Department of Dermatology

－The 60th Seminar－

🔬 Mapping the T Cell Repertoire to a Model System of the Human Gut Microbiome

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📅 **Date:** October 8, 2025

🕔 **Time:** From 5:00 PM

📍 **Venue:** Shared Conference Room, 8th Floor, North Ward（北病棟 8 階共通カンファレンス室）

👤 **Guest Speaker:**

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Mapping the T cell repertoire to a model system of the human gut microbiome

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Certain gut bacteria elicit strong, antigen-specific T cell responses. While past studies used mono-colonization to identify immunomodulatory strains, this doesn't reflect how strains behave within complex communities. We colonized germ-free mice with a defined >100-strain community and profiled T cell responses to each strain. Surprisingly, many T cells recognized multiple strains. Screening 92 TCR hybridomas revealed that most TCRs were polyspecific, including 13 abundant clonotypes targeting 18 Firmicutes. These TCRs shared a conserved antigen: a substrate-binding protein (SBP) from an ABC transporter. Treg and Th17 cells specific for the SBP are abundant in community-colonized and SPF mice. Our work reveals that T cell recognition of Firmicutes is focused on a widely conserved cell-surface antigen, opening the door to new therapeutic strategies in which colonist-specific immune responses are rationally altered or redirected.

Reference

[1] Nagashima, K.; Zhao, A.; Atabakhsh, K.; Bae, M.; Blum, J. E.; Weakley, A.; Jain, S.; Meng, X.; Cheng, A. G.; Wang, M.; Higginbottom, S.; Dimas, A.; Murugkar, P.; Sattely, E. S.; Moon, J. J.; Balskus, E. P.; Fischbach, M. A. *Mapping the T Cell Repertoire to a Complex Gut Bacterial Community. Nature*, 2023, doi: 10.1038/s41586-023-06431-8.

[2] Nagashima, K. *Blockbuster T cells in the gut: A high-resolution view of immune modulation by the gut microbiome is presented. Science*, 2024, 385 (6704), 36-37

[3] Cheng, A. G.; Ho, P.-Y.; Jain, S.; Meng, X.; Wang, M.; Yu, F. B.; Iakiviak, M.; Brumbaugh, A. R.; Nagashima, K.; Zhao, A.; Patil, A.; Atabakhsh, K.; Weakley, A.; Yan, J.; Higginbottom, S.; Neff, N.; Sonnenburg, J. L.; Huang, K. C.; Fischbach, M. A. *Design, Construction and In Vivo Augmentation of a Complex Gut Bacterial Community. Cell*, 2022, 185 (19), 3617-3636.

[4] Nagashima, K.; Sawa, S.; Nitta, T.; Tsutsumi, M.; Okamura, T.; Penninger, J. M.; Nakashima, T.; Takayanagi, H. *Identification of Subepithelial Mesenchymal Cells That Induce IgA and Diversify Gut Microbiota. Nature immunology*, 2017, 18 (6), 675–682.