

 MILESTONE 19

Modern culturing efforts expand the culturable microbiota

High-throughput anaerobic culturing enabled the recovery of a large part of the diverse human gut microbiota and the creation of individual culture collections.

ORIGINAL ARTICLE Goodman, A. L. et al. Extensive personal human gut microbiota culture collections characterized and manipulated in gnotobiotic mice. *Proc. Natl Acad. Sci. USA* **108**, 6252–6257 (2011).
FURTHER READING Lagier, J. C. et al. Culturing the human microbiota and culturomics. *Nat. Rev. Microbiol.* **1**, 540–550 (2018).



Credit: Rickvan Arda / Alamy Stock Photo

 MILESTONE 20

Global human microbiome

Genetic variation occurs between human populations living in different places, but little was known about variation in microbiomes. To investigate how gut microbiomes differ among human populations, Yatsunen et al. characterized bacterial species in faecal samples from

cohorts living in different regions, including the Amazonas of Venezuela, rural Malawi and US metropolitan areas. The authors found pronounced differences in the composition and functions in the gut microbiomes between these geographically distinct cohorts.

ORIGINAL ARTICLE Yatsunen, T. et al. Human gut microbiome viewed across age and geography. *Nature* **486**, 222–227 (2012).

FURTHER READING Schnorr, S. L. et al. Gut microbiome of the Hadza hunter-gatherers. *Nat. Commun.* **5**, 3654 (2014) | O'Keefe, S. J. D. et al. Fat, fibre and cancer risk in African Americans and rural Africans. *Nat. Commun.* **6**, 6342 (2014) | Obregon-Tito, A. J. et al. Subsistence strategies in traditional societies distinguish gut microbiomes. *Nat. Commun.* **6**, 6505 (2015) | Nishijima, S. et al. The gut microbiome of healthy Japanese and its

microbial and functional uniqueness. *DNA Res.* **23**, 125–133 (2016) | Das, B. et al. Analysis of the gut microbiome of rural and urban healthy Indians living in sea level and high-altitude areas. *Sci. Rep.* **8**, 10104 (2018) | Pasolli, E. et al. Extensive unexplored human microbiome diversity revealed by over 150,000 genomes from metagenomes spanning age, geography, and lifestyle. *Cell* **176**, 649–662 (2019) | Nayfach, S., Shi, Z. J., Seshadri, R., Pollard, K. S. & Kyrpides, N. Novel insights from uncultivated genomes of the global human gut microbiome. *Nature* <https://doi.org/10.1038/s41586-019-1058-x> (2019).



Credit: N. Wallington / Springer Nature Limited

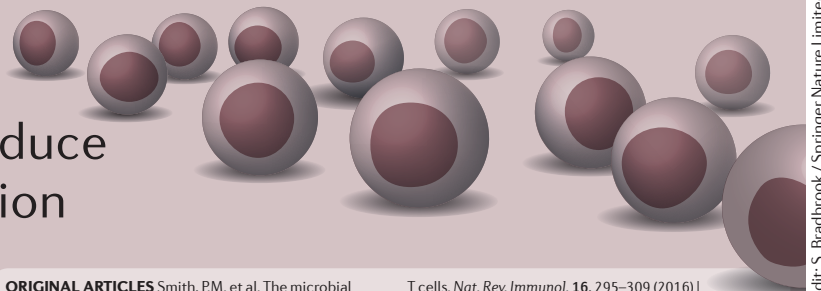
 MILESTONE 21

Microbially-produced short-chain fatty acids induce regulatory T cell production

Regulatory T cells (Tregs) are crucial in maintenance of immune homeostasis. In 2013, three studies found that microbiota-derived short-chain fatty acids promote the expansion and differentiation of Tregs, revealing a form of chemical-mediated communication between the commensal microbiota and the immune system that affects immune mechanisms.

ORIGINAL ARTICLES Smith, P.M. et al. The microbial metabolites, short-chain fatty acids, regulate colonic Treg cell homeostasis. *Science* **341**, 569–573 (2013) | Atarashi, K. et al. Treg induction by a rationally selected mixture of Clostridia strains from the human microbiota. *Nature* **500**, 232–236 (2013) | Arpaia, N. et al. Metabolites produced by commensal bacteria promote peripheral regulatory T-cell generation. *Nature* **504**, 451–455 (2013).
FURTHER READING Tanoue, T., Atarashi, K. & Honda, K. Development and maintenance of intestinal regulatory

T cells. *Nat. Rev. Immunol.* **16**, 295–309 (2016) | Round, J. L. & Mazmanian, S. K. Inducible Foxp3+ regulatory T-cell development by a commensal bacterium of the intestinal microbiota. *Proc. Natl Acad. Sci. USA* **107**, 12204–12209 (2010) | Geuking, M. B. et al. Intestinal bacterial colonization induces mutualistic regulatory T cell responses. *Immunity* **34**, 794–806 (2011) | Lathrop, S. K. et al. Peripheral education of the immune system by colonic commensal microbiota. *Nature* **478**, 250–254 (2011).



Credit: S. Bradbrook / Springer Nature Limited