High dietary folic acid intake is associated with genomic instability in peripheral lymphocytes of healthy adults.

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**Supplemental Table S1:** Food Survey



**Supplemental Table s2: General participants characteristics.** 

**N**, number of participants; **SD**, standard deviation; **M**, males; **F**, Females. **BMI**: body mass index, **WHR**: waist to hip ratio. p-value refer to comparison between M &F.

**Supplemental Table S3**: Mean systemic markers.

|  |  |  |
| --- | --- | --- |
| Systemic Markers | Mean (SD) | Normal Rang |
| Serum folate (µg/L) a | 14.8 (5.12) | 2 - 20 |
| RBC folate (µg/L) a | 608.32 (168.4) | 140 - 628 |
| Homocysteine (µmol/L) | 21.41 (7.82) | 4 -15 |
| Serum B12 (pg/ml) | 459.5 (186.5) | 200 - 950 |
| MMA (nmol/L) | 125.7 (49.1) | 87 - 318 |
| Plasma B6 (µg/L) | 18.9 (15.4) | 5 - 50 |
| Plasma B2 (µg/L) | 20.21 (23.6) | 4 - 24 |
| HGB (g/dL) | 14.92 (1.81) | **M**: 13.5 -17.5 **F:** 12 - 15.5 |
| HCT (%) | 48.1 (5.7) | **M**: 42 - 54 **F:** 38 - 46 |
| RBC (106/L) | 5.10 (0.6) | **M**: 4.7 - 6.1 **F:** 4.2 - 5.4 |
| WBC (109/L) | 6.26 (1.68) | 4.5 - 11 |
| Neut (%) | 51.6 (10.7) | 45 - 75 |
| Lymph (%) | 36.4 (8.9) | 20 - 40 |
| Mono (%) | 8.1 (2.3) | 2 – 8 |
| MCV (fL) | 94.6 (8.7) | 80 - 96 |
| MCH (pg) | 29.3 (2.1) | 23 - 31 |
| MCHC (g/dL) | 31.1 (1.74) | 32 - 36 |
| RDW-SD (fL) | 46.6 (5.6) | 39 - 46 |
| PLT (103/µl) | 264.3 (63.93) | 150 - 400 |
| MPV (fL) | 11.19 (0.83) | 7 – 11 |

**Supplemental Table S4: Nutrient intake.**

|  |  |  |
| --- | --- | --- |
| *Nutrient Intake* | *Mean (SD)* | *RDA or AI c* |
| Protein (g) | 89.3 (37.2) | 0.8 g/kg/day |
| Choline (mg) | 306.5 (130.5) | M: 550 mg/ day F: 425 mg/day |
| Iron (mg) | 14.9 (6.8) | M: 8 mg/ day F: 18 mg/day |
| Vitamin B1 (mg) | 1.31 (0.54) | M: 1.2 mg/ day F: 1.1 mg/day |
| Vitamin B2 (mg) | 1.22 (0.81) | M: 1.3 mg/ day F: 1.1 mg/day |
| Vitamin B3 (mg)a | 21.2 (10.2) | M: 16 mg/ day F: 14 mg/day |
| Vitamin B6 (mg) | 1.54 (0.92) | M: 1.3 mg/ day F: 1.3 mg/day |
| Vitamin B12 (mcg) | 4.94 (12.2) | M: 2.4 mcg/ day F: 2.4 mcg/day |
| Folate (mcg) | 401.76 (230.9) | M: 400 mcg/ day F: 400 mcg/day |
| Folate (mcg DFE) b | 495.9 (303.8) |

a recommendation is expressed as niacin equivalent (NE)

b recommendation is expressed as dietary folate equivalent (DFE)

C recommendations are expressed as Recommended Dietary allowance (RDA) or Adequate Intake (AI) for group ages (19-50 yr). n=33

**Supplemental Table S5: Proposed comparison structures.**

**Structure 1, serum folate tertiles**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Tertiles (n) | T1(11) | T2(11) | T3(11) | p- value |
| Serum Folate (ng/ml) | 9.3 (1.9) | 14.4 (1.3) | 20.6 (2.8) | < 0.0001 |
| RBC Folate (ng/ml) | 563.5 (144.7) | 571.6 (119.5) | 689.9 (210.9) | 0.14 |
| Homocysteine (µmol/L) | 27.4 (7.2) | 20.0 (6.2) | 16.8 (6.3) | 0.002 |
| Total folate Intake (µg DFE) | 576.0 (339.4) | 626.3 (336.4) | 484.8 (209.4) | ns |
| Folic acid intake (µg DFE) | 204.2 (204.8) | 233.7 (169.1) | 187.1 (89.6) | <0.0001 |
| FAR | 0.31 (0.01) | 0.36 (0.01) | 0.42 (0.02) | ns |

**Structure 2, total folate intake tertiles**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Tertiles (n) | T1(11) | T2(11) | T3(11) | p- value |
| Total folate intake (µg DFE) | 289.8 (73.4) | 490.5 (59.4) | 906.9 (237.9) | < 0.0001 |
| Folic acid intake (µg DFE) | 98.6 (53.6) | 152.2 (39.1) | 374.2 (168.3) | < 0.0001 |
| FAR | 0.36 (0.03) | 0.32 (0.01) | 0.41 (0.01) | ns |
| Serum Folate (ng/ml) | 13.9 (4.4) | 15.4 (4.8) | 15.0 (6.3) | ns |
| RBC Folate (ng/ml) | 637.2 (215.7) | 571.3 (145.1) | 616.5 (143.6) | ns |
| Homocysteine (µmol/L) | 25.5 (7.7) | 19.0 (4.8) | 19.6 (9.2) | 0.09 |

**Structure 3, folic acid intake tertiles**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Tertiles (n) | T1(11) | T2(11) | T3(11) | p- value |
| Folic acid (µg DFE) | 85.6 (35.6) | 155.9 (18.5) | 383.4 (157.8) | <0.0001 |
| Folate (µg DFE) | 362.4 (124.2) | 503.9 (240.9) | 820.7 (298.1) | <0.0001 |
| FAR | 0.24 (0.01) | 0.38 (0.02) | 0.46 (0.01) | 0.003 |
| Serum Folate (ng/ml) | 13.9 (4.5) | 14.5 (5.2) | 15.9 (5.1) | ns |
| RBC Folate (ng/ml) | 583.7 (210) | 605.6 (146.2) | 635.7 (153.9) | ns |
| Homocysteine (µmol/L) | 24.1 (7.1) | 21.4 (8.3) | 18.8 (7.8) | ns |

**Structure 4, folic acid:total folate intake ratio tertiles (FAR).**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Tertiles (n) | T1(11) | T2(11) | T3(11) | p- value |
| FAR | 0.2 (0.06) | 0.35 (0.04) | 0.54 (0.02) | < 0.0001 |
| Folic acid (µg DFE) | 99.1 (51) | 180.7 (92.5) | 345.1 (184.5) | < 0.0001 |
| Folate (µg DFE) | 492.0 (253.9) | 510.2 (240.4) | 684.9 (369.1) | ns |
| Serum Folate (ng/ml) | 13.6 (4.8) | 14.5 (5.2) | 16.2 (5.5) | ns |
| RBC Folate (ng/ml) | 581.7 (205.8) | 625.9 (144.2) | 617.3 (168.4) | ns |
| Homocysteine (µmol/L) | 23.2 (7.0) | 20.5 (7.8) | 20.4 (8.9) | ns |

FAR; folic acid; total folate intake ration, DFE; (dietary folate equivalent), Data presented as mean (± SD), n=33. P values denotes significant difference between tertiles.

**Supplementary Table S6:** Qiagen- RT2 qPCR Primers

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Gene Symbol | Gene name | NM\_Number | Band Size | Reference position | Catalog number |
| MLH1 | mutL homolog 1 | NM\_000249 | 102 | 1822 | PPH00196F-200 |
| ACTB | Beta Actin | NM\_001101 | 174 | 730 | PPH00073G-200 |
| UNG | Uracil-DNA glycosylase | NM\_003362 | 84 | 2068 | PPH01727E-200 |
| MGMT | O-6-methylguanine-DNA methyltransferase | NM\_002412 | 87 | 160 | PPH01519F-200 |
| MTHFR | Methylenetetrahydrofolate reductase (NAD(P)H) | NM\_005957 | 103 | 2107 | PPH00027F-200 |
| MTR | 5-methyltetrahydrofolate-homocysteine methyltransferase | NM\_000254 | 128 | 3883 | PPH10237A-200 |
| HPRT1 | Hypoxanthine phosphoribosyltransferase 1 | NM\_000194 | 57 | 332 | PPH01018C-200 |