

**Table S1 .** Summary of the main human metabolomics studies on virus infections

<b>Metabolomics approaches</b>	<b>Method</b>	<b>Type of virus</b>	<b>Cohort/ Biofluid</b>	<b>Key metabolites</b>	<b>Biomarker association</b>	<b>Authors</b>
Targeted	FIA–MS/MS	SARS-CoV-2	39 patients/ Serum	kynurenine, 3-methylhistidine, ornithine, p-cresol sulfate, C24, and sphingomyelin	Predictive biomarkers of intensive care unit and mechanical ventilation duration in critically ill for Coronavirus disease	Taleb et al. [1]
Targeted	FIA–MS/MS	SARS-CoV-2	115 patients/ Serum	palmitic , docosapentaenoic , docosahexaenoic and oleic acids	Associated with increased SARS-CoV-2 severity in diabetic and hypertensive patients, offering potential novel diagnostic and therapeutic targets.	Elrayess et al. [2]
Untargeted	<sup>1</sup> H NMR	SARS-CoV-2	30 patients/ plasma	pyruvate ,3-hydroxybutyrate, citrate and free amino acids (alanine, glycine, glutamine, histidine)	Assess metabolites alterations due to SARS-CoV-2 infection and evaluate the response to tocilizumab treatment	Meoni et al. [3]
Untargeted	ESI-MS/MS	influenza	not mentioned/ PBMCs	monodehydroascorbate radical, L-gluconate, orotidine 5'-phosphate, CDP-ethanolamine, 3-dehydrosphinganine, Sphingosine, S-formylglutathione, Resolvin E1, 3,4-dihydroxymandelate, monodehydroascorbate, putrescine	Understand the replication and pathogenesis mechanisms of influenza	Karimi et al. [4]
Targeted	CE-TOF-MS	influenza	34 pediatric patients / Serum	succinic acid, undecanoic acid, kynurenine, decanoic acid, cysteine and quinolinic acid	Biomarker discovery to understand the pathophysiology of encephalopathy linked to influenza.	Torii et al. [5]

Untargeted	UPLC-MS and GC-TOF-MS	HIV	87 HIV-positive and 148 HIV+ NCDs/ Plasma	plasmalogen, phosphatidylcholines, phosphatidylethanolamines, and glutamine	Metabolites may serve as crucial targets for investigating the pathophysiology of non-communicable diseases (NCDs) in HIV infection and developing treatments	Ding et al.[6]
Untargeted	<sup>1</sup> H NMR	HIV	34 HIV-1 positive patients, 29 patients were receiving combination antiretroviral therapy treatment and 5 patients had not been treated with antiretroviral agents before/ Serum	choline, lactate, glycerol glucose, valine, and alanine.	Differentiate between individuals with HIV-1 positive and receiving antiretroviral treatment, and HIV-1 negative	Hewer et al. [7]
Untargeted	HPLC-HESI MS/MS	HBV	30 CHB patients, 29 LC patients, and 30 HCC patients/ Serum	1,2-diacyl-3-β-D-galactosyl- <i>sn</i> glycerol, 5-hydroxy-6 <i>E</i> ,8 <i>Z</i> ,11 <i>Z</i> ,14 <i>Z</i> ,17 <i>Z</i> -eicosapentaenoic acid, glycyrrhizic acid ,taurodeoxy cholic acid	Differentiate between CHB, LC, and HCC patients. This can aid in the early detection and treatment of patients with HCC	Pan et al. [8]
Untargeted	UHPLC-Q-TOF/MS	HBV	199 hepatic disease patients /Serum	alanine transaminase, L-lactate dehydrogenase , alkaline phosphatase , aspartate transaminase, and gamma-glutamyl transferase	Changes that occur in patients with HBV replication and compare the metabolic alterations in the progression of liver disease induced by HBV infection	Yu et al. [9]
Untargeted	<sup>1</sup> H NMR	HBV	90 patients with CHB/ Serum	glutamine , glutamate , methionine and tricarboxylic acid	Changes during the transition from immune tolerance to immune clearance phase and display distinct metabolomic	Nguyen et al.[10]

					profiles at different stages of medical treatment	
Targeted	MSI-CE-MS and <sup>1</sup> H-NMR	HCV	20 patients with HCV and 14 / Serum	hypoxanthine, acetoacetate, hydroxybutyric acid, lactic acid and glucose	Differentiation of liver disease severity and progression of liver fibrosis	Shanmugan -athan et al. [11]
Targeted and Untargeted	GC-MS and UPLC-MS/MS	HCV	30 HCC patients, 27 hepatitis C cirrhosis disease controls and 30 healthy / Serum	12-hydroxyeicosa-tetraenoic acid (12-HETE), 15-HETE, sphingosine, $\gamma$ -glutamyl, xanthine, serine, glycine, aspartate, acylcarnitines and dicarboxylic acids	Metabolites were found to be associated with the presence of HCC and correlated with cirrhosis	Fitian et al. [12]
Untargeted	<sup>1</sup> H NMR	HCMV	31 patients of HCMV and 22 controls/ Urine	betaine , glycine, alanine, dimethylamine, succinate,1-methylnicotinamide, acetate, and oxoglutarate	Confirms the usefulness of metabolomics for studying HCMV infection in clinical applications	Frick et al. [13]
Untargeted	GC-MS	HCMV	127 patients with HCMV infantile hepatitis, HCMV ICH, and HCMV EHBA/ Plasma	carbamic acid, glutamate, L-aspartic acid, L-homoserine, and noradrenaline	Potential diagnostic tool that could be used to distinguish ICH from EHBA as well as to explore the pathogenesis of HCMV-induced liver injury	Li et al.[14]
Untargeted	<sup>1</sup> H NMR	Arbovirus: West Nile Virus and rabies	27 patients with infections that included Lyme disease, West Nile Virus meningoencephalitis, multiple sclerosis, rabies, and Histoplasma meningitis and 25 controls/ CSF	ketones, pyruvate, carnitine, glycine, glutamate, 2-oxoglutarate, sobutyrate, fructose, N-acetylneuraminate, and serine	Used as a rapid screening test to enhance diagnostic accuracy and improve patient outcomes	French et al. [15]

Untargeted	<sup>1</sup> H NMR	viral meningitis (VM)	children diagnosed with BM (n=85), TBM (n=47), and VM (n=35), as well as controls (n=24)/ CSF	beta-hydroxybutyrate, lactate, alanine, acetate, acetone, acetoacetate, pyruvate, glutamine, citrate, creatine/creatinine, glucose, and urea	The combined use of NMR spectroscopic data and other routine clinical features may improve the differential diagnosis of meningitis in children	Subramanian et al.[16]
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