

## NAME

**Sidonia Fagarasan**

## CURRENT POSITION & TITLE

Team Leader, Laboratory for Mucosal Immunity, Center for Integrative Medical Sciences (IMS) RIKEN Yokohama Institute

Professor, Division of Integrated High-Order Regulatory Systems, Center for Cancer Immunotherapy and Immunobiology, Kyoto University Graduate School of Medicine, Kyoto University, Kyoto, Japan

## EDUCATION/TRAINING

- “Iuliu Hatieganu” University of Medicine and Pharmacy, Cluj, Romania. Degree: Medical Doctor.
- Residency and specialty in Clinical Laboratory, Microbiology, Biochemistry and Hematology, University of Medicine and Pharmacy, Cluj, Romania.
- Mombusho Visiting Researcher, Department of Medical Chemistry, Kyoto University, Faculty of Medicine, Kyoto, Japan.
- Kyoto University: PhD degree.

## RESEARCH

Our works on mucosal immunity uncovered an unanticipated role of the immune system in regulating the indigenous microbial communities, mucosal barrier integrity and whole-body homeostasis. We revealed the symbiotic role of IgA, elucidated the cellular and molecular mechanisms of IgA synthesis and demonstrated the instrumental role of adaptive immunity for controlling the development and maintenance of complex gut bacterial communities. We demonstrated the critical role of T cells, and the unique regulatory roles of signaling receptors (ex. PD-1) and transcription factors (ex. Foxp3, Bcl-6) for the IgA synthesis promoting mutualistic relationships with the gut microbiota. We showed that bacterial overgrowth caused by mucosal antibody defects activates peripheral immune system fueling the cycle of systemic activation and autoimmunity.

Recently we applied systems biology approaches to long-range extra-intestinal effects of the microbiota-immune interactions. Combining metabolomics, immunological analysis and mouse behavioral studies, we reveal the impact of chronic systemic immune activation on the brain biochemistry controlling the emotional responses.

## SELECTED PEER-REVIEWED PUBLICATIONS

**Fagarasan S**, Muramatsu M, Suzuki K, Nagaoka H, Hiai H, Honjo T. Critical roles of activation-induced cytidine deaminase in the homeostasis of gut flora. *Science*. 2002 Nov 15;298(5597):1424-7. PMID: 12434060.

Suzuki K, Meek B, Doi Y, Muramatsu M, Chiba T, Honjo T, **Fagarasan S**. Aberrant expansion of segmented filamentous bacteria in IgA-deficient gut. *Proc Natl Acad Sci U S A*. 2004 Feb 17;101(7):1981-6. PMID: 14766966.

Tsuji M, Suzuki K, Kitamura H, Maruya M, Kinoshita K, Ivaylo II, Itoh K, Littman DR, **Fagarasan S**. Requirement for Lymphoid tissue inducer cells in isolated follicle formation and T cell-independent immunoglobulin A generation in the gut. *Immunity*. 2008, 29, 261-271. doi: 10.1016/j.immuni.2008.05.014. PMID: 18656387.

Tsuji M, Komatsu N, Kawamoto S, Suzuki K, Kanagawa O, Honjo T, Hori S, **Fagarasan S**. Preferential generation of follicular B helper T (T<sub>FH</sub>) cells from Foxp3<sup>+</sup> T cells in gut Peyer's patches. *Science*, 2009, 323, 1488-1492. doi: 10.1126/science.1169152. PMID: 19286559.

Kawamoto S, Tran TH, Maruya M, Suzuki K, Doi Y, Yumi T, Kato ML, **Fagarasan S**. The inhibitory receptor PD-1 regulates IgA selection and bacterial composition in the gut. *Science* 2012, 336(6080):485-9. doi: 10.1126/science.1217718. PMID: 22539724.

Kawamoto S, Maruya M, Kato LM, Suda W, Atarashi K, Doi Y, Tsutsui Y, Qin H, Honda K, Okada T, Hattori M, **Fagarasan S**. Foxp3(+) T cells regulate immunoglobulin a selection and facilitate diversification of bacterial species responsible for immune homeostasis. *Immunity*. 2014 Jul 17;41(1):152-65. doi: 10.1016/j.immuni.2014.05.016.PMID: 25017466

Miyajima M., Zhang B., Sugiura Y., Sonomura K., Guerrini M.M., Tsutsui Y., Maruya M., Vogelzang A., Chamoto K., Honda K., Hikida T., Qin H., Sanuki R., Suzuki K., Furukawa T., Ishihama Y., Matsuda F., Suematsu M., Honjo T., **Fagarasan S**. Metabolic shift induced by systemic activation of T cells in PD-1 deficient mice perturbs brain monoamines and emotional behavior. *Nat Immunol*. 2017, Dec 18 (12):1342-1352. doi: 10.1038/ni.3867. PMID:29058703.

## **HONOURS & AWARDS**

2005: Young Scientist Award from the Ministry of Education, Culture, Sport, Science and Technology, Japan.

2012: Achievements Award from the Japanese Society for Immunology.

2013: NISTEP Award from the Ministry of Education, Culture, Sport, Science and Technology, Japan.

2020: 1<sup>st</sup> Kobayashi Award