The 11th Leading Seminar Report

Lecturer:	**Dr. Koichi Araki**
	(Assistant professor, Emory Vaccine Center,
	Department of Microbiology and Immunology,
	Emory University School of Medicine, USA)
Date:	October 8th, 2014, 14:00-17:00
Venue:	Lecture Hall
Number of participants:	72
Organaizer:	Tomohiro Okagawa
	(Laboratory of Infectious Diseases, DC3)

<Leading Seminar (lecture)>

- **Seminar Title**

"Kinetics and role of autophagy during effector and memory CD8 T cell differentiation"

- **Abstract**

Immunological memory is the capacity of the adaptive immune system to remember pathogen for rapid and greater response upon re-encounter with the same pathogen. This concept is the basis of vaccination against infectious diseases. CD8 T cells are a critical component of the adaptive immune system and play an essential role in controlling viral as well as intracellular bacterial and parasitic infections. There is also considerable interest in CD8 T cell-mediated tumor immunity. Thus, inducing effective memory CD8 T cells is a major goal of vaccines against such diseases. We have previously shown that mTOR is a major regulator of memory CD8 T cell differentiation. Treatment of mice with rapamycin, an mTOR inhibitor, following acute lymphocytic choriomeningitis virus (LCMV) infection enhanced not only the quantity but also the quality of virus specific memory CD8 T cells. Experiments using RNAi showed that mTOR acts intrinsically in antigen specific CD8 T cells through the mTORC1 pathway to regulate memory T cell differentiation. Our study identifies a molecular pathway regulating memory formation and also provides a strategy for improving the functional qualities of vaccine or infection induced memory T cells. Now an important question is how mTOR regulates memory CD8 T cell differentiation. mTOR controls a variety of events essential for cellular homeostasis and growth/proliferation. One of the downstream targets of mTOR is autophagy that is an evolutionarily conserved intracellular degradation process. In this seminar, I will present our recent work on kinetics and functional role of autophagy in antigen specific CD8 T cells during viral infection, and will discuss how autophagy is dynamically regulated during memory CD8 T cell differentiation

During Dr. Araki's lecture

- **<u>Questions and Answers</u> (partially paraphrased)**

Q: Do the autophagy-deficient T cells affect memory T cell formation?

A: Although I didn't show the results of phenotypic analysis on the memory phase, P14 cells (LCMV-specific $CD8^+$ T cells) observed at 30 dpi was memory $CD8^+$ T cells. Few antigen-specific T cells survived until the memory phase in *Atg7*$^{fl/fl}$ *Gzmb*-Cre mice.

Q: Is this *in vivo* model of autophagy-deficient T cells possible to apply for the other experimental infections?

A: LCNV infection induces the higher promoter activity of *Granzyme B* gene, so we used *Gzmb* promoter for the conditional knockout of *Atg7*. In most infections, it is difficult to activate the *Gzmb* promoter activity sufficiently, but this conditional knockout system is also used in the infection model of Adenovirus type 5.

Active discussion following the lecture

<Post-seminar session>

- **Summary**

In this session, we asked Dr. Araki to talk about his carrier decisions after his PhD course and experience in the US.

Dr. Araki is a graduate of our veterinary school. He received the degree of doctor of veterinary medicine from Hokkaido university in 2000. He finished his PhD course at Lab. of Public health of our Graduate School of Veterinary Medicine in 2004. His PhD work was “Studies on the mechanism of persistent infection of hantavirus in mice”, and mainly studied the role of CD8 T cells on the Hantavirus infection. When he was a D4 student, he found and got interested in the paper from Dr. Rafi Ahmed’s lab., which he currently belongs to, and get in touch with Dr. Ahmed soon. Finally, he was invited to Dr. Ahmed’s lab. at Emory University School of Medicine and worked as a postdoctoral fellow from 2004 to 2011. At present, he works as an assistant professor in Emory Vaccine Center and Department of Microbiology and Immunology.

The reasons why he decided to go to Dr. Ahmed’s lab. were that he was interested in the research on antigen-specific T cells using MHC-tetramer and infection models and there was no lab. which was familiar with this kind of research in Japan. During the life in the U.S., he faced the difficulty of social life, especially language. He was emphasized the necessity of English skill. In addition, he also mentioned the special importance of “Quality of data” and “Work hard” on a scientific research as what he learned in the Dr. Ahmed’s lab.

His talk was very helpful to the graduate students to think about our post-graduate carrier.

Post-seminar session

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<From student organizer>

It was my great honor to conduct the 11th Leading Seminar as a student organizer. Fortunately, Dr. Araki kindly accepted our offer to come and give lectures about the kinetics and role of autophagy on effector $CD8^+$ T cell survival and memory formation.

Dr. Araki is one of the leading scientists in the field of immunological memory of $CD8^+$ T cells. The reasons why I invited Dr. Araki to the Leading Seminar are that his research is quite unique on immunology and he is a graduate of our veterinary school. I think the participants of this Leading Seminar agree that the scientific data with high quality and interesting story is very persuasive and helpful for scientific progress. I also hope PhD students take some messages back from his carrier path talk.

Finally, I am most grateful that Dr. Araki came back to Hokudai and had a lecture at our Leading Seminar. I also would express my gratitude to Leading Program Coordinator Professor Horiuchi, Leading Office staff Ms. Maki and Ms. Hashimoto, Seminar staff Dr. Aoshima and all the members of Laboratory of Infectious Diseases for helping to make the leading seminar successful.

Tomohiro Okagawa (Laboratory of Infectious Diseases, DC3)

Group photo with Dr. Araki