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TRANSLATIONAL METABOLOMICS RESEARCH LABORATORY

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EXPERT/FACULTY REVIEW OF LABORATORY RESULTS

Date/City: *August 11, 2017/Los Angeles, CA, United States of America*

Expert Opinion: *Physiological Metabolic Adaptation to Nutritional Ketosis*

In Reference: *Mr. Matej Toth (matej.toth@gmail.com; +421908762371; www.matejtoth.sk)*

Laboratory data matrices attached with signatures

To Whom it may concern,

Background: Mr. Matej Toth has been consuming a natural low carbohydrate diet since the spring of 2014, while he also maintains a competitive sporting curriculum with regular exercise regimens. This change in the dietary ketone (fat) intake ratio is accompanied by blood chemistry laboratory profile changes, which are the scope of this report. Mr. Toth is requesting an expert review of his laboratory results obtained since 2009 with particular emphasis on the apparent drop in circulating ferritin (InterPro: IPR008331) concentrations as the biological end point of his dieting and exercise protocols. This expert identified below has performed such evaluation with regard of circulating ferritin, blood cell counts and hemoglobin on the basis of decreased carbohydrate and increased ketone intake ratio. This expert found that Mr. Toth's laboratory findings constitute a natural metabolic adaptation to low carbohydrate consumption during competitive exercise routines that are in physiological ranges. The expert identified below herein states that he performed the analyses at the academic consultant recharge basis as a current active member of the University of California faculty. The report does not constitute a conflict of interest at the academic rate as described in UCLA and LABIOMED Conflict of Interest (COI) guidelines that can be obtained directly from the Compliance Office Staff. This report can be used as a Level "C" evidence, based on prominent academic consensus regarding laboratory findings in nutritional ketosis during exercise for sports medicine.

Discussions: Plasma ferritin carries iron in a soluble and non-toxic form in blood. It is a globular protein of 24 subunits forming a nanocage with multiple iron–protein interactions. Although it is the primary intra-mitochondrial and intracellular iron-storage protein in eukaryotes, it also appears in plasma as the iron carrier. Ferritin, i.e. apoferritin conjugated with iron, is an important marker of an individual's iron stores [1]. Iron carrying and storage capacities have profound effects on mitochondrial and cellular substrate oxidation, glucose disposal and overall metabolism as described elsewhere [2,3]. In general, improved mitochondrial metabolism in the presence of low glycogenic substrates, when replaced by ketogenic substrates, also known as low carbohydrate diet, improves tricarboxylic acid cycle flux and turnover, whereby there are less requirements for aconitase (aconitate hydratase; EC 4.2.1.3) activity, less number of circulating erythrocytes, less hemoglobin, less hematocrit values and thus less circulating ferritin and iron stores in an individual. Aconitate hydratase catalyses the stereo-specific isomerization of citrate to isocitrate by cis-aconitate as the intermediary product in the

tricarboxylic acid cycle with an active $[Fe^4S^4]^{2+}$ cluster, which has less requirements for iron when mitochondrial metabolism and turnover are improved during low carbohydrate dieting. Peripheral blood counts with erythroid lineage ontogeny, i.e.: erythrocytes and hemoglobin also decrease during low carbohydrate dieting and excercise.

Low carbohydrate consumption with accompanying ketosis improves mitochondrial substrate oxidation by two basic mechanisms 1) it is the increased proton availability from food due to a higher hydrogen saturation of carbons in ketosis and 2) deuterium depletion to improve proton transfers in mitochondria during low carbohydrate consumptions [4,5].

In the light of improved ATP synthesis with less oxygen equilibriums for each glycogenic acetyl-CoA unit to oxidize completely, which are replaced by highly saturated ketogenic substrates in low carbohydrate diets, there are less iron binding, storing and transporting capacities needed in athletes, as seen in Mr. Toth's blood chemistry profile. A summary of those finding are given in Table 1.

The gradual changes with significantly altered blood plasma chemistry profiles are readily seen in astronauts of the NASA NEEMO22 project (https://twitter.com/hashtag/NASA_NEEMO22) using natural nutritional ketosis to maintain and improve fitness and performance without the use of drugs or supplements.

It is the opinion of the expert identified below that Mr. Toth has naturally adapted to a low carbohydrate diet with exercise, which can be achieved without the use of drugs. The laboratory findings Mr. Toth presented specifically reflect the precise time course of such natural adaptation to low carbohydrate dieting as a physiological course.

Please do not hesitate to contact my office in case there are additional clarifications necessary in the above referenced case.

Sincerely,

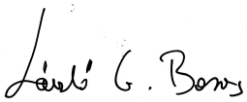

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Table 1. Time course of Mr. Matej Toth's blood profile changes during low carbohydrate dieting with exercise

Výsledky krvi (2017-2009)																
		Apr 13_ 2017	Mar09_ 2017	Jan31_ 2017	Jan16_ 2017	Oct11_ 2016	Aug04_ 2016	May19_ 2016	Mar09_ 2016	Jan26_ 2016	Nov12_ 2015	Aug17_ 2015	Aug13_ 2015	Jul20_2015	Mar16_ 2015	Mar12_ 2015
Erytrocyty (RBC)	erythrocytes	4.94	5.1	4.92	4.69	5.16	5.04	4.77	5.07	4.7	4.96	4.66	4.55	4.65	4.99	4.83
Hemoglobín (HGB)	hemoglobin	142	146	141	136	151	146	138	146	138	143	137	136	137	143	137
Hematokrit (HCT)	hematocrit	0.42	0.43	0.42	0.4	0.43	0.44	0.42	0.44	0.42	0.43	0.41	0.4	0.4	0.43	0.41
Feritín	ferritin		340.2		418.8		533.2		370.1	468.9	635.7		402.4			377.7

Výsledky krvi (2017-2009)																	
	Dec18_ 2014	Jun12_ 2014	Jun02_ 2014	Dec17_ 2013	Feb06_ 2013	Jul26_ 2012	Jun08_ 2012	Mar30_ 2011	Aug23_ 2010	Jul14_ 2010	Apr13_ 2010	Jan29_ 2010	Aug06_ 2009	May14_2009	Apr29_ 2009	Mar30_ 2009	Jan07_ 2009
Erytrocyty (RBC)	5.26	5.17	4.44	5.77	5.49	5.37	5.42	5.72	5.38	5.45	5.45	6.1	5.35	5.41	5.64	5.31	5.76
Hemoglobín (HGB)	150	145	130	165	155	148	152	160	152	152	153	172	154	154	160	152	158
Hematokrit (HCT)	0.44	0.42	0.39	0.46	0.45	0.45	0.44	0.47	0.44	0.45	0.44	0.5	0.45	0.45	0.47	0.45	0.46
Feritín	364.5			514.2			615	507	710	795	640		661				

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References:

1. Theil EC. Ferritin protein nanocages-the story. Nanotechnol Percept. 2012;8(1):7-16.

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