

Supplementary Table S2. Summary of the major mass-spectrometry-based studies performed on the syphilis patients or neurosyphilis patients to date. Table includes details about the numbers of sample, the analysis method, and the type of mass spectrometer used and biomarkers identified in previous study.

Research model	Sample cohort (no. of samples)	Analytical apparatus	Biomarkers identified	Study (year)	Ref.
Human serum	syphilis (20); healthy control (20)	UHPLC-Q-TOF/MS analy	trimethylamine N-oxide, l-arginine, lysoPC(18:0), betaine and acetylcarnitine	Liu LL <i>et al.</i> (2019)	[1]
Human CSF	neurosyphilis (18); syphilis/non-neurosyphilis (18); syphilis-free(18)	UHPLC-Q-TOF/MS	L-gulono-gamma-lactone, D-mannose, N-acetyl-L-tyrosine, hypoxanthine, and S-methyl-5'-thioadenosine	Liu LL <i>et al.</i> (2019)	[2]
Human CSF	Neurosyphilis (15); non-neurosyphilis (14)	LC-MS	Bilirubin, L-histidine, prostaglandin E2, alpha-kamlolenic acid, and butyryl-L-carnitine and palmitoyl-L-carnitine	Qi S <i>et al.</i> (2019)	[3]

[1] Liu L.L., Lin Y., Zhuang J.C., Ren J., Jiang X.Y., Chen M.H., et al. (2019). Analysis of serum metabolite profiles in syphilis patients by untargeted metabolomics. *J Eur Acad Dermatol Venereol.* 3(7):1378-1385. doi: 10.1111/jdv.15530.

[2] Liu L.L., Lin Y., Chen W., Tong M.L., Luo X., Lin L.R., et al. (2019). Metabolite Profiles of the Cerebrospinal Fluid in Neurosyphilis Patients Determined by Untargeted Metabolomics Analysis. *Front Neurosci.*, 26;13:150. doi: 10.3389/fnins.2019.00150.

[3] Qi S., Xu Y., Luo R., Li P., Huang Z., Huang S., et al. (2019). Novel Biochemical Insights in the Cerebrospinal Fluid of Patients with Neurosyphilis Based on a Metabonomics Study. *J Mol Neurosci.* 69(1):39-48. doi: 10.1007/s12031-019-01320-0.