ADVANCED MATERIALS TECHNOLOGIES

Supporting Information

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Porous PDMS-Based Microsystem (ExoSponge) for Rapid Cost-Effective Tumor Extracellular Vesicle Isolation and Mass Spectrometry-Based Metabolic Biomarker Screening

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Supplementary Information

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Keywords: Porous PDMS, microsystems, circulating biomarkers, PDMS Sponge, extracellular vesicles, liquid biopsy

Contents

Figures & Table

S1. EV isolation using ExoSponge

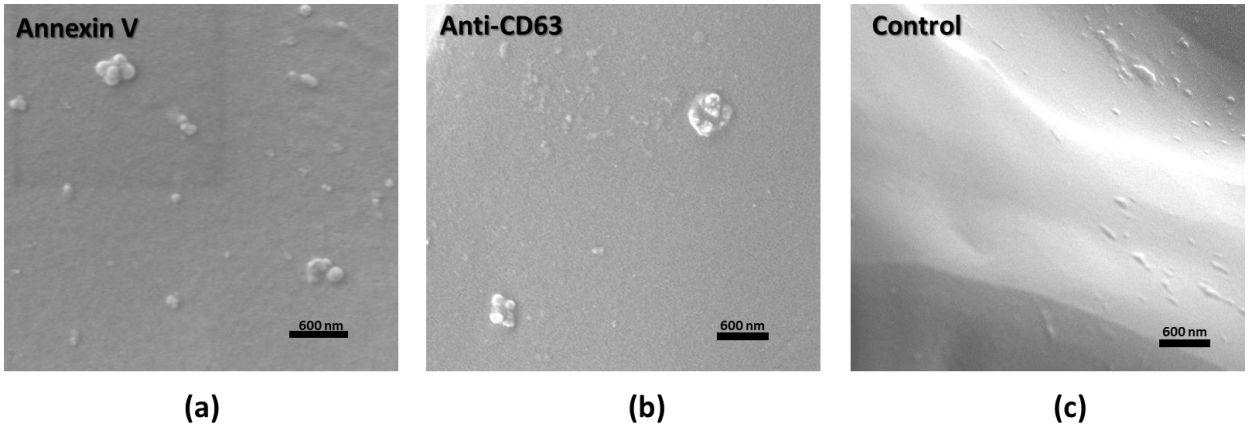

Figure S1. SEM imaging demonstrating on device EV capture. (**a**) Annexin V protein conjugated device with effective exosome (30-150 nm) isolation. (**b**) CD-63 antibody conjugated device surface (**c**) Control device surface with only Silane-GMBS Neutravidin conjugation

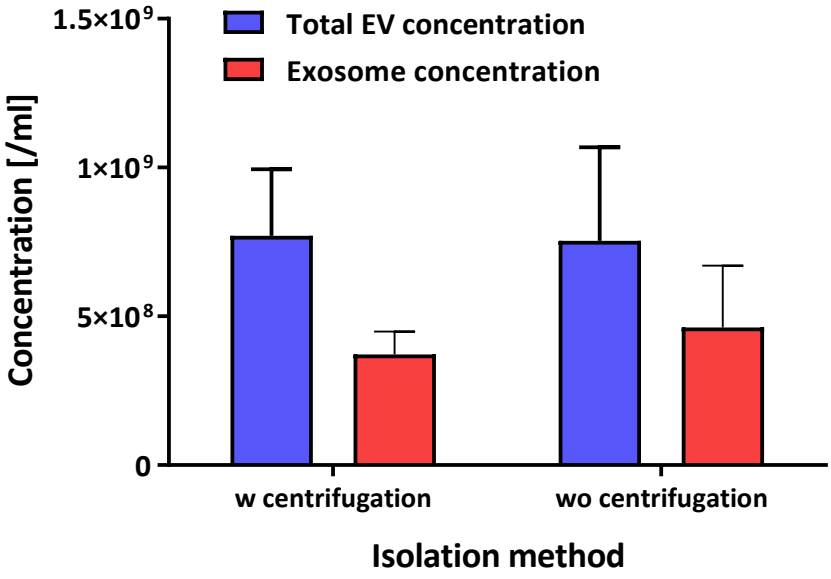

Figure S2. EV isolation comparison with/without additional external force (centrifugation) during incubation

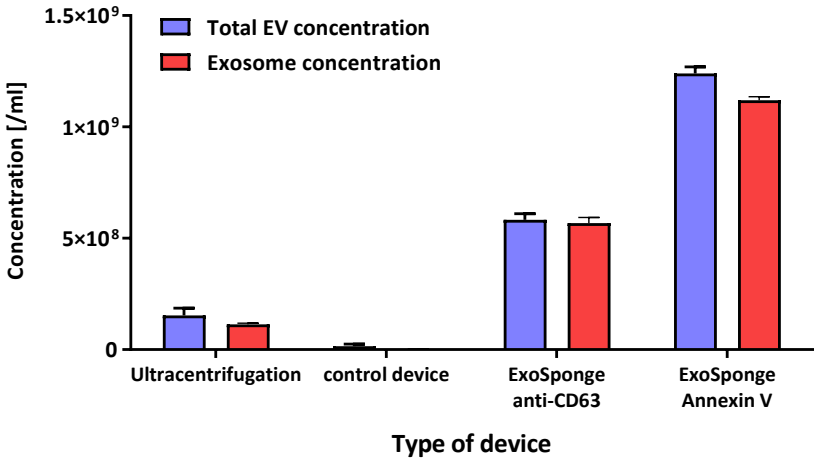

Figure S3. EV isolation comparison with ultracentrifugation and ExoSponge with various conjugation conditions

S2. Patients information

Table S1. Clinical information of the patient samples

Cancer Type	Sample ID	Sample description						
		Sex	Age	Stage	Adenocarcinoma subtype	Mutation	Treatment	Tumor origin
Lung cancer patient	***LC1***	F	61	IV	EGFR	EGFR Exon 19 deletion	Tarceva	Left upper lobe
	LC2	F	58	IV	EGFR	EGFR mutation	Carboplatin/ pemetrexed	Left upper lobe
	LC3	F	70	I	EGFR	EGFR Exon 19 deletion	Tagrisso	Left upper lobe
	LC4	F	55	IV	ROS1	ROS1 Mutation	Crizotinib	Neck
	LC5	F	40	IV	ROS1	ROS1 rearrangement	Crizotinib, Entrectinib	Lymph node
	LC6	F	63	IV	ROS1	ROS1	Carboplatin/ pemetrexed	Left upper lobe

S3. MSEA raw data

Table S2. Extended contents of MSEA data

Metabolite Set	Total Cmpd	Hits	Statistic Q	Expected Q	Raw p	Holm p	FDR	Enrichment Ratio
COBALAMIN (AND FOLATE) DEFICIENCY	3	1	25.252	14.286	0.20439	1	0.89552	1.767604648
METHYLMALONIC ACIDURIA, CBLB TYPE	2	1	25.252	14.286	0.20439	1	0.89552	1.767604648
PRIMARY BILIARY CIRRHOSIS	3	1	17.349	14.286	0.30465	1	0.89552	1.214405712
PHENYLKETONURIA	7	2	16.527	14.286	0.31518	1	0.89552	1.156866863
METHYLMALONIC ACIDURIA, CBLA TYPE	4	2	16.269	14.286	0.32112	1	0.89552	1.138807224
MALNUTRITION	8	2	15.037	14.286	0.34221	1	0.89552	1.052568949
BIOTINIDASE DEFICIENCY	5	2	13.725	14.286	0.36793	1	0.89552	0.960730785
METHYLMALONIC ACIDURIA (MMA)	8	2	13.454	14.286	0.38325	1	0.89552	0.941761165
MAMMARY TUMOR-BEARING MICE	3	3	13.493	14.286	0.38636	1	0.89552	0.94449111
SOTOS SYNDROME	2	1	12.113	14.286	0.39821	1	0.89552	0.847893042
CHRONIC RENAL FAILURE	13	3	11.227	14.286	0.43675	1	0.89552	0.785874283
AIDS	6	1	9.2837	14.286	0.46308	1	0.89552	0.649846003
DEMENTIA	2	1	9.2837	14.286	0.46308	1	0.89552	0.649846003
GAMMA-GLUTAMYLTRANSFERASE DEFICIENCY	4	1	9.2837	14.286	0.46308	1	0.89552	0.649846003
MULTIPLE SCLEROSIS	39	1	9.2837	14.286	0.46308	1	0.89552	0.649846003
21-HYDROXYLASE DEFICIENCY (CYP21)	11	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
3-BETA-HYDROXYSTEROID DEHYDROGENA	9	1	9.2647	14.286	0.46356	1	0.89552	0.64851603

SE DEFICIENCY								
3-METHYL-CROTONYL-GLYCINURIA	4	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
ACTH DEFICIENCY, ISOLATED | ADRENAL HYPOPLASIA. ADDISON DISEASE, X-LINKED	4	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
BECKWITH-WIEDEMANN SYNDROME. EXOMPHALOS-MAKROGLOSSIA-GIGANTISM SYNDROME | EXERCISE-INDUCED-HYPERINSULINSM [EIHI] | HYPOGLYCEMIA, FAMILIAL NEONATAL	2	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
BETA-KETOTHIOLASE DEFICIENCY	8	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
CARNITINE DEFICIENCY, MYOPATHIC	3	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
CARNITINE PALMITOYL TRANSFERASE DEFICIENCY (I)	5	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
CARNITINE PALMITOYL TRANSFERASE DEFICIENCY (II)	8	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
CARNITINE TRANSPORTER DEFECT. PRIMARY SYSTEMIC CARNITINE DEFICIENCY	4	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
CYSTIC FIBROSIS (CF)	4	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
DIABETES MELLITUS, INSULIN-DEPENDENT	5	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
FAMILIAL HYPERINSULIN	3	1	9.2647	14.286	0.46356	1	0.89552	0.64851603

EMIA AND HYPERPROINSULINEAMIA WITH MILD DIABETES								
GALACTOSEMIA I	6	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
GLUCOCORTICOID DEFICIENCY, FAMILIAL ISOLATED. MIGEON SYNDROME | HYPOADRENOCORTICISM, FAMILIAL	2	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
GLUTARIC ACIDURIA II	8	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
GLYCEROL INTOLERANCE SYNDROM	3	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
GLYCEROL KINASE DEFICIENCY	2	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
GLYCOGENOSIS, TYPE III. CORI DISEASE, DEBRANCHER GLYCOGENOSIS	3	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
GROWTH HORMONE DEFICIENCY	4	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
KETOTIC HYPOGLYCEMIA	2	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
MALONYL-COA DECARBOXYLASE DEFICIENCY	3	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
MEDIUM CHAIN ACYL-COA DEHYDROGENASE DEFICIENCY (MCAD)	10	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
NEONATAL HEMOCHROMATOSIS	2	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
PERSISTANT HYPERINSULINEMIC HYPOGLYCEMIA OF INFANCY, PHHI	3	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
REYE	2	1	9.2647	14.286	0.463	1	0.8955	0.64851603

SYNDROME					56		2	
REYE SYNDROME LIKE MANIFESTATIONS	2	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
VERY-LONG-CHAIN ACYL COA DEHYDROGENASE DEFICIENCY (VLCAD)	21	1	9.2647	14.286	0.46356	1	0.89552	0.64851603
ALCOHOLISM	6	1	7.8324	14.286	0.50201	1	0.89552	0.548257035
METABOLITES AFFECTED BY GENDER	9	5	11.215	14.286	0.51005	1	0.89552	0.785034299
HARTNUP DISEASE	2	1	6.5394	14.286	0.54101	1	0.89552	0.457748845
SPASTIC ATAXIA	5	1	6.5394	14.286	0.54101	1	0.89552	0.457748845
TYROSINEMIA I	5	2	6.7727	14.286	0.54529	1	0.89552	0.474079518
SEPTIC SHOCK	2	1	5.8152	14.286	0.56507	1	0.89552	0.407055859
EARLY MARKERS OF MYOCARDIAL INJURY	14	5	10.982	14.286	0.5709	1	0.89552	0.768724626
2-KETOGLUTARATE DEHYDROGENASE COMPLEX DEFICIENCY	2	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
3-HYDROXY-3-METHYLGLUTARYL-COA LYASE DEFICIENCY	4	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
3-METHYLGLUTACONIC ACIDURIA (TYPE I)	3	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
ASPHYXIA [DD]	7	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
CARNITINE-ACYLCARNITINE TRANSLOCASE DEFICIENCY	4	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
CHRONIC PROGRESSIVE EXTERNAL	3	2	6.0688	14.286	0.57555	1	0.89552	0.424807504

OPHTHALMOPLEGIA AND KEARNS-SAYRE SYNDROM								
FRUCTOSE INTOLERANCE, HEREDITARY	5	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
FRUCTOSE-1,6-DIPHOSPHATASE DEFICIENCY	5	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
GLYCOGEN SYNTHETASE DEFICIENCY	3	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
GLYCOGENOSIS (TYPE IA, IB, IC) | GLYCOGENOSIS, TYPE VI. HERS DISEASE	5	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
LONG CHAIN ACYL-COA DEHYDROGENASE DEFICIENCY (LCAD)	5	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
LONG-CHAIN-3-HYDROXYACYL-COA DEHYDROGENASE DEFICIENCY (LCHAD)	10	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
PHOSPHOENOLPYRUVATE CARBOXYKINASE DEFICIENCY 2 (PEPCK2)	5	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
RESPIRATORY CHAIN DEFICIENCIES	4	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
SHORT CHAIN ACYL-COA DEHYDROGENASE DEFICIENCY (SCAD)	4	2	6.0688	14.286	0.57555	1	0.89552	0.424807504
TRANSALDOLASE DEFICIENCY	6	1	5.1069	14.286	0.59048	1	0.89552	0.35747585
RHABDOMYOLYSIS	4	2	9.1565	14.286	0.59099	1	0.89552	0.640942181
GLUTARIC ACIDURIA I	3	1	4.9052	14.286	0.59811	1	0.89552	0.343357133
DICARBOXYLIC AMINOACIDURIA. GLUTAMATE-ASPARTATE TRANSPORT DEFECT	2	2	7.0157	14.286	0.61165	1	0.89552	0.491089178

ISOVALERIC ACIDEMIA	9	2	5.898	14.286	0.63741	1	0.89552	0.412851743
GLUTATHIONE SYNTHETASE DEFICIENCY	8	1	3.9397	14.286	0.6375	1	0.89552	0.275773485
AUTISM	8	3	6.1796	14.286	0.63845	1	0.89552	0.432563349
PROPIONIC ACIDEMIA	8	2	5.6612	14.286	0.65995	1	0.89552	0.396276074
HYPERBARIC OXYGEN EXPOSURE	9	2	6.3726	14.286	0.67394	1	0.89552	0.446073079
DIABETES MELLITUS (MODY), NON-INSULIN-DEPENDENT	19	9	7.9128	14.286	0.68482	1	0.89552	0.553884922
PYRUVATE DEHYDROGENASE DEFICIENCY (E3)	7	4	5.2467	14.286	0.7011	1	0.89552	0.367261655
LESCH-NYHAN SYNDROME	5	2	4.0124	14.286	0.70308	1	0.89552	0.280862383
MYOCARDIAL ISCHEMIA	6	4	6.8865	14.286	0.70409	1	0.89552	0.482045359
MAPLE SYRUP URINE DISEASE	9	4	5.9715	14.286	0.70852	1	0.89552	0.41799664
HYPERINSULINISM-HYPERAMMONEMIA SYNDROME	2	1	2.3506	14.286	0.717	1	0.89552	0.164538709
LYSINURIC PROTEIN INTOLERANCE (LPI)	4	1	2.3506	14.286	0.717	1	0.89552	0.164538709
2,4-DIENOYL-COA REDUCTASE DEFICIENCY	3	1	2.2589	14.286	0.72241	1	0.89552	0.158119838
2-HYDROXYGLUTARIC ACIDEMIA (L)	2	1	2.2589	14.286	0.72241	1	0.89552	0.158119838
HYPERLYSINEMIA I, FAMILIAL | HYPERPIPECOLATEMIA	2	1	2.2589	14.286	0.72241	1	0.89552	0.158119838
PYRUVATE CARBOXYLASE DEFICIENCY	10	5	3.6691	14.286	0.75313	1	0.89552	0.256831863
CARBAMOYL PHOSPHATE SYNTHETASE DEFICIENCY	3	2	1.8803	14.286	0.76073	1	0.89552	0.131618368

(CPS)								
HYPERLYSINEMIA II OR SACCHAROPINURIA	3	2	1.8396	14.286	0.76503	1	0.89552	0.128769425
XANTHINURIA	2	1	1.5719	14.286	0.76737	1	0.89552	0.110030799
AGING-RELATED METABOLITES	6	1	1.537	14.286	0.76992	1	0.89552	0.107587848
CITRULLINEMIA TYPE I | CITRULLINEMIA TYPE II, ADULT-ONSET	3	1	1.4339	14.286	0.77761	1	0.89552	0.100370993
SHORT-BOWEL SYNDROME (PERMANENT INTESTINAL FAILURE)	2	1	1.4339	14.286	0.77761	1	0.89552	0.100370993
HEMODIALYSIS	14	4	4.63	14.286	0.79875	1	0.89552	0.324093518
ANOXIA	8	3	2.4216	14.286	0.79907	1	0.89552	0.16950861
HOMOCYSTINURIA DUE TO DEFECT OF N(5,10)-METHYLENE THF DEFICIENCY | HOMOCYSTINURIA (CBLE)	2	1	1.1572	14.286	0.79985	1	0.89552	0.08100238
METHIONINE ADENOSYL TRANSFERASE DEFICIENCY | METHYLMALONIC ACIDURIA AND HOMOCYSTINURIA, CBLC TYPE | METHYLMALONIC ACIDURIA AND HOMOCYSTINURIA, CBLD TYPE	2	1	1.1572	14.286	0.79985	1	0.89552	0.08100238
S-ADENOSYLHOMOCYSTEINE HYDROLASE DEFICIENCY	5	1	1.1572	14.286	0.79985	1	0.89552	0.08100238
CONTINUOUS AMBULATORY	15	7	2.3437	14.286	0.80816	1	0.89552	0.164055719

PERITONEAL DIALYSIS (CAPD)								
3-HYDROXYISOBUTYRIC ACIDURIA	3	1	1.0572	14.286	0.80856	1	0.89552	0.07400252
3-METHYLGLUTACONIC ACIDURIA (TYPE II), X-LINKED	4	1	1.0572	14.286	0.80856	1	0.89552	0.07400252
ACYL COA DEHYDROGENASE 9 DEFICIENCY | PYRUVATE DEHYDROGENASE DEFICIENCY (E2)	2	1	1.0572	14.286	0.80856	1	0.89552	0.07400252
CONGENITAL LACTIC ACIDOSIS	2	1	1.0572	14.286	0.80856	1	0.89552	0.07400252
ETHYLMALONIC ENCEPHALOPATHY (EPEMA)	2	1	1.0572	14.286	0.80856	1	0.89552	0.07400252
LEIGH`S SYNDROME, SUBACUTE NECROTIZING ENCEPHALOPATHY, SNE	2	1	1.0572	14.286	0.80856	1	0.89552	0.07400252
LIVER DISEASE, LIVER FAILURE, UNSPECIFIC	2	1	1.0572	14.286	0.80856	1	0.89552	0.07400252
METHANOL POISONING	2	1	1.0572	14.286	0.80856	1	0.89552	0.07400252
MITOCHONDRIAL-ENCEPHALOPATHY-LACTIC ACIDOSIS-STROKE (MELAS) | MYOCLONIC EPILEPSY AND RAGGED RED FIBER DISEASE (MERRF) | PYRUVATE DEHYDROGENASE DEFICIENCY (E1)	2	1	1.0572	14.286	0.80856	1	0.89552	0.07400252
PYRIDOXAMINE	3	1	1.0572	14.286	0.808	1	0.8955	0.07400252

5-PRIME-PHOSPHATE OXIDASE DEFICIENCY					56		2	
PYRUVATE DEHYDROGENASE E3-BINDING PROTEIN DEFICIENCY	3	1	1.0572	14.286	0.80856	1	0.89552	0.07400252
SEPSIS, NEONATAL [DD]	2	1	1.0572	14.286	0.80856	1	0.89552	0.07400252
VALPROATE THERAPY: ANTICONVULASANT HYPERSENSITIVITY SYNDROME VALPROATE ASSOCIATED HEPATOTOXICITY	5	1	1.0572	14.286	0.80856	1	0.89552	0.07400252
ARGININOSUCCINIC ACIDURIA (ASL)	6	4	2.4454	14.286	0.81399	1	0.89552	0.171174577
ORNITHINE TRANSCARBAMYLASE DEFICIENCY (OTC)	10	7	2.2549	14.286	0.81803	1	0.89552	0.157839843
METABOLITES AFFECTED BY EXERCISE	5	2	3.6982	14.286	0.82246	1	0.89552	0.258868823
HYPERORNITHINEMIA WITH GYRATE ATROPHY (HOGA)	4	4	2.2762	14.286	0.82373	1	0.89552	0.159330813
N-ACETYLGLUTAMATE SYNTHETASE DEFICIENCY. NAGS DEFICIENCY	5	3	1.5791	14.286	0.82747	1	0.89552	0.110534789
HYPERPROLINEMIA, TYPE II	2	2	2.1083	14.286	0.82781	1	0.89552	0.147578048
STROKE	5	2	3.4146	14.286	0.83524	1	0.89552	0.23901722
DELTA-PYRROLIDINE-5-CARBOXYLATE SYNTHASE DEFICIENCY	5	3	1.8616	14.286	0.83558	1	0.89552	0.130309394

SCHIZOPHRENIA	26	6	2.8328	14.286	0.83686	1	0.89552	0.198292034
CREATINE DEFICIENCY, GUANIDINOACETATE METHYLTRANSFERASE DEFICIENCY	4	2	0.89635	14.286	0.83928	1	0.89552	0.062743245
HEART FAILURE	10	3	2.3756	14.286	0.84025	1	0.89552	0.166288674
CRITICAL ILLNESS (MAJOR TRAUMA, SEVERE SEPTIC SHOCK, OR CARDIOGENIC SHOCK)	6	4	4.0176	14.286	0.84133	1	0.89552	0.281226375
ACUTE SEIZURES	14	7	3.1178	14.286	0.84197	1	0.89552	0.218241635
DIFFERENT SEIZURE DISORDERS	24	7	3.1178	14.286	0.84197	1	0.89552	0.218241635
HYPERORNITHINEMIA-HYPERAMMONEMIA-HOMOCITRULLINURIA [HHH-SYNDROME]	3	2	1.65	14.286	0.84429	1	0.89552	0.11549769
SHORT BOWEL SYNDROME (UNDER ARGININE-FREE DIET)	4	2	1.65	14.286	0.84429	1	0.89552	0.11549769
NEONATAL INTRAHEPATIC CHOLESTASIS	12	2	1.3567	14.286	0.85472	1	0.89552	0.094967101
PEARSON SYNDROM	3	2	1.2993	14.286	0.85705	1	0.89552	0.090949181
HOMOCYSTINURIA, CYSTATHIONINE BETA-SYNTHASE DEFICIENCY	5	2	1.0733	14.286	0.86381	1	0.89552	0.075129497
REFRACTORY LOCALIZATION-RELATED EPILEPSY	10	4	2.1239	14.286	0.86879	1	0.89552	0.148670027
FUMARIC ACIDURIA	3	2	0.64437	14.286	0.94144	1	0.95666	0.045104998
ARGININEMIA.	5	1	0.05346	14.286	0.956	1	0.9566	0.00374268

HYPERARGININEMIA, ARGINASE DEFICIENCY			8		66		6	5
CIRRHOSIS	23	1	0.053468	14.286	0.95666	1	0.95666	0.003742685
L-ARGININE:GLYCINE AMIDINOTRANSFERASE DEFICIENCY	2	1	0.053468	14.286	0.95666	1	0.95666	0.003742685