

(別紙) 研究成果の概要 (英文)

Title of research project	Development of a new dose-response model based on survival characteristics of <i>Campylobacter</i> during food digestion process
Research project number	1802
Research period	FY 2018 – FY2019
Name of principal research investigator (PI)	Shigenobu Koseki

Abstract/Summary

The objective of this study was to develop a dose-response model that expresses the relationship between the ingestion amount of a pathogenic bacteria and the probability of infection of *Campylobacter* spp. Although the conventional dose-response model of food-borne pathogenic bacteria has been mathematically expressed by associating the cause (amount of ingested bacteria) and the result (probability of infection), in reality, there are some key bioreaction fields in the human body (gastric acid, invasion of epithelial cells, etc.) from ingestion of contaminated food to the establishment of infection in the intestinal tract. In this study, we aimed to break away from the conventional dose-response model in which the reaction process was unknown, estimate the survival / death probability at each key reaction site, and predict the infection probability at low doses. Then, we have developed a mathematical model that predicts the probability of infection. In concrete, this study examined the following four processes. First of all, we examined the probability of survival / death of *Campylobacter* during gastric digestion. Survival characteristics of *Campylobacter* in the stomach, which is the first barrier of food digestion process, are clarified from the survival behavior when exposed with various chicken dishes in artificial gastric juice, and a prediction model that enables estimation of survival probability was developed. Second, we investigated the survival/death in a competitive environment with intestinal flora in the small intestinal digestive process. The survival probability of *Campylobacter* that passed through the digestive process in the stomach under the condition of competing with the intestinal bacterial flora in the small intestine, which is the second barrier of the digestive process, was clarified. And then, we evaluated the probability of colonization and invasion of small intestinal epithelial cells. The invasion probability to the intestinal epithelial cells, which is the final process of establishment of *Campylobacter* infection, was clarified by using a cultured cell line using Caco-2 cells, and the invasion probability could be estimated. Finally, we developed a dose-response model that integrates the results of each Key Event mentioned above. A new dose-response model that can consider the amount of bacteria ingested, the type of food eaten, and the amount of food intake was developed by integrating the predictive probabilities for each of the above three levels of Key Event. Moreover, it was clarified that the developed model is valid by comparison with the conventional proposal model.

※次のただし書（Disclaimer）を枠で囲って記載すること。

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1. List of papers published on the basis of this research

Hiura, S., Abe, H., Koyama, K., and Koseki, S. Transforming kinetic model into a stochastic inactivation model: Statistical evaluation of stochastic inactivation of individual cells in a bacterial population. *Food Microbiology*, 91, 103508, 2020.

2. List of presentations based on this research

- 1) 武岡晃平, 小山健斗, 安部大樹, 川村周三, 小関成樹. 人工胃液中におけるカンピロバクターの生残特性の解明と数理モデル化, 日本食品科学工学会北海道支部大会, 2018年12月2日, 札幌市(藤女子大学)
- 2) Kohei Takeoka, Hiroki Abe, Kento Koyama and Shige Koseki. Modeling the Survival Kinetics of *Campylobacter jejuni* in Simulated Gastric Fluid. IAFP 2019 Annual meeting, 21-24 July 2019, Louisville, Kentucky, USA.
- 3) Satoko Hiura, Kento Koyama, Hiroki Abe, Shige Koseki. Stochastic evaluation for survival bacterial numbers and the time-to-inactivation by using Weibull modelling and Monte Carlo simulation. 11th International Conference on Predictive Modelling in Food, 17-20 September 2019, Braganza, Portugal.

3. The number and summary of patents and patent applications

None

4. Others (awards, press releases, software and database construction)

Young Researcher Best Oral Presentation for Satoko Hiura in 11th International Conference on Predictive Modelling in Food, 17-20 September 2019, Braganza, Portugal.