A systematic review. Psychol Med. 2015; 45(12): 2461-80.

8. Cho Y, Ryu S, Huh I, et al. Effects of genetic variations in NRG1 on cognitive domains in patients with schizophrenia and healthy individuals. Psychiatr Genet. 2015; 25(4): 147-54.

9. Matosin N, Newell KA, Quide Y, et al. Effects of common GRM5 genetic variants on cognition, hippocampal volume and mGluR5 protein levels in schizophrenia. Brain Imaging Behav. 2018; 12(2): 509-517.

10. Baek JH, Kim JS, Ryu S, et al. Association of genetic variations in DTNBP1 with cognitive function in schizophrenia patients and healthy subjects. Am J Med Genet B Neuropsychiatr Genet. 2012; 159B(7): 841-9.

11. Varela-Gomez N, Mata I, Perez-Iglesias R, et al. Dysbindin gene variability is associated with cognitive abnormalities in first-episode non-affective psychosis. Cogn Neuropsychiatry. 2015; 20(2): 144-56.

12. Vyas NS, Lee Y, Ahn K, et al. Association of a Serotonin Receptor 2A Gene Polymorphism with Visual Sustained Attention in Early-Onset Schizophrenia Patients and their Non-Psychotic Siblings. Aging Dis. 2012; 3(4): 291-300.

13. Sun Z, Ma Y, Li W, et al. Associations between the DBH gene, plasma dopamine beta-hydroxylase activity and cognitive measures in Han Chinese patients with schizophrenia. Schizophr Res. 2018; 193: 58-63.

14. Yates D. Synaptic plasticity: Micro-level disruption. Nat Rev Neurosci. 2015; 16(7): 373.

15. Kim AH, Parker EK, Williamson V, et al. Experimental validation of candidate schizophrenia gene ZNF804A as target for hsa-miR-137.

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General Psychiatry

Schizophr Res. 2012; 141(1): 60-64.

16. Kwon E, Wang W, and Tsai LH. Validation of schizophrenia-associated genes CSMD1, C10orf26, CACNA1C and TCF4 as miR-137 targets. Mol Psychiatry. 2013; 18(1): 11-2.

17. Abdolmaleky HM, Cheng KH, Russo A, et al. Hypermethylation of the reelin (RELN) promoter in the brain of schizophrenic patients: a preliminary report. Am J Med Genet B Neuropsychiatr Genet. 2005; 134B(1): 60-6.

18. Li M, Li Y, Qin H, et al. Genome-wide DNA methylation analysis of peripheral blood cells derived from patients with first-episode schizophrenia in the Chinese Han population. Mol Psychiatry. 2020.

19. Santarelli DM, Beveridge NJ, Tooney PA, et al. Upregulation of dicer and microRNA expression in the dorsolateral prefrontal cortex Brodmann area 46 in schizophrenia. Biol Psychiatry. 2011; 69(2): 180-7.

20. Liu S, Zhang F, Wang X, et al. Diagnostic value of blood-derived microRNAs for schizophrenia: results of a meta-analysis and validation. Sci Rep. 2017; 7(1): 15328.

21. Orsolini L, Sarchione F, Vellante F, et al. Protein-C Reactive as Biomarker Predictor of Schizophrenia Phases of Illness? A Systematic Review. Curr Neuropharmacol. 2018; 16(5): 583-606.

22. Sanada K, Montero-Marin J, Barcelo-Soler A, et al. Effects of Mindfulness-Based Interventions on Biomarkers and Low-Grade Inflammation in Patients with Psychiatric Disorders: A Meta-Analytic Review. Int J Mol Sci. 2020; 21(7).

23. Bora E. Peripheral inflammatory and neurotrophic biomarkers of cognitive impairment in schizophrenia: a meta-analysis. Psychol Med. 2019; 49(12): 1971-1979.

24. Frydecka D, Krzystek-Korpacka M, Lubeiro A, et al. Profiling inflammatory signatures of schizophrenia: A cross-sectional and meta-analysis study. Brain Behav Immun. 2018; 71: 28-36.

25. Orlovska-Waast S, Kohler-Forsberg O, Brix SW, et al. Cerebrospinal fluid markers of inflammation and infections in schizophrenia and affective disorders: a systematic review and meta-analysis. Mol Psychiatry. 2019; 24(6): 869-887.

26. Feng T, McEvoy JP, and Miller BJ. Longitudinal study of inflammatory markers and psychopathology in schizophrenia. Schizophr Res. 2020; 224: 58-66.

27. Joaquim HPG, Costa AC, Gattaz WF, et al. Kynurenine is correlated with IL-1beta in plasma of schizophrenia patients. J Neural Transm (Vienna). 2018; 125(5): 869-873.

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28. Pedraz-Petrozzi B, Elyamany O, Rummel C, et al. Effects of inflammation on the kynurenine pathway in schizophrenia - a systematic review. J Neuroinflammation. 2020; 17(1): 56.

29. Miller BJ, Buckley P, Seabolt W, et al. Meta-analysis of cytokine alterations in schizophrenia: clinical status and antipsychotic effects. Biol Psychiatry. 2011; 70(7): 663-71.

30. Rasmussen H, Frokjaer VG, Hilker RW, et al. Low frontal serotonin 2A receptor binding is a state marker for schizophrenia? Eur Neuropsychopharmacol. 2016; 26(7): 1248-50.

31. Carlborg A, Jokinen J, Nordstrom AL, et al. CSF 5-HIAA, attempted suicide and suicide risk in schizophrenia spectrum psychosis. Schizophr Res. 2009; 112(1-3): 80-5.

32. Wieselgren IM and Lindstrom LH. CSF levels of HVA and 5-HIAA in drug-free schizophrenic patients and healthy controls: a prospective study focused on their predictive value for outcome in schizophrenia. Psychiatry Res. 1998; 81(2): 101-10.

33. Kumar J, Liddle EB, Fernandes CC, et al. Glutathione and glutamate in schizophrenia: a 7T MRS study. Mol Psychiatry. 2020; 25(4): 873-882.

34. Coughlin JM, Yang K, Marsman A, et al. A multimodal approach to studying the relationship between peripheral glutathione, brain glutamate, and cognition in health and in schizophrenia. Mol Psychiatry. 2020.

35. Catak Z, Kocdemir E, Ugur K, et al. A Novel Biomarker Renalase and Its Relationship with its Substrates in Schizophrenia. J Med Biochem. 2019; 38(3): 299-305.

36. Qin XY, Wu HT, Cao C, et al. A meta-analysis of peripheral blood nerve growth factor levels in patients with schizophrenia. Mol Psychiatry. 2017; 22(9): 1306-1312.

37. Rao S, Martinez-Cengotitabengoa M, Yao Y, et al. Peripheral blood nerve growth factor levels in major psychiatric disorders. J Psychiatr Res. 2017; 86: 39-45.

38. Chu CS, Chu CL, Wu CC, et al. Serum nerve growth factor beta, brain- and glial-derived neurotrophic factor levels and psychopathology in unmedicated patients with schizophrenia. J Chin Med Assoc. 2018; 81(6): 577-581.

39. Cakici N, Sutterland AL, Penninx B, et al. Altered peripheral blood compounds in drug-naive first-episode patients with either schizophrenia or major depressive disorder: a meta-analysis. Brain Behav Immun. 2020; 88: 547-558.

40. Yang Y, Liu Y, Wang G, et al. Brain-derived neurotrophic factor is associated with cognitive impairments in first-episode and chronic

schizophrenia. Psychiatry Res. 2019; 273: 528-536.

41. Fang X, Chen Y, Wang Y, et al. Depressive symptoms in schizophrenia patients: A possible relationship between SIRT1 and BDNF. Prog Neuropsychopharmacol Biol Psychiatry. 2019; 95: 109673.

42. Heitz U, Papmeyer M, Studerus E, et al. Plasma and serum brain-derived neurotrophic factor (BDNF) levels and their association with neurocognition in at-risk mental state, first episode psychosis and chronic schizophrenia patients. World J Biol Psychiatry. 2019; 20(7): 545-554.

43. Weickert CS, Lee CH, Lenroot RK, et al. Increased plasma Brain-Derived Neurotrophic Factor (BDNF) levels in females with schizophrenia. Schizophr Res. 2019; 209: 212-217.

44. Yang Y, Wang J, Xiong Z, et al. Prevalence and clinical demography of hyperhomocysteinemia in Han Chinese patients with schizophrenia. Eur Arch Psychiatry Clin Neurosci. 2020.

45. Trzesniowska-Drukala B, Kalinowska S, Safranow K, et al. Evaluation of hyperhomocysteinemia prevalence and its influence on the selected cognitive functions in patients with schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry. 2019; 95: 109679.

46. Liu Y, Tao H, Yang X, et al. Decreased Serum Oxytocin and Increased Homocysteine in First-Episode Schizophrenia Patients. Front Psychiatry. 2019; 10: 217.

47. Zhang Y, Zhao J, Wang W, et al. Homocysteine, but not MTHFR gene polymorphism, influences depressive symptoms in patients with schizophrenia. J Affect Disord. 2020; 272: 24-27.

48. Kinoshita M, Numata S, Tajima A, et al. Cumulative effect of the plasma total homocysteine-related genetic variants on schizophrenia risk. Psychiatry Res. 2016; 246: 833-837.

49. Fryar-Williams S and Strobel JE. Biomarkers of a five-domain translational substrate for schizophrenia and schizoaffective psychosis. Biomark Res. 2015; 3: 3.

50. Cao B, Sun XY, Zhang CB, et al. Association between B vitamins and schizophrenia: A population-based case-control study. Psychiatry Res. 2018; 259: 501-505.

51. Tomioka Y, Numata S, Kinoshita M, et al. Decreased serum pyridoxal levels in schizophrenia: meta-analysis and Mendelian randomization analysis. J Psychiatry Neurosci. 2018; 43(3): 194-200.

52. Yazici AB, Akcay Ciner O, Yazici E, et al. Comparison of vitamin B12, vitamin D and folic acid blood levels in patients with schizophrenia,

drug addiction and controls. J Clin Neurosci. 2019; 65: 11-16.

53. Ishiwata S, Hattori K, Sasayama D, et al. Plasma and cerebrospinal fluid G72 protein levels in schizophrenia and major depressive disorder. Psychiatry Res. 2017; 254: 244-250.

54. Lin E, Lin CH, Lai YL, et al. Combination of G72 Genetic Variation and G72 Protein Level to Detect Schizophrenia: Machine Learning Approaches. Front Psychiatry. 2018; 9: 566.

55. Akyol ES, Albayrak Y, Aksoy N, et al. Increased serum G72 protein levels in patients with schizophrenia: a potential candidate biomarker. Acta Neuropsychiatr. 2017; 29(2): 80-86.

56. Nguyen TT, Kosciolek T, Maldonado Y, et al. Differences in gut microbiome composition between persons with chronic schizophrenia and healthy comparison subjects. Schizophr Res. 2019; 204: 23-29.

57. Maes M, Kanchanatawan B, Sirivichayakul S, et al. In Schizophrenia, Increased Plasma IgM/IgA Responses to Gut Commensal Bacteria Are Associated with Negative Symptoms, Neurocognitive Impairments, and the Deficit Phenotype. Neurotox Res. 2019; 35(3): 684-698.

58. Severance EG, Gressitt KL, Stallings CR, et al. Probiotic normalization of Candida albicans in schizophrenia: A randomized, placebo-controlled, longitudinal pilot study. Brain Behav Immun. 2017; 62: 41-45.

59. Bousman CA, Bengesser SA, Aitchison KJ, et al. Review and Consensus on Pharmacogenomic Testing in Psychiatry. Pharmacopsychiatry. 2021; 54(1): 5-17.

60. Xu M, Xing Q, Li S, et al. Pharacogenetic effects of dopamine transporter gene polymorphisms on response to chlorpromazine and clozapine and on extrapyramidal syndrome in schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry. 2010; 34(6): 1026-32.

61. Arranz M, Collier D, Sodhi M, et al. Association between clozapine response and allelic variation in 5-HT2A receptor gene. Lancet. 1995; 346(8970): 281-2.

62. Arranz MJ, Munro J, Birkett J, et al. Pharmacogenetic prediction of clozapine response. Lancet. 2000; 355(9215): 1615-6.

63. Li J, Hashimoto H, and Meltzer HY. Association of Serotonin2c Receptor Polymorphisms With Antipsychotic Drug Response in Schizophrenia. Front Psychiatry. 2019; 10: 58.