MILESTONE 22

# Production of antibiotics by the human microbiota

Identification of biosynthetic gene clusters for antibiotics in the genomes of the human microbiota, suggests new sources of antimicrobial drugs whose species-specific production has the potential to modulate the local microbial community structure.

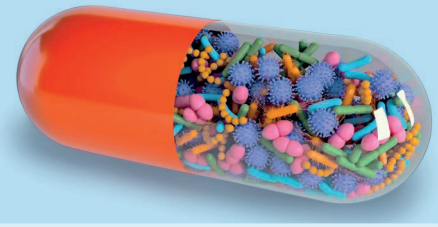
Credit: V. Summersby / Springer Nature Limited

**ORIGINAL ARTICLE** Donia, M. S. et al. A systematic analysis of biosynthetic gene clusters in the human microbiome reveals a common family of antibiotics. *Cell* **158**, 1402–1414 (2014).
**FURTHER READING** Zipperer, A. et al. Human commensals producing a novel antibiotic impair pathogen colonization. *Nature* **535**, 511–516 (2016).

MILESTONE 23

# Host-targeted drugs affect microbiota populations

Commonly used medications affect gastrointestinal microbial abundances and bacterial gene expression, which may both positively and negatively contribute to the effects on human health associated with drug treatment.



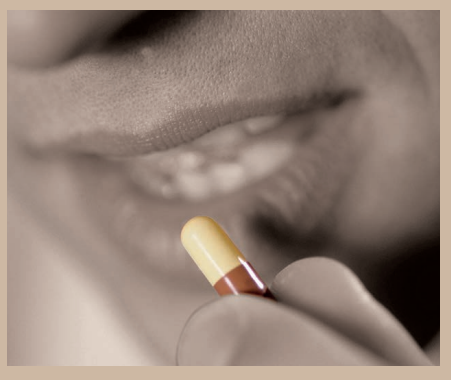
Credit: Science Photo Library / Alamy Stock Photo

**ORIGINAL ARTICLES** Tsuda A et al. Influence of proton-pump inhibitors on the luminal microbiota in the gastrointestinal tract. *Clin. Transl. Gastroenterol.* **6**, e89 (2015) | Freedberg, D. E. et al. Proton pump inhibitors alter specific taxa in the human gastrointestinal microbiome: a crossover trial. *Gastroenterology* **149**, 883–885 (2015) | Forslund, K. et al. Disentangling type 2 diabetes and metformin treatment signatures in the human gut microbiota. *Nature* **528**, 262–266 (2015).
**FURTHER READING** Maurice, C. F., Haiser, H. J. & Turnbaugh, P. J. Xenobiotics shape the physiology and gene expression of the active human gut microbiome. *Cell* **152**, 39–50 (2013) | Maier L. et al. Extensive impact of non-antibiotic drugs on human gut bacteria. *Nature* **555**, 623–628 (2018) | Zimmermann, M. et al. Separating host and microbiome contributions to drug pharmacokinetics and toxicity. *Science* **363**, eaat9931 (2019).

MILESTONE 24

# Human microbiota affects response to cancer therapy

Following earlier studies in mouse models, gut microbiota composition was shown to affect the response of melanoma patients, and those suffering from advanced lung or kidney cancer, to immune checkpoint therapy, as well as tumour control.



Credit: ImageSource

**ORIGINAL ARTICLES** Routy, B. et al. Gut microbiome influences efficacy of PD-1-based immunotherapy against epithelial tumors. *Science* **359**, 91–97 (2018) | Gopalakrishnan, V. et al. Gut microbiome modulates response to anti-PD-1 immunotherapy in melanoma patients. *Science* **359**, 97–103 (2018) | Matson, V. et al. The commensal microbiome is associated with anti-PD-1 efficacy in metastatic melanoma patients. *Science* **359**, 104–108 (2018).
**FURTHER READING** Tanoue, T. et al. A defined commensal consortium elicits CD8 T cells and anti-cancer immunity. *Nature* **565**, 600–605 (2019) | Iida, N. et al. Commensal bacteria control cancer response to therapy by modulating the tumor microenvironment. *Science* **342**, 967–970 (2013) | Viaud, S. et al. The intestinal microbiota modulates the anticancer immune effects of cyclophosphamide. *Science* **342**, 971–976 (2013) | Taur, Y. et al. The effects of intestinal tract bacterial diversity on mortality following allogeneic hematopoietic stem cell transplantation. *Blood* **124**, 1174–1182 (2014) | Sivan, A. et al. Commensal Bifidobacterium promotes antitumor immunity and facilitates anti-PD-L1 efficacy. *Science* **350**, 1084–1089 (2015) | Vétizou, M. et al. Anticancer immunotherapy by CTLA-4 blockade relies on the gut microbiota. *Science* **350**, 1079–1084 (2015).

MILESTONE 25

# Metagenome-assembled genomes provide unprecedented characterization of human-associated microbiota

Advances in computational methods, recently pioneered in the environmental microbiology field, enable the reconstruction of bacterial genomes from metagenomic datasets. This approach was used to identify thousands of new uncultured candidate bacterial species from the gut and other body sites, of global populations from rural and urban settings, substantially expanding the known phylogenetic diversity and improving classification of understudied, non-Western populations.

Credit: N. Wallington / Springer Nature Limited

**ORIGINAL ARTICLES** 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) | Almeida, A. et al. A new genomic blueprint of the human gut microbiota. *Nature* https://doi.org/10.1038/s41586-019-0965-1 (2019) | Nayfach, S. et al. New insights from uncultivated genomes of the global human gut microbiome. *Nature* https://doi.org/10.1038/s41586-019-1058-x (2019).