LETTER TO THE EDITOR

Nucleotide sugars correlate with leukocyte telomere length as part of a dyskeratosis congenita metabolomic plasma signature

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Table S1. Summary of metabolites distinguishing DC patients from control subjects: relationship to AATL and *TERC* only mutants.

Metabolite	P Value Rank Test[a]	P Value Welch's T test	Chronological Age Link	TERC Mutants only (n =12)[a]
1,2,3 Propane TCA	0.002	0.006		0.01
5-Aminopentanoate	0.02	0.04		0.04
Acetylalanine	0.0002	0.002		0.002
Acetylleucine	0.002	0.0007	Depletion linked to neurodegeneration[1,2]	0.0008
ADMA	0.0007	0.02	Increases with cardiovascular risk [3]	0.34
ADP ribose	0.0001	8.9 x 10-5		0.02
Alanylglycine	3.5 x 10-7	7.8 x 10-7		0.00007
Allantoin	0.0008	0.002	Yes Inhibitor of collagenase[4]	0.0001
Argenine	0.003	0.001	Depletion associated with Alzheimer's Disease[5]	0.04
Ascorbate	0.0008	0.006	Declines with age and associated with frailty. May also be protective against cognitive decline[6]	0.007
Aspartate	0.0009	3 x 10-5	Yes	0.003
Beta Alanine	0.009	0.01		0.04
Beta hydroxyisovaleric acid	0.0045	0.003	Yes muscle deterioration[7]	0.002
Cinnamic Acid	0.03	0.02	Antioxidant protects against skin ageing[8]	0.25
CMP	0.0009	0.01		0.05
Cystine	0.009	0.007	Oxidative defence protects against hippocampus degeneration[9]	0.1
Cytidine	0.01	0.01		0.11
Deoxyuridine	0.005	0.03		0.0005
Glycerate	0.002	0.0007	Yes[10]	0.04
Hydroxykynurenine	0.002	0.0007	Depletion and increase linked to neurodegeneration[11]	0.004

Hydroxylysine	0.0007	0.01	Yes Collagen Degradation[12]	0.004
Hypoxanthine	0.000008	0.04	Yes[10]	0.69
Indoleacetate	0.006	0.003	Yes[10]	0.10
Kynurenine	0.004	0.006	Depletion linked to neurodegeneration Alzheimer's and Parkinson's[11]	0.32
N-acetylalanine	0.0001	0.002	Yes[10]	0.03
N-acetylleucine	0.0003	0.0007	Depletion linked to neurodegeneration[1,2]	0.04
N-acetylisoleucine	0.002	0.002	Yes cognitive function	0.02
N-acetylneuranimate	0.049	0.05	Increase linked to neurodegeneration	0.01
N-Formyl-L-methionine	0.035	0.045		0.05
N-methylglutamate	0.002	0.001		0.004
Phosphoglycerate[c]	0.00002	0.00004	Pentose phosphate pathway	0.0006
Nor-valine	0.01	0.01	Depletion associated with Alzheimer's Disease[13]	0.84
Ophthalmate	0.002	0.005		0.03
Ornithine	<6 x 10-7	1.5 x 10-8	Yes	0.000009
Paraxanthine	0.0002	9 x 10-5	Yes Depletion linked to neurodegeneration[14]	0.008
Quinate	0.03	0.125		1.0
Quinolate	0.000009	6.4 x 10-6	Accumulation linked to neurodegeneration and immunosuppression[15]	0.007
Quinolate Carboxylate	0.01	0.02	Accumulation linked to neurodegeneration and immunosuppression[15]	0.12
S-Adenosyl methionine	0.04	0.03	Yes Enhances ageing Substrate for methylation.	0.001

Sarcosine	<6 x 10-7	1.7 x 10-7	Frailty Sarcopenia[16] Caloric restriction Macroautophagy[17]	0.00004
Trans-4-hydroxyproline	0.02	0.02	Collagen degradation[18]	0.65
Tryptamine	0.02	0.06		0.15
UDP-Glucose[d]	<6 x 10-7	1.7 x 10-7	Frailty, Cognitive Decline[19]	0.00006
Uridine monophosphate	0.006	0.005	Age-related cognitive decline[20]	0.004
Xanthine	0.000006	2.5 x 10-6	Yes[10]	0.0004
Xanthurenate	0.01	0.02	Depletion linked to Alzheimer's Disease and Ageing[21]	0.06

[a] Wilcoxon-Mann-Whitney Test; [c] 2-phosphoglycerate and 3-phosphoglycerate were not resolved by our analytical method; [d] may also contain contributions from UDP-galactose, if present.

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Table S2. The relationship of DC patient metabolites to clinical indicators and the age of control samples.						
Metabolite	WBC[a]	Platelets[a]	Hb[a]	MCV[a]	Patients with skin symptoms[b]	Recent v Old Controls[b]
Alanylglycine	0.85	0.14	0.41	0.75	0.68	0.002+
Allantoin	0.09	0.002	0.06	0.71	0.50	0.67
Beta hydroxyisovaleric acid	0.27	0.003	0.42	0.07	0.20	0.05
Cystathionine	0.66	0.29	0.25	0.62	0.0042	0.81
Deoxyuridine	0.08	0.001	0.68	0.82	0.15	0.50
Hydroxylysine	0.3	0.2	0.51	0.4	0.63	0.04+
Kynurenine	0.28	0.8	0.16	0.94	0.47	0.02
N-acetylalanine+	0.69	0.77	0.42	0.005+	0.44	0.12
N-acetylleucine	0.3	0.02	0.95	0.95	0.58	0.08
N-acetylneuranimate	0.008	0.002	0.45	0.06	0.69	0.72
N-methylglutamate	0.98	0.66	0.88	0.48	0.042	0.86
Ornithine	0.08	0.04	0.06	0.006	0.014	0.10
S-Adenosyl methionine	0.28	0.006	0.3	0.005	0.32	0.99
Sarcosine	0.58	0.95	0.96	0.46	0.67	2.24E-05+
Trans-4-hydroxyproline	0.73	0.95	0.41	0.05	0.0057	0.42
Xanthurenate	0.63	0.42	0.05	0.73	0.74	0.01

[a]Linear regression analysis; [b] Wilcoxon-Mann-Whitney Test; [c] 2-phosphoglycerate and 3-phosphoglycerate not distinguishable by analytical method; [d] potential interferences from UDP-galactose.

+ Going in the opposite direction from DC and therefore indicating the true difference between DC and control subjects may be greater than indicated.