

**LEMBAR**  
**HASIL PENILAIAN SEJAWAT SEBIDANG ATAU PEER REVIEW**  
**KARYA ILMIAH : JURNAL ILMIAH**

Judul Artikel Ilmiah : The Efficacy of Education with the WHO Dengue Algorithm on Correct Diagnosing and Triaging of

Penulis Artikel Ilmiah : Patrick PYT PAUWELS, Job FM METSEMAKERS, Ari Budi HIMAWAN, Tri Nur KRISTINA

Status Pengusul : Penulis pertama/ **penulis anggota/ penulis korespondensi**

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Prof. Dr. Drg. Oedijani, MS  
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Judul Artikel Ilmiah : The Efficacy of Education with the WHO Dengue Algorithm on Correct Diagnosing and Triaging of Dengue-Suspected Patients; Study in Public Health Center.

Penulis Artikel Ilmiah : Patrick PYT PAUWELS, Job FM METSEMAKERS, Ari Budi HIMAWAN, Tri Nur KRISTINA Tri Nur KRISTINA2

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Reviewer 2

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## Autism phenotype in fragile X premutation males is not associated with *FMR1* expression: a preliminary evaluation

Tanjung Ayu SUMEKAR<sup>1,2</sup>, Tri Indah WINARNI<sup>1,2</sup>, Yi MU<sup>3</sup>, Weerasak CHONCHAIYA<sup>1,4</sup>, Flora TASSONE<sup>1,5</sup>, Christine IWAHASHI<sup>5</sup>, Katherine CHEUNG<sup>5</sup>, Sultana MH FARADZ<sup>2</sup>, Paul J HAGERMAN<sup>1,5</sup>, Danh V NGUYEN<sup>6,7</sup>, Randi J HAGERMAN<sup>1,8</sup>

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### ABSTRACT

To explore the association between autism phenotype and *FMR1* protein (FMRP), *FMR1* mRNA and CGG repeat length in 31 male *FMR1* premutation carriers aged 3.0 to 27.9 years old (mean 13.0 ± SD 6.5) using the ADOS communication, social interactive and total scores. FMRP levels were determined using the sandwich Enzyme-linked Immunosorbent Assay (ELISA) method, *FMR1* mRNA expression levels were measured by qRT-PCR, and CGG repeat size was determined using Southern blot and PCR analyses. There was no significant difference in FMRP, CGG repeat length, and *FMR1* mRNA between fifteen subjects without (ASD / PDDNOS / autism and sixteen subjects with ASD / PDDNOS / autism. ADOS scores were not significantly associated with either FMRP or *FMR1* mRNA, This preliminary evaluation found that autism phenotype is not associated with the level of expression of either *FMR1* mRNA or FMRP. However, CGG was significantly negative associated with both ADOS communication score ( $p=0.0173$ ) and ADOS total score ( $p=0.0358$ ).

Key-words: Autism, CGG, *FMR1* mRNA, FMRP, Fragile-X Premutation

The expansion of the CGG repeat in the premutation range (55-200 CGG repeats) of the fragile X mental retardation 1 gene (*FMR1*) can lead to a range of clinical involvement, including psychological problems<sup>1,2</sup>; fragile X-associated primary ovarian insufficiency (FXPOI)<sup>3,4</sup>; immune-mediated disorders<sup>5,6</sup>; hypertension<sup>7</sup>; fragile X-associated tremor/ataxia syndrome (FXTAS)<sup>8-10</sup> and neurodevelopmental disorders, such as autism spectrum disorders (ASD) and attention deficit hyperactivity disorder (ADHD)<sup>11,12</sup>. Some of behaviours associated with autism such as avoidance of eye gaze, hand flapping, repetitive behaviours, and speech perseverations have been reported in more than 60% of all individuals with fragile X syndrome (FXS)<sup>13-15</sup>.

A lack or deficiency of the *FMR1* protein (FMRP) in individuals with the full mutation (>200 CGG repeats) leads to the clinical features of FXS<sup>16</sup>. However, FMRP may be also mildly

deficient in some individuals with the premutation, particularly those with CGG repeats in the upper premutation range as well as the premutation CGG Knock-In (CGG KI) mouse model<sup>17-20</sup>. In addition, elevated level of *FMR1* mRNA, which rises with increased CGG-repeat number, is the most consistent molecular abnormality observed in both human and mouse premutations<sup>20-23</sup>. Elevated mRNA also leads to central nervous system (CNS) toxicity and neurological disease, such as FXTAS and psychopathology in older carriers<sup>1,2,24</sup>.

Although most individuals with the premutation are unaffected by intellectual disability, a subgroup of children experience ASD, ADHD, anxiety, seizures, and learning difficulties or intellectual disability<sup>12,13,25-29</sup>. The prevalence of ASD in boys with the premutation whose parents sought medical attention for their sons' behaviour problems in the clinic (probands) is

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## Effects of Different Types of Dietary Fibers on Fermentation by Intestinal Flora

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Kenichiro UEMURA, Yoshiaki MURAKAMI, and Taijiro SUEDA

*Department of Surgery, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Japan*

### ABSTRACT

**Purpose:** A treatment for chronic constipation is dietary fiber intake. This study aimed to determine the effects of different types of dietary fibers on the microbiota in the large intestine.

**Methods:** Nine healthy volunteers participated in this study. Breath hydrogen test was used to determine the dietary fiber fermentations. The presence of hydrogen in the breath indicates intestinal bacterial activities. Participants fasted overnight and ate white bread (200 g) with 10 g of each type of dietary fiber: (1) cellulose, (2) soy fiber, (3) guar gum, and (4) control (without any dietary fiber). Samples were collected before and every 1 hour after eating, for 8 h. Another test compared the effects between cellulose and guar gum with a loaded food, which activates intestinal fermentation, and samples were collected using the same methods.

**Results:** During 8 h of measurements, breath hydrogen concentration in the soy fiber group were higher than that of the control, but were not significantly different. Changes in the guar gum group were similar to those in the control. However, breath hydrogen concentrations in the cellulose group did not increase even after eating white bread that caused large intestinal fermentation  $2.9 \pm 0.7$  ppm, which was significantly lower than that of the guar gum group ( $7.4 \pm 1.7$  ppm,  $p < 0.01$ ). In the study with a well-fermented food intake, cellulose reduced breath hydrogen concentrations, but its difference with that of the guar gum group was statistically non-significant.

**Conclusion:** Cellulose might have a suppressive effect on large intestinal fermentation. Therefore, this compound may be beneficial in treating chronic constipation.

**Key words:** *intestinal flora, dietary fiber, breath hydrogen, fermentation*

Microorganisms in the lower gut ferment dietary fibers and produce hydrogen, methane, and carbon dioxide gases. Some portion of these gases enters the blood stream and is excreted via the lungs<sup>15,16,22</sup>. The hydrogen breath test, which is based on the premise that hydrogen gas in humans is produced exclusively by colonic fermentation, uses expired hydrogen levels as indirect indicators of disturbances in the intestinal flora<sup>12,15,17</sup>. The test is widely used to detect a battery of non-structural gastrointestinal disorders, particularly carbohydrate malabsorption, small intestinal bacterial overgrowth, and irritable bowel syndrome. The breath test is also used in food metabolism studies and various indicators of intestinal flora<sup>1–4,13,18,19,23,25–29</sup>.

Dietary fiber is one of the most important tools for the treatment of constipation, as it increases the volume of feces and adds water<sup>7,14</sup>. However, some of the fibers cause excessive fermentation in the intestines, which may lead to diarrhea or gas production<sup>20</sup>. Determining the good dietary fiber with less fermented substrate for the treatment of constipation is difficult. Therefore, this

study aimed to compare different types of dietary fibers and determine suitable treatment measures to resolve constipation.

### PATIENTS AND METHODS

#### Basal analysis: fasting breath hydrogen data on healthy Japanese subjects

A total of 35 healthy volunteers (21 men and 15 women, aged 21–65 years) fasted after their usual dinner until the following morning (~0800) when hydrogen breath tests were conducted at Hiroshima University School of Medicine. End-alveolar breath samples were obtained by having the subjects exhale end-expiratory samples into 500-ml plastic bags fitted with stopcocks. Samples were analyzed for hydrogen concentration with a HCMA-T1™ Gas Chromatograph (Abilit Corporation, Osaka, Japan). Data were presented as normalized breath-hydrogen concentrations in parts per million (ppm).

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