Press Release

Keio University

NCGM

September 18, 2019
Keio University
National Center for Global Health and Medicine

Discovery of a Novel Link between Food Intake and Mucosal Immune Response —Dietary Factors Are Necessary for Mucosal Immune Homeostasis—

A joint team from Keio University and the National Center for Global Health and Medicine (NCGM) has uncovered a novel link between nutritional signals and immune cell dynamics and functionality, according to research published in *Cell*. The discovery could help develop treatment courses that enhance vaccine efficacy via dietary intervention.

1. Main Points of Research

- Fasting drastically reduces lymphocyte levels in Peyer's patches.
- Naive B cells migrate to the bone marrow during fasting and then back to the Peyer's patches upon refeeding.
- Nutritional signals are essential to maintain CXCL13 expression by stromal cells.
- Fasting causes the death of matured B cells and attenuates antigen-specific IgA response.

2. Background of Research

Inappropriate calorie intake is a global health problem. In developing countries, nutritional deficiency often compromises vaccination efficacy and increases the risk of infectious diseases. On the other hand, excessive food intake accompanied by a lack of exercise has augmented the incidence of obesity in industrialized countries, which is a significant risk factor for cardiovascular disease, metabolic syndrome, and autoimmune disorders. These observations indicate that nutritional status potentially influences immune responses; however, how nutritional signals regulate cellular dynamics and functionality remains unclear.

3. Content of Research and Results

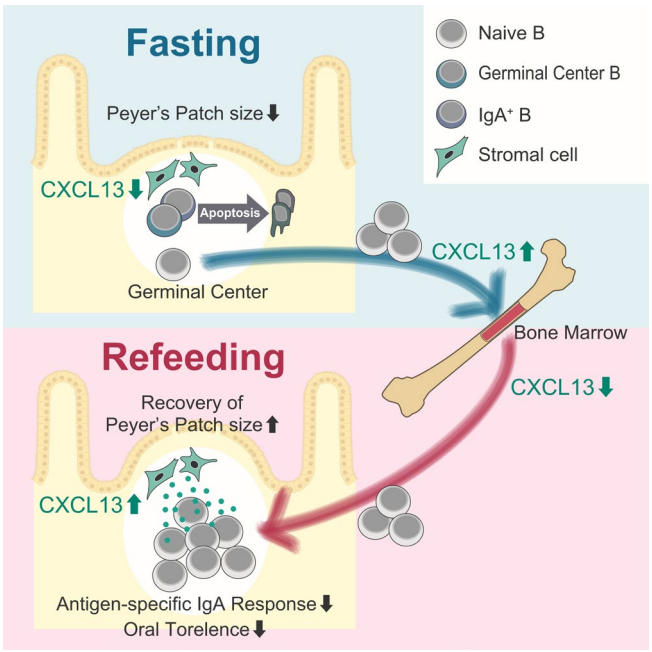
In the current study, a group led by Motoyoshi Nagai, Taeko Dohi, and Koji Hase of Keio University, and Yuki I. Kawamura of NCGM found that temporary fasting drastically reduces the number of lymphocytes by approximately 50% in Peyer's patches (PPs), the inductive sites of gut immune responses. Subsequent refeeding seemingly restored the number of lymphocytes, but their cellular composition was conspicuously altered.

A large portion of matured B cells, including germinal center and IgA^+ B cells, were lost via apoptosis during fasting. Meanwhile, naive B cells migrated from PPs to the bone marrow during fasting and then back to PPs during refeeding when stromal cells sensed nutritional signals and upregulated CXCL13 expression to recruit naive B cells.

Furthermore, the team found that temporal fasting before oral immunization with ovalbumin abolished the induction of antigen-specific IgA. This result indicates that nutritional deprivation impairs mucosal immunity and causes low efficacy of oral vaccines, especially in developing countries.

4. Future Developments

"Our study uncovered a novel link between nutritional signals and immune cell dynamics and functionality; however, further studies should be conducted to completely understand the underlying molecular mechanisms," says Motoyoshi Nagai. "We hope that our study may one day help develop treatment courses for enhancing vaccine efficacy via dietary intervention," Koji Hase added.



5. Funding Information
This work was supported by AMED-Crest, the Japan Society for the Promotion of Science, and other organizations.

6. Details of Journal Article
Nagai M. *et al.,* Fasting-refeeding impacts immune cell dynamics and mucosal immune responses. *Cell*, August 22, 2019
DOI: 10.1016/j.cell.2019.07.047

*Please direct any requests or inquires to the contact information provided below.

【Inquiries about research】
Keio University Faculty of Pharmacy, Department of Biochemistry,
Professor Koji Hase
TEL: +81- (0)3- 5400- 2654 FAX: +81-(0)3- 5400- 2484 E-mail: hase-kj@pha.keio.ac.jp
http://square.umin.ac.jp/keio-dbc/

Yuki I. Kawamura
Chief, Section of Gastrointestinal Pathophysiology
Department of Gastroenterology
The Research Center for Hepatitis and Immunology
Research Institute
Tel: +81-(0)47-375-4754 FAX: +81-(0)47-375-4766
E-mail: kawamura@hospk.ncgm.go.jp

【Inquiries about press release】
Keio University Office of Communications and Public Relations (Ms.Kurihara)
TEL:+81-(0)3-5427-1541 Fax: +81-(0)3-5441-7640 Email: m-pr@adst.keio.ac.jp
https://www.keio.ac.jp/

Office of Public Relations
Bureau of Strategic Planning
National Center for Global Health and Medicine
TEL: +81-(0)3-5273-5258 Fax: +81-(0)3-5273-5254
E-mail: press@hosp.ncgm.go.jp