Supplementary Table S1: Summary of BCa Metabolomic studies reviewed

	First author, Year	Methods	Samples	Altered metabolites	Notes	AUC	Altered pathways	Refs
Urine	Pakisanti, 2010	GC/TOFMS OPLS-DA	24 BCa (any stage) vs 51 non BCa controls	Senecioic acid 2-Butenedioic acid Ribonic acid 2,5-Furandicarboxylic acid Sumiki's acid 2-Propenoic acid Glycerol Gluconic acid Valerate Fructose Citric acid Ribitol	Decreased			[66]
				Melibiose Uridine L-Valine	Increased			
	Putluri, 2011	PLSDA	83 BCa vs 51 Controls Group 1: 13 BCa (prior to surgery) vs 13 Controls (age matched with no history of BCa) Group 2: 28 BCa vs 16 Controls (with prior history of BCa but disease free of benign after treatment) Group 3: 34 BCa vs 11 Controls(with prior history of BCa but disease free of benign after treatment) Group 4: 8 BCa vs 11 Controls (age matched with no history of BCa)	Palmitic acid Creatine Histamine Uracil Guanine D−Ribonolactone Pipecolic acid Thymine S−Adenosylmethionine Niacinamide Hippuric acid N12−Acetylspermidine Serine Lysine Spermidine Carnitine Tyrosine 3−Hydroxykynurenine Phenylalanine Valine 4−Pyridoxic acid Hypoxanthine Kynurenine Histidine Leucine/ Isoleucine	Group 1 Group 2 Group 3 Group 4 Group 2 NMIBC vs MIBC	0.790 0.670 0.620 0.760 0.840		[67]
	Shen, 2015	UPLC-TOF-HRMS OPLS-DA	23 BCa (early stages) vs 21 non BCa controls	Nicotinuric acid Aspartateaspartateglycinetriptophan Trehalose	Increased	0.774 0.743 0.776		[68]
				Glycinecysteinealaninelysine Inosinic acid Ureidosuccinic acid	Decreased	0.834 0.720 0.752		
	Cheng, 2018	LC-HRMS OPLS-DA	26 NMIBC vs 39 Healthy Controls	Metabolite panel: Dopamine 4-sulfate, mg00/1846z,9z,12z,15z/00, aspartyl-histidine Tyrosyl-methionine		0.838	Fatty acid metabolism Increased Fatty acid oxidation	[69]

			43 LG NMIBC vs 43 Healthy controls	Metabolite panel: 3-hydroxy-cis-5-tetradecenoylcarnitine 6-ketoestriol Beta-cortolone tetrahydrocorticosterone heptylmalonic acid		0.899	Decreased Tryptophan metabolism	
			43 LG NMIBC without hematuria vs 37 HG NMIBC without hematuria	Metabolite panel: N-acetyl-4-o-acetylneuraminic acid 4-(2-aminophenyl)-2 4-dioxobutanoic acid 6-keto-decanoylcarnitine 3-hydroxydecanoyl carnitine 2-hydroxylauroylcarnitine		0.755		
			18 LG NMIBC with hematura vs 69 HG with hematuria	Metabolite panel Indolylacryloylglycine histidinyl-histidine indoleacrylic acid N-acetyl-5-methoxykynuramine l-3-hydroxykynurenine		0.827		
	Jin, 2014	HPLC-MS OPLS-DA	138 BCa vs 121 Healthy controls	Succinate Pyruvate Oxoglutarate Carnitine Phosphoenolpyruvate Trimethyllysine Isovalerylcarnitine Octenoylcarnitine Acetyl-Coa	increased	0.937	Fatty acid oxidation	[20]
				Melatonin Glutarylcarnitine Decanoylcanitine	decreased			
	Loras 2018	UPLC-TOF-MS PLS-DA	27/33 BCa vs 10/11 Controls (patient 2 weeks post-TURBT)	Phenylalanine Tryptophan Kynurenine hydroxykynurenine phenylacetylglutamine		0.94	phenylalanine, arginine, proline, and tryptophan	[70]
			BCa vs Patient under surveillance			0.75		
			Controls vs patient under surveillance			0.53		
	Liu, 2018	OPLSA-DA	33 BCa vs 44 age- and sex- matched healthy subjects	Metabolite panel Trans-2-dodecenoylcarnitine serinyl-valine feruloyl-2-hydroxyputrescine 3-hydroxynonanoyl carnitine		0.956	Amino acid metabolism and fatty acid oxidation upregulated, phenylalanine metabolism and xenobiotics (e.g., caffeine) metabolism were downregulated	[73]
			15 HG BCa vs 18 LG BCa	Indolylacryloylglycine N_2-galacturonyl-L-lysine aspartyl-glutamate		0.891		
	Pinto, 2021	VOCs headspace solid-phase	53 BCa: 26 Ta/is 17 T1 10 ≥T2 vs 53 Healthy controls	(1S)-1,5-dimethyl-6,8 dioxabicyclo[3.2.1] octane 2-butanone 2-furaldehyde	Decreased	0.800		[104]

		microextraction-GC-MS PCA PLS-DA		2-methylbutanal Formaldehyde Hexanal 4-heptanone Carvone Piperitone 2 unknows				
				1-methylnaphthalene 2-methylnonane 2-methylnaphthalene 2,4-dimethylheptane 2,6-dimethylnonane 4-methyloctane P-cresol 1,2,4-trimethylbenzene 4 unknowns	Increased	0.787		
				17 Metabolite set (excluding unknowns)	BCa vs HC Ta/is vs HC T1 vs HC ≥T2 vs HC T1 vs Ta/is ≥T2 vs Ta/is ≥T2 vs T1	0.851 0.761 0.910 0.820 0.837 0.938 0.894		
Serum	Cao, 2012	1H-NMR OPLS-DA	BCa vs Calculi vs Healthy controls	Isoleucine/leucine tyrosine Lactate Glycine, Citrate	Decreased			[84]
				V/ldl Glucose Acetoacetate				
	Lin,2012	LC-MS OPLS-DA	24 BCa vs 24 KC vs 24 Healthy controls	Eicosatrienol Azaprostanoic acid	BCa specific biomarkers	0.980 0.977		[85]
				Acetylphenylalanine Methyl hippuric acid	Common genitourinary biomarkers	0.847 0.828		
	Liu, 2020	LC-MS	64 BCa vs 74 KC vs 141 Healthy controls	Homocysteine Thiolactone Acetylcysteine Methionine Sulfoximine 9,10,13-trihome Avenoleic acid (10E,12Z)-(9S)-9-Hydroperoxyoctadeca-10 12-dienoic acid 16-Hydroxy-10-oxohexadecanoic acid	Decreased in cancer groups	0.942		[86]
				9S, 10R-Epoxy-6Z-nonadecene	Increased in cancer groups			
	Bansal,2013	1HNMR OPLS-DA	36 LG BCa vs 31 HG BCa vs 32 Healthy controls	Dimethylamine (DMA) Malonate Lactate Glutamine Histidine Valine		0.910 0.905 0.897 0.891 0.899. 0878		[87]

	Zhou, 2016	GC-MS-SIM and nontargeted GC-MS PLS-DA	53 HG BCa vs 48 age and sex matched Healthy controls	Gluconic acid Xylitol 2-keto-gluconic acid Ribose, Arabitol Hypoxanthine Uridine Hypotaurine Kynurenine N-acetylserine	Increased		PPP cycle TCA cycle and fatty acid biosynthesis	[88]
			39 LG BCa vs 48 age and sex matched Healthy Controls	Oleic acid Serine 3-indolepropionic acid Glyoxylic acid Glycolic acid Hippuric acid				
			101 HG/LG BCa vs 48 Healthy Controls	Fumaric acid Malic acid Dsaccharic acid	increased	0.863		
	Tan, 2016	UHPLS-QTOFMS	LG BCa vs HG BCa	Inosine N1- acetyl-N2-formyl-5-methoxykynuramine phosphatidylserine		0.961		[89]
	Vantaku, 2019	LC-MS	18 AA BCa VS 54 EA BCa	Taurine Glutamine Glutamate Aspartate Serine Hypoxanthine Uric acid	Increased in AA		one-carbon, tryptophan and nucleotide metabolisms (e.g. purine catabolic pathway)	[90]
Tissue	Putluri, 2011	LC-MS	27 benign adiacent vs 31 BCa vs 25 matched pairs	Serine Asparagine Valine Tryptophan Phenylalanine Histidine	Increased			[67]
	Tripathi, 2013	1H-HRMS-NMR – GC-MS crossvalidation PCA and PLS-DA	17 ta-t1 BCa tissues vs 16 T2 BCa tissues vs 26 benign/healthy tissues vs	branched-chain amino acids (BCAAs), Lactate Alanine Ace Glutamic acid GSH Glutamine Aspartate Cre ChoCC Taurine myo-Inositol Phenylalanine, Tyrosine	Increased in BCa vs healthy No clear segregation observed between ta-t1 and t2	0.970	aerobic glycolysis (Warburg effect) TCA cycle anaplerosis	[91]
	Piyarathna, 2017	LC-MS	126 BCas vs 39 benign adiacent/normal	phosphocholines phosphatidylethanolamines plasmenyl Pes	Increased		cyclooxygenase-2 pathways implicated in tumor growth and metastasis	[92]
				Triglyceride	Decreased			

	Yang, 2019	LC-HRMS UPLC PCA	48 samples collected in 4 groups: Pre-gemcitabine normal, pre-gemcitabine BCa, post-gemcitabine normal, and post-gemcitabine BCa	Bilirubin	Decreased in BCa tissues pre-gemcitabine and insignificant level after gemcitabine		glutathione, purine and thiamine metabolism	[93]
				Retinal	In T2 stage BCa vs normal Decreased And insignificant difference after gemcitabine			
Cell lines	Dettmer, 2013	LC-QTOFMS PCA (Principal Component Analysis	Cluster 1 HCC and 5 other cell lines of different origin (JB2 BCa LINE) Cluster 2: Renal Cell Carcinoma and BCa RT4 CLUSTER 3: primary hepatocytes Cluster 4: Mammary carcinoma lines and THE T47D melanoma cell line Cluster 5: SW 480 AND SW620 colon carcinoma lines	dipeptides Val-Leu and Leu-Leu	Increased in RT4 (cluster 2) Decreased in JB2 (Cluster 1)		carrier-mediated uptake or extracellular hydrolysis followed by uptake of amino residues by amino acid transporters . pathways related to increased use of di and tripeptides ad substrates of increased bioenergetic and biosintetic demand in cancer cells	[98]
	Conde, 2015	(1H-NMR) and spectra analysis	RT4 (less invasive) vs TCCSUP cell lines (more invasive)	glucose	Decreased in both		metabolism of pyruvate	[99]
				Pyruvate	Decreased in TCCSUP			
				Alanine	Increased in TCSSUP			
	Petrella, 2020	1H-NMR spectroscopy exometabolome analysis OPLS-DA	5637 vs RT112 vs RT4 cell lines	Glucose Glutamine serine BCAAs arginine	Decreased in each one line(consumed) Glucose: similar		Glycolysis is the Most Active Metabolic Pathway in 5637 Cells RT Cells Show an Active Oxidative Metabolism	[100]
				Alanine Lactate Pyruvate formate	Increased in each one line (excreted) Lactate: 5637/RT112 > RT4 Alanine: RT4 > RT112 > 5637			

Rodrigues, 2019	GC-MS endometabolome analysis PCA PLS-DA	J82 vs 5637 Cell lines	Glycine Myristic acid Palmitic acid palmitoleic acid	Decreased in J82	0.960 1.000 1.000 1.000	Ammonia recycling, fatty acid biosynthesis, and methionine and glutamate metabolisms	[101]
			Leucine Methionine Valine Aspartic acid	Increased in J82	0.880 0.920 0.920 0.960		
Iliou, 2020	1H-NMR spectroscopy PCA PLS-DA	RT4 (grade I) RT112 (grade II) T24 (grade III) TCCSUP (grade IV)	Myo-inositol Creatine phosphate Histidine Malate Succinate, Acetate AMP ADP ATP GTP UMP Oxypurinol	Increased in T24 Decreased In RT4 and TCCSUP		Metabolic inversion	[102]
			Uracil Propylene glycol	Decreased in T24 and TCCSUP			
			Tryptophan Formate Uracil Adenine Propylene glycol Choline	Ratio decreased in grade III (T24) compared to grade I (RT4)			
Rodrigues, 2018	HSSPME/GC–MS VOCs extraction OPLS-DA	Scaber J82 5637 SV-HUC-1 (normal)	2-pentadecanone A-terpineol 2-methylbutan-2-ol 1-phenylethanol 2-phenylpropan-2-ol 2-hydroxy-2-methyl-1-phenylpropan-1-one	Scaber vs SV-HUC-1 Ph7	1.000	synthesis of fatty acids for membrane formation or β-oxidation of fatty acids for energy production, amino acids metabolism, oxidative stress and inflammation process	[103]
			Benzoic acid 2-methyl-2-heptanol 1-butanol A-methylstyrene unknown 25	Scaber vs SV-HUC-1 Ph2	1.000		
			4-methylbenzaldehyde cyclohexanone 2-pentadecanone 2-phenylpropan-2-ol phenol dodecane 4-methylheptan2-one γ-dodecalactone unknown 24	J82 vs SV-HUC-1	1.000		
			1-phenylethanol 4-methylnonane dodecane γ-dodecalactone unknowns 10 and 24	5637 vs SV-HUC-1	1.000		

				benzaldehyde 2-nonanone 4-methylheptan-2-one dodecane 2 3-dimethylhexane hexadecane tetradecane	Increased in BCa lines medium vs normal line mediun	1.000		
				2-phenylpropanol isopentanol	Decreased in BCa cell lines medium vs normal line medium	1.000		
				acetophenone α-terpineol nonanal 2-phenylpropan-2-ol 4-methylnonane 6-methylheptan-2-one	Decreased in J82 and Scaber vs 5637 medium	1.000		
				Dodecanol dodecanal γ-nonalactone	Increased in J82 and Scaber vs 5637 medium	1.000		
				1-phenylethanol α-terpineol (2E,4E)-Deca-2,4-dienal Benzaldehyde Benzoic acid Geranylacetone 2-pentadecanone γ-nonalactone	Increased in J82 vs Scaber	1.000		
				Phenol Nonanal n-butyl acetate acetophenone Cyclohexanone Naphthalene	Decreased in J82 vs 5637 medium	1.000		