# SUPPLEMENTAL MATERIALS

Literature search strategy

I. **Supplemental Table 1**: Search strategy used for the Embase database (1974 – May 03, 2019)

| # | Searches | Results |
|---|---|---|
| 1 | folic acid/ or folic acid deficiency/ or folate metabolism/ or folic acid blood level/ | 58040 |
| 2 | ((folic acid or folate) adj5 (deficien* or enriched or exposure or fortifi* or intake* or metaboli* or restrict* or supplement*)).tw,kw. | 18839 |
| 3 | 1 or 2 [folic acid] | 60884 |
| 4 | diet supplementation/ or dietary supplement/ or diet/ | 286116 |
| 5 | (diet or diets or dietary or nutrition*).tw,kw. | 832232 |
| 6 | 4 or 5 [diet] | 902701 |
| 7 | mouse model/ | 49397 |
| 8 | (((mice or mouse) adj3 model*) or mouse?model*).tw,kw. | 240688 |
| 9 | exp mouse/ or (mice or mouse).tw,kw. | 1887144 |
| 10 | animal experiment/ or animal model/ or controlled study/ or (control or experimental or studies or study).tw. | 15978494 |
| 11 | 9 and 10 | 1523441 |
| 12 | 7 or 8 or 11 [mouse model] | 1549257 |
| 13 | 3 and 6 and 12 [folic acid + diet + mouse model] | 811 |
| 14 | limit 13 to (yr=2009-current and english) | 564 |
| 15 | limit 13 to (yr=2014-current and english) [2014-current] | 278 |
| 16 | 14 not 15 [2009-2013] | 286 |

II. **Supplemental Table 2**: Search strategy used for the Ovid Medliner database (January 1946 – May 03, 2019)

| # | Searches | Results |
|---|---|---|
| 1 | Folic Acid/ or Folic Acid Deficiency/ | 28103 |
| 2 | ((folic acid or folate) and (deficien* or enriched or exposure or fortifi* or intake* or metaboli* or restrict* or supplement*)).tw,kf,hw. | 26935 |
| 3 | 1 or 2 [folic acid] | 38978 |
| 4 | dietary supplements/ or diet/ | 193527 |
| 5 | (diet or diets or dietary or nutrition*).tw,kf. | 665083 |
| 6 | 4 or 5 [diet] | 723740 |
| 7 | (((mice or mouse) adj6 model*) or mouse?model*).tw,kf. | 182795 |
| 8 | exp mice/ or (mice or mouse).tw,kf. | 1667354 |
| 9 | exp animal experimentation/ or exp Models, Animal/ or Control Groups/ or (control or experimental or studies or study).tw. | 10711182 |
| 10 | 8 and 9 | 916438 |
| 11 | 7 or 10 [mouse model] | 957195 |
| 12 | 3 and 6 and 11 [folic acid + diet + mouse model] | 514 |
| 13 | limit 12 to (yr=2009-current and english) | 316 |
| 14 | limit 12 to (yr=2014-current and english) [2014-current] | 164 |
| 15 | 13 not 14 [2009-2013] | 152 |

III. **Supplemental Table 3**: Search strategy used for the Food Science and Technology Abstracts (FSTA) database (January 1969 – May 03, 2019)

| # | Searches | Results |
|---|---|---|
| 1 | Folic Acid/ or exp Folates/ or Folate Deficiency/ | 2794 |
| 2 | ((folic acid or folate) and (deficien* or enriched or exposure or fortifi* or intake* or metaboli* or restrict* or supplement*)).ti,ab,hw. | 4068 |
| 3 | 1 or 2 [folic acid] | 4817 |
| 4 | food supplements/ or diet/ | 41464 |
| 5 | (diet or diets or dietary or nutrition*).mp. | 198897 |
| 6 | 4 or 5 [diet] | 201480 |
| 7 | (((mice or mouse) adj6 model*) or mouse?model*).ti,ab,hw. | 4150 |
| 8 | (mice or mouse).ti,ab,hw. | 23346 |
| 9 | animal models/ or (control or experimental or studies or study).ti,ab. | 508085 |
| 10 | 8 and 9 | 20030 |
| 11 | 7 or 10 [mouse model] | 20275 |
| 12 | 3 and 6 and 11 [folic acid + diet + mouse model] | 121 |
| 13 | limit 12 to (yr=2009-current and english) | 108 |
| 14 | limit 12 to (yr=2014-current and english) [2014-current] | 65 |
| 15 | 13 not 14 [2009-2013] | 43 |

IV. **Supplemental Table 4**: Search strategy used for the Global Health (1973 – April 24, 2019) and the International Pharmaceutical Abstracts (1970 – April 2019) database.

| # | Searches | Results |
|---|---|---|
| 1 | Folic Acid/ or Folic Acid Deficiency/ | 14591 |
| 2 | ((folic acid or folate) adj5 (deficien* or enriched or exposure or fortifi* or intake* or metaboli* or restrict* or supplement*)).ti,ab. | 8413 |
| 3 | 1 or 2 [folic acid] | 15806 |
| 4 | food supplements/ | 25638 |
| 5 | (diet or diets or dietary or nutrition*).ti,ab,hw. | 458619 |
| 6 | 4 or 5 [diet] | 466279 |
| 7 | (((mice or mouse) adj3 model*) or mouse?model*).ti,ab. | 22712 |
| 8 | exp mice/ or (mice or mouse).ti,ab. | 182291 |
| 9 | Animal Models/ or (control or experimental or studies or study).ti,ab. | 2039976 |
| 10 | 8 and 9 | 132861 |
| 11 | 7 or 10 [mouse model] | 135764 |
| 12 | 3 and 6 and 11 [folic acid + diet + mouse model] | 293 |
| 13 | limit 12 to (yr=2009-current and english) | 199 |
| 14 | limit 12 to (yr=2014-current and english) [2014-current] | 98 |
| 15 | 13 not 14 [2009-2013] | 101 |
| 16 | remove duplicates from 14 | 98 |
| 17 | remove duplicates from 15 | 101 |

Mouse strains and substrains

I. **Supplemental Table 5**: Mouse strains and substrains identified in the studies.

| Strains | Substrains | Substrain frequency | Total Frequency |
|---|---|---|---|
| **Unreported** | | | 2 |
| **BALB/C** | | | 48 |
| **C57BL/6** | | | 184 |
| **C3H** | | | 11 |
| **CD1** | | | 14 |
| **SWISS** | | 6 | 8 |
| | Swiss Webster | 1 | |
| | Swiss albino | 1 | |
| **AJ** | | | 7 |
| **129** | | 11 | 22 |
| | 129S2/SvHsd | 1 | |
| | 129S1/SvlmJ | 6 | |
| | 129P2/OlaHsd | 4 | |
| **CAST/EIJ** | | | 3 |
| **FVB** | | | 5 |
| **PWK/PHJ** | | | 3 |
| **WSB/EIJ** | | | 6 |
| **Big Blue** | | | 3 |
| **CBA** | | | 3 |
| **Intercrossed outbred** | | | 1 |
| **Intercrossed Inbred** | | | 7 |
| | Swiss-Webster/129/SvJae/C57BL/6 | 1 | |
| | 129S6/SvEv x C57BL/6J | 3 | |
| | 129Sv x C57BL/6J | 2 | |
| | B6SJF1/J | 1 | |
| **634Mui/J** | | | 1 |
| **Athymic nu/nu** | | | 2 |
| **Beige Nude XID** | | | 1 |
| **SCID** | | | 2 |
| | CB-17/ICR SCID | 1 | |
| | NOD/SCID | 1 | |
| **Kumming** | | | 5 |
| **Mutamouse** | | | 1 |
| **SJL** | | | 1 |
| **SMV** | | | 2 |
| **SWV** | | | 1 |
| **DBA** | | | 2 |
| | DBA/6J | 1 | |
| | DBA/2J | 1 | |
| **Tg** | | | 5 |
| | Ts65Dn | 1 | |
| | TgCRND8 | 2 | |
| | Tg2576 | 1 | |
| | 3xTg | 1 | |
| **LPT/LeJ** | | | 1 |
| **LM/BC** | | | 3 |
| **NIH** | | | 2 |
| **Curly Tail** | | | 1 |
| **CF1** | | | 1 |
| **ICR** | | | 3 |

Reporting Dietary Interventions

I. **Supplementary Table 6:** Nutrition-specific Essential 6 checklist of details that should be included when reporting nutrition research that utilizes animal models.

| CONCEPT | | RECOMMENDATIONS | Section/line or reason for not reporting |
|---|---|---|---|
| **Rationale for Use** | 1 | Have you provided a rationale for the relevance of the animal model used to the:<br>a. Health outcome being investigated<br>b. Food substance under investigation | |
| **Health Outcomes** | 2 | a. Have you provided a rationale for investigating the relation between the food substance of interest and the health outcome?<br>b. Have you outlined your primary core outcomes and/or secondary core outcomes under investigation?<br>c. Did you utilize and report the use of a verified biomarkers of health status to certify experimental dietary intake-heath outcome investigation?<br>d. Have you provided a rationale for investigating non-oral interventions and explained how it affects the interpretation of results?<br>e. Did you provide comment on the choice of tissues analyzed for health outcome? | |
| **Base Diet** | 3 | a. Use an open-formula diet to minimize experimental variability and improve precision and reproducibility. If a closed-formula diet was utilized, did you provide details of formulation (i.e., complete ingredient list and their relative concentrations), manufacturer and catalogue number and lot numbers in the publication?<br>b. Have you verified the food substance of interest concentrations in the diet itself and/or through a validated biomarker of exposure in the animals?<br>c. Have you provided details on method used to verify nutritional composition of diet? | |
| **Intervention Dose** | 4 | a. Have you given full details on the concentration of dose used in the intervention, including that of the comparison diet (control) and explain whether or not nutritional components was modified in the base diet or administered differently?<br>b. Have you reported the total exposure (base diet plus added amount, if applicable)?<br>c. Did you track and report food consumption (and body weight) during the intervention to certify exposure?<br>d. Have you provided a rationale for the doses used and relevance to adequate intakes (when established for an essential nutrient) or usual intakes for other food substances? | |
| **Duration of Exposure** | 5 | Have you provided a brief description to justify chosen duration of dietary intervention, including how it relates to the development of the outcome being measured? | |
| **Cofounding variables** | 6 | a. Have you commented on randomizations, blinding, statistical methods and actions to reduce bias?<br>b. Have you commented on environmental factors that may influence dietary intake and act as confounding factors? | |