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Understanding the influence of dietary folic acid as a biomarker of Down syndrome with measurement of key regulatory enzymes and metabolites in the methylation pathways of folate synthesis, using a cognitive mouse model Ts65Dn

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Folate is critical for one carbon metabolism and has been implicated in mediation of Down syndrome symptoms. Both younger (<17 years) and older (>35 years) mothers are more prone to the experience of a Down syndrome infant. Red blood cell levels of folate of both mother and infant are low, implicating a dietary effect upon Down syndrome. Inconsistencies within the literature show dietary folate restriction to have preventive effects, whereas excess folate intake demonstrates adverse outcomes. MTHFR (methylenetetrahydrofolate) is a key enzyme in folate metabolism and low dietary intake of folic acid may restrict this enzyme in Down syndrome offspring and their mothers. The effect of dietary folic acid upon four other regulatory enzymes of protein methylation and transulfuration are involved. Ts65Dn mouse model has been successfully used to demonstrate a reversal of the cognitive behaviors of Down syndrome using the Beta2 adrenergic agonist, Formoterol. The Ts65Dn mouse was used to study dietary folic acid intervention and its' effect upon the most likely enzyme of folate metabolism (MTHFR) and cognitive assessments that may have preventive effect on Down syndrome. The hypothesis was measurement of the response of Ts65Dn mice to 3 different dietary intake levels of folic acid, 0,2 and 7 ppm with changes in MTHFR activity and plasma 5-methyl-THF metabolic concentration. MTHFR activity and concentration of 5-methyl-THF assays were completed. The results of both assays demonstrate positive metabolic results from varying the levels of dietary folic acid in the diet consumed by the Down syndrome mouse. Differences between the Ts65Dn model of Down syndrome and control mice were assessed by measurement of MTHFR activity and 5-CH3-THF concentrations in plasma. The study was conducted over a period of 6 months and with a total of 56 male mice provided the following dietary treatments (DS=Down Syndrome; C=Control; F=Folate; N=normal; L-low; H=High); n=9, DSNF; n=8, CNF; n=10 DSLF; n=10 CLF; n=9 DSHF; n=10 CHF. Statistical analysis revealed that the Control and Down syndrome mice were significantly different in terms of growth (p=0.003) and nesting behavior (p=0.000); with the Down syndrome having lower weight gain (M=1.9 g) and nesting behavior (M=2.35) compared to control weight gain (M=6.4 g) and nesting behavior (M=4.40). An analysis of the MTHFR activity has demonstrated no statistical difference between the control and Down syndrome mice in plasma MTHFR activity and yet, the Ts65Dn mice responded to the varying levels of dietary folic acid with changes in MTHFR activity and in plasma concentrations of 5-methyl THF. Dietary folic acid does impact the folate metabolism of the Ts65Dn mouse.

Biography

Susan Edgar Helm has completed her PhD in Physiological Chemistry at Univeristy of California Davis. She is the Director of the undergraduate and graduate Nutritional Science program at Pepperdine Unviersity, a private Liberal Arts Institution in Malibu, CA.

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