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29 SEPTEMBER – 27 NOVEMBER 2015

## IMMUNOBIOTIC STUDIES TO ADVANCED ANALYSIS OF IMMUNOBIOTIC MUCOSAL IMMUNOREGULATION

### 1) ACTIVITIES WITH MY HOST RESEARCHER

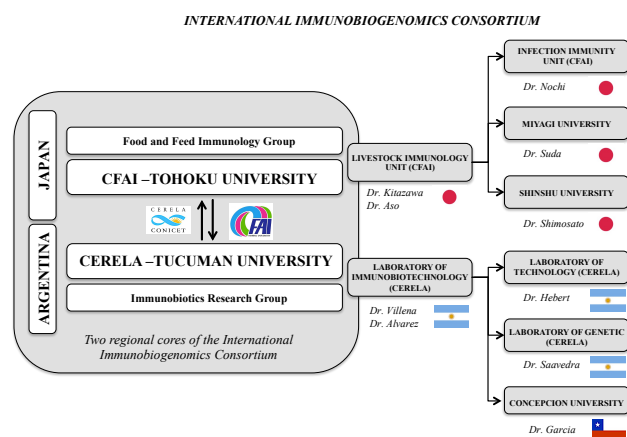
The principal activity of my visit to Japan using the JSPS Invitation Fellowships for Overseas Researchers was to analyze results, define general and specific objectives, set priorities, allocate tasks and strengthen the research collaboration between the Laboratory of Immunobiotechnology (CERELA) and the Food and Feed Immunology Group (Tohoku University).

The visit was undoubtedly of great importance to strengthening cooperation activities already underway between the groups of Argentina and Japan, and to start new tasks in collaboration. The opportunity to have several meetings with my host researcher Dr. Kitazawa and his research group allowed us:

- The completion of the project “**Non-viable lactic acid bacteria and their cellular fractions as alternatives for the development of immunoregulatory products for the prevention of respiratory infections in immunocompromised hosts**” (*Project 1*), through the writing of a final report and the discussion and organization of the related publications, that are now in preparation.

- The advance in the project “**Prevention of respiratory superinfections using immunomodulatory cellular fractions from immunobiotic lactic acid bacteria. Role of pattern recognition receptors and signaling pathways**” (*Project 2*), through the fixing of new goals and forward steps.

- The initiation of a new project in collaboration “**Immunobiogenomics: genomics-based studies to provide insights into how immunobiotic bacteria stimulate the mucosal immune system**” (*Project 3*). Bioinformatics and functional genomics of probiotic bacteria is an exiting new field. We have entered into a new era of research for probiotic bacteria, characterized by a complete genetic characterization. The genomics applied to probiotic bacteria, which is often called probiogenomics, have provided access to the complete genetic make-up of probiotic bacteria. We believe that the detailed comparative studies of probiotic bacteria with immunomodulatory activities (**immunobiotics**) can give us important information regarding the molecules and receptors involved in the stimulation of local and distal mucosal sites. In this regard, studying comparatively the genomes of these bacteria by using bioinformatics tools could be an effective way to determine the cellular components/gens involved in the immunoregulatory effects. Previous genome analyses of probiotic bacteria focused mainly on predicted metabolic features, relying on functional annotation, and genome composition and synteny. However, these types of analyses could also help us to answer some of the most interesting questions regarding the beneficial effects of immunobiotics: What enables related organisms to present different immunoregulatory effects and what genes are involved in their unique capabilities? Which genes are unique within these related strains? How can new genetic targets be used to selected new immunobiotic strains? Therefore, we decided to start a new project in collaboration titled “**Immunobiogenomics**”. The main objective of this project is to sequence immunobiotic strains belonging to our research groups and compare them using bioinformatics tools, to search similarities and differences that could explain their differential immunoregulatory effects. These studies will be completed with transcriptomics studies to evaluate the response of host cells to the different immunobiotic strains. During the visit I had the opportunity to talk with several Japanese researchers and discuss about this new project. Some of them become interested in our project and decided to join it. Therefore, as a result of these several discussions, we conformed an international group called **International Immunobiogenic Consortium** that gathers researchers from Japan, Argentina and Chile that have the goal of collaborating in genomic studies of immunobiotics with different immunoregulatory capacities. This consortium will have two regional cores, one in Japan directed by my host researcher Dr. Kitazawa (CFAI-Japan core) and one in Argentina directed by myself (CERELA-South America core). During the visit several collaborative activities have been fixed for the next year, including research in collaborations, seminars and exchange of researchers and students.



## LIST OF RESEARCH DISCUSSION WITH MY HOST RESEARCHER

Date	Activities
1 October	Interview with Dr. <b>Hisashi Aso</b> and Dr. <b>Haruki Kitazawa</b> to set up my activities for the International Education and Research Center for Food and Agricultural Immunology (CFAI) – Tohoku University.
5 October	Discussion with Dr. <b>Haruki Kitazawa</b> to set up my research and academic activities for the Food and Feed Immunology Group, Graduate School of Agricultural Science – Tohoku University.
5 October	Discussion of results with Dr. <b>Haruki Kitazawa</b> and preparation of the final report of our ongoing research project: <b>Non-viable lactic acid bacteria and their cellular fractions as alternatives for the development of immunoregulatory products for the prevention of respiratory infections in immunocompromised hosts (Project 1)</b> .
13-14 October	Analysis and discussion with Dr. <b>Haruki Kitazawa</b> of the results and next objectives of our ongoing research project: <b>Prevention of respiratory superinfections using immunomodulatory cellular fractions from immunobiotic lactic acid bacteria. Role of pattern recognition receptors and signaling pathways (Project 2)</b> .
21-22 October	Discussion with Dr. <b>Haruki Kitazawa</b> to define general and specific objectives, set priorities, allocate tasks and formalize the research collaboration for the new project <b>Immunobiogenomics: genomics-based studies to provide insights into how immunobiotic bacteria stimulate the mucosal immune system (Project 3)</b> .

## 2) ACTIVITIES WITH OTHER JAPANESE RESRACHERS

The JSPS fellowship was an excellent mechanism for promoting and strengthening scientific collaborations between Japan and Argentina because it allowed me to have many discussions with other Japanese scientists. Dr. Kitazawa prepared an excellent schedule of meetings, visits and discussions for me, and their accompaniment on my visits was very helpful and enjoyable.

My visits to several laboratories located in different universities of Japan and the discussions of research projects in the field of immunology were excellent opportunities for information exchange, and I found the open and honest discussions very valuable. In particular, meeting with Drs. Yoshihito Suda, Tomonori Nochi and Takeshi Shimosato were excellent for strengthening scientific collaborations since new research projects in collaboration with those researchers were established. Moreover, as a result of those meetings, the three Japanese researchers were included as members of the International Immunobiogenomic Consortium.

## LIST OF ACTIVITIES WITH OTHER JAPANESE RESRACHERS

Date	Place	Activities
19 October	Department of Food, Agriculture and Environment, Miyagi University, Sendai.	Discussion with Dr. <b>Yoshihito Suda</b> and setting of new goals to continue work in collaboration.
26 October	Infection Immunology Unit, International Education and Research Center for Food Agricultural Immunology (CFAI), Graduate School of Agricultural Science, Tohoku University, Sendai.	Discussion with Dr. <b>Tomonori Nochi</b> and setting of goals to start work in collaboration.
16 October	Department of Molecular Preventive Medicine, Graduate School of Medicine, Tokyo University, Tokyo.	Visit to the laboratory and discussion with Dr. <b>Kouji Matsushima</b> and Dr. <b>Satoshi Ueha</b> .
16 November	Faculty of Agriculture, Shinshu University, Kamiina Nagano.	Visit to the laboratory and discussion with Dr. <b>Sachi Tanaka</b> and Dr. <b>Shinichi Yonekusa</b>
17 November	Laboratory of Food Molecular Biotechnology, Faculty of Agriculture, Shinshu University, Kamiina Nagano.	Discussion with Dr. <b>Takeshi Shimosato</b> and setting of goals to start work in collaboration.

### 3) ACTIVITIES WITH TOHOKU UNIVERSITY STUDENTS

I had meetings and discussions with several students belonging to the Food and Feed Immunology Group of Tohoku University. Dr. Kitazawa accompanied me for all discussions to analyze results, and define future objectives for each research project of students: Hikaru Ida, Yuki Masumizu, Nana Sato and Brian Tzu-An Chao.

In addition, we have several meetings with the Japanese students Hisakazu Kobayashi and Asuka Tada and the Argentinean student Leonardo Albarracin who accompanied me in this trip, to discuss research activities included in the project “**Immunobiogenomics: genomics-based studies to provide insights into how immunobiotic bacteria stimulate the mucosal immune system**”. These three students are the first members of our groups that will be involved in genomic and transcriptomics studies of immunobiotics. During the meetings we defined general and specific objectives, set priorities, and allocate tasks for each student.

#### LIST OF RESEARCH DISCUSSIONS WITH TOHOKU UNIVERSITY STUDENTS

Date	Activities
7 October	Interview and discussion with Dr. <b>Haruki Kitazawa</b> and students <b>Leonardo Albarracin</b> (Tucuman University - Argentina) and <b>Hisakazu Kobayashi</b> (Tohoku University - Japan).
15 October	Interview and discussion with Dr. <b>Haruki Kitazawa</b> and student <b>Hikaru Ida</b> (Tohoku University - Japan).
19 October	Interview and discussion with Dr. <b>Haruki Kitazawa</b> and students <b>Leonardo Albarracin</b> (Tucuman University - Argentina) and <b>Asuka Tada</b> (Tohoku University - Japan).
2 November	Interview and discussion with Dr. <b>Haruki Kitazawa</b> and student <b>Yuki Masumizu</b> (Tohoku University - Japan).
4 November	Interview and discussion with Dr. <b>Haruki Kitazawa</b> and student <b>Nana Sato</b> (Tohoku University - Japan).
5 November	Interview and discussion with Dr. <b>Haruki Kitazawa</b> and student <b>Brian Tzu-An Chao</b> (Tohoku University - Japan).
11 November	Interview and discussion with Dr. <b>Haruki Kitazawa</b> and students <b>Leonardo Albarracin</b> (Tucuman University - Argentina) and <b>Hisakazu Kobayashi</b> (Tohoku University - Japan).
13 November	Interview and discussion with Dr. <b>Haruki Kitazawa</b> and students <b>Leonardo Albarracin</b> (Tucuman University - Argentina) and <b>Asuka Tada</b> (Tohoku University - Japan).

### 4) FORMAL LECTURES

I gave three formal lectures during my fellowship in two Japanese universities: Tohoku University (Sendai) and Shinshu University (Kamiina Nagano). Lectures were aimed to give Japanese researchers and students detailed information about Argentina culture and science. Specifically, lectures were dedicated to show the Argentinean scientific system and the advances made by our research institute in the cellular and molecular mechanisms involved in the beneficial effects of immunobiotics in respiratory infections. Those lectures were an excellent opportunity to talk and discuss with Japanese students of different ages.

#### LIST OF FORMAL LECTURES

Date	Place	Lecture
9 October	Laboratory of Animal Products Chemistry, Graduate School of Agricultural Science, Tohoku University, Sendai.	Science English Course II: <b>Science and Technology in Argentina</b>
6 November	International Education and Research Center for Food Agricultural Immunology (CFAI), Graduate School of Agricultural Science, Tohoku University, Sendai.	2015 CFAI 7th Special Lecture: <b>Modulation of respiratory immune response by beneficial bacteria: impact on the prevention of viral respiratory infections</b>
16 November	Faculty of Agriculture, Shinshu University, Kamiina Nagano.	Special Lecture: <b>Immunobiotechnological applications of lactic acid bacteria for the prevention of respiratory infections</b>

## 5) FORMAL SEMINARS

As planned, I participated in two formal seminars with researchers and students of our groups to have general discussions of results and future activities.

### LIST OF FORMAL SEMINARS

Date	Place	Lecture
20 November	Conference room of Akiu Grand Hotel, Sendai.	Feed and Food Immunology Group Seminar
24 November	International Education and Research Center for Food Agricultural Immunology (CFAI), Graduate School of Agricultural Science, Tohoku University, Sendai.	International CERELA-CFAI Immunobiotics and Immunobiogenomic Consortium Seminar

## 6) OTHER ACTIVITIES

I was also able to attend several CFAI 2015 Food and Agricultural Immunology Joint Lectures during my stay in Japan. I was very impressed with the very organized and systematic approach being undertaken by CFAI professors to give students an overview of several aspects of Food and Agricultural Immunology. I should confess that it was one of my favorite activities during my visit to Japan. I really enjoyed listening to the lectures of CFAI professors and learning about the application of immunology in other fields.

### LIST OF OTHER ACTIVITIES

Date	Activities
6 October	Attendance to the CFAI 2015 Food and Agricultural Immunology Joint Lecture <b>Overview of Food and Agricultural Immunology</b> , Prof. <b>Haruki Kitazawa</b>
13 October	Attendance to the CFAI 2015 Food and Agricultural Immunology Joint Lecture <b>Immunobiotic Applications based on Livestock Immunology</b> , Prof. <b>Haruki Kitazawa</b>
20 October	Attendance to the CFAI 2015 Food and Agricultural Immunology Joint Lecture <b>Overview of Vaccine Development based on Mucosal Immunity</b> , Prof. <b>Tomonori Nochi</b>
27 October	Attendance to the CFAI 2015 Food and Agricultural Immunology Joint Lecture <b>Recognition and exclusion of pathogens in innate immunity</b> , Prof. <b>Shoichiro Kurata</b>
15-16 October	Attendance to the <b>Annual Meeting of Japanese Association for Food Immunology</b> in Tokyo
10 November	Attendance to the CFAI 2015 Food and Agricultural Immunology Joint Lecture <b>Overview of Innate Immune System of Mollusks and Crustaceans</b> , Prof. <b>Keisuke Takahashi</b>
24 November	Attendance to the CFAI 2015 Food and Agricultural Immunology Joint Lecture <b>Overview of Plant Immune System</b> , Prof. <b>Hideki Takahashi</b>