Data Article

Fecal metabolomic dataset of American ginseng-treated DSS mice: Correlation between ginseng enteric inflammation inhibition and its biological signatures

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ABSTRACT

Although anti-inflammatory effects of American ginseng metabolites have been investigated at systemic and cellular levels, the biological signatures of ginseng microbial metabolite-induced bioactivities are still unknown. To fill this knowledge gap and to support the findings published in the companion research article entitled “American ginseng microbial metabolites attenuated DSS-induced colitis and abdominal pain” (Wang et al., 2018), we are here to provide datasets of enteric microbiome biotransformation and fecal metabolomics. For the microbiome biotransformation study, data were obtained from C57BL6 mice treated with a broad-spectrum antibiotic metronidazole. After oral administration of ginseng extract, we observed that compound K (CK) was undetectable in metronidazole-treated mouse stools but was detected in stools from vehicle-treated mice, suggesting biotransformation of CK is gut microbial dependent. In the fecal metabolomic study, three small molecules which were associated with gut inflammation were identified. In the DSS mice, the levels of lactate, linoleic acid, and malic acid increased significantly in the model group. After ginseng treatment, the expressions of these metabolites...
reduced significantly. Thus, the selective fecal endogenous metabolites could be used as biological signatures reflecting severity of enteric inflammation and ginseng treatment outcomes. Our results showed the enteric microbiome plays a key role for CK conversion, and the effects of CK on enteric inflammation can be demonstrated by the metabolomics data.

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Specifications table

| Subject area                  | Gastrointestinal inflammation |
|-------------------------------|--------------------------------|
| More specific subject area    | Colitis, gut inflammation, intestinal microbiome, biological signature |
| Type of data                  | Figures                       |
| How data was acquired         | LC/TOF-MS and GC/TOF-MS        |
| Data format                   | Analyzed                      |
| Experimental factors          | Ginsenoside compound K was determined in mouse fecal samples with or without metronidazole treatment. Fecal metabolomic profiles of DSS mice and ginseng treated DSS mice were investigated. |
| Experimental features         | Metabolomic fecal profiling from DSS model group and ginseng treated group |
| Data source location          | Data was collected at University of Chicago, Chicago, IL, USA |
| Data accessibility            | Data is provided within this article |
| Related research article      | C.Z. Wang, H. Yao, C.F. Zhang, L. Chen, J.Y. Wan, W.H. Huang, et al., American ginseng microbial metabolites attenuate DSS-induced colitis and abdominal pain, Int. Immunopharmacol. 64 (2018) 246–251. [1] (DOI:10.1016/j.intimp.2018.09.005) |

Value of the data

- Broad-spectrum antibiotics-treated mouse is a reliable model for initial ginseng biotransformation observation.
- Enteric microbiome induced compound K possesses different biological activities from its parent compound.
- Fecal endogenous metabolites can be used as biological signatures reflecting enteric inflammation.
- Gut disease severity and treatment outcome can be quantified by metabolomics analysis.

1. Data

1.1. In vivo verification of the requirement of enteric microbiome in ginsenoside compound K (CK) biotransformation

As shown in Fig. 1A, the major ginsenosides in American ginseng extract are Rb1, Rc, Rd, Re, and Rg1, and Rb1 is the primary constituent [2]. After oral ingestion, CK was detected in stools from vehicle control mice, which have normal gut microbiota. In contrast, for the mice pretreated with a broad-spectrum antibiotic metronidazole, CK was not detected in stools (Fig. 1B). Our data suggests that enteric microbiome is required for the biotransformation of CK (Fig. 1C) [3,4].
1.2. Metabolomic profiling for biological signatures of ginseng effects on gut inflammation

Using the criteria of VIP > 1 and P-value < 0.05, three fecal endogenous metabolites, lactate, linoleic acid, and malic acid, had different expressions in the model and control groups. The metabolite levels were significantly higher in the model group. After ginseng intervention, the levels of...
these three metabolites decreased significantly ($P < 0.05$ or $P < 0.01$) (Fig. 2). Previous studies have shown that lactate is found in greater abundance in patients with active IBD [5,6]. Linoleic acid is essential for the synthesis of prostaglandins and their breakdown product PGE2 [7], which is considered as a marker of bowel inflammation [7,8]. In addition, the malic acid level in plasma and colon tissue significantly increased in DSS mice [9,10]. Therefore, these three inflammation-related metabolites could be used as biological signatures reflecting gut inflammatory severity and ginseng treatment outcomes.

2. Experimental design, materials, and methods

2.1. Chemicals and regents

Ginsenosides Rb1, Rc, Rd, Re, Rg1, and CK were obtained from the Delta Information Center for Natural Organic Compounds (Xuancheng, AH, China). Solvents and other chemical and biological regents were obtained from Fisher Scientific (Pittsburgh, PA, USA) or Sigma-Aldrich (St. Louis, MO, USA).

2.2. Plant materials, extract preparation and analysis

The root of American ginseng (Panax quinquefolius L.) was collected from Roland Ginseng, LLC (Wausau, WI, USA). The extraction and LC/MS analysis of American ginseng was carried out as described by Yao et al. [2].

2.3. Microbiome biotransformation of American ginseng extract

This experiment employed 6–8 week-old male C57BL6 mice from Jackson Laboratories (Bar Harbor, ME, USA). All mice received sterile chow diets. Mice were given either un-supplemented drinking water or drinking water supplemented with metronidazole (600 μg/ml) for 7 days ($n = 3$ per group). Mice then received American ginseng extract in drinking water (30 mg/kg/day) for 3 days. Then mouse stool samples were collected for ginseng metabolite analysis.

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Fig. 2. Metabolomic analysis of stool samples in weeks 4 and 8. Three metabolites responsible for the differential expression between the model and control groups were identified. Ginseng treatment restored the expressions of these metabolites. Ordinate values are peak area ratios, that is, relative concentrations (peak area of each groups/peak area of control group) of each metabolite. """"$P < 0.01$ compared with the control group; **$P < 0.05$ and """"$P < 0.01$ compared with the model group.
Stool samples were extracted using methanol. HPLC/TOF-MS analysis was carried out as described [11]. Extracted ion chromatograms with a 0.01 Da mass window in negative mode (m/z 667.44–667.45) was used for CK detection.

2.4. Fecal metabolomic analysis

Male C57BL6 mice (6–8 week-old) were separated into three groups (n = 5 per group): control, DSS model, and DSS + ginseng groups. The animals in the DSS and DSS + ginseng groups received 2.5% DSS in drinking water for 7 consecutive days [12,13]. The animals in DSS + ginseng group also consecutively received American ginseng extract in drinking water (30 mg/kg/day) from one week before DSS treatment to 70 days. Stool samples were collected at day 28 (week 4) and day 56 (week 8).

Stool samples were extracted using water and methanol with homogenization [12,14]. Before analysis, a two-step derivation process was conducted using methoxyamine and BSTFA containing 1% TMCS. GC/TOF-MS analysis and data treatment was carried out as described [12,15]. The corresponding fold change was calculated, the most changed small molecules were identified and the results were compared to the control.

2.5. Statistical analysis

Data were expressed as mean ± S.D. A student’s t-test and a one-way ANOVA were used to test the significance of the differences between ginseng treatment and model groups. The statistical significance was set at P < 0.05.

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Transparency document. Supporting information

Transparency data associated with this article can be found in the online version at https://doi.org/10.1016/j.dib.2018.10.131.

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