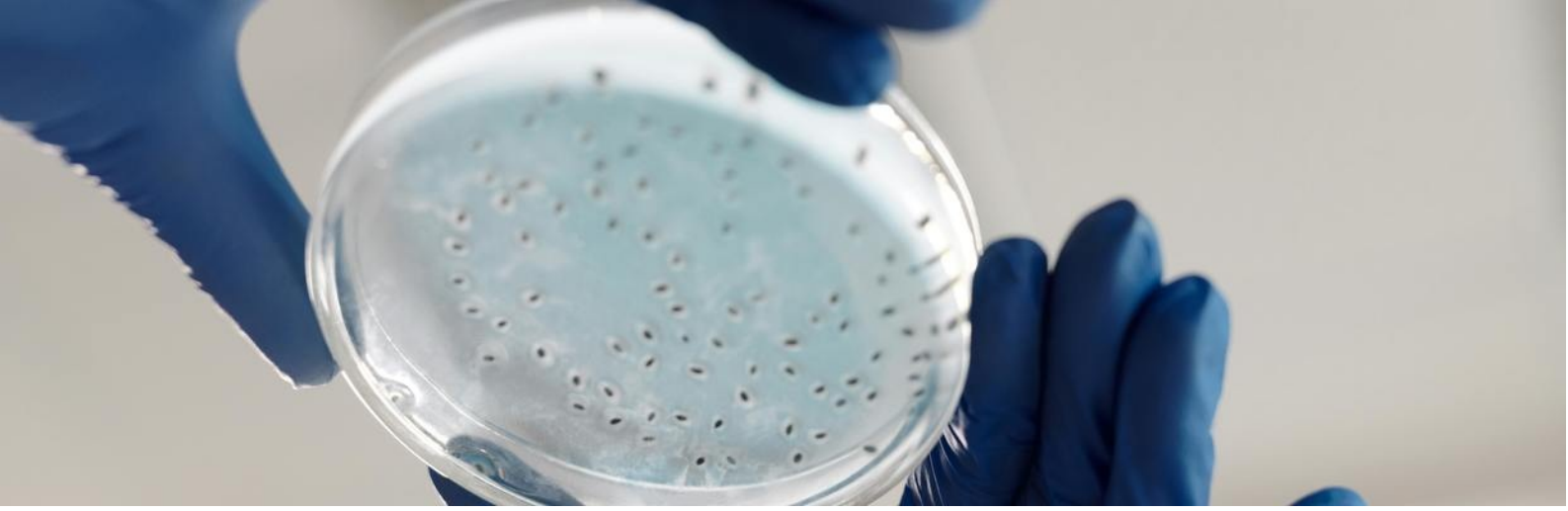

Spotlight on Microbial & Cellular Frontiers

Authors: Rohita Biswas, Cinthya Souza Simas, Sara Tóth Martínez, María Belén Moyano, Felicitas S. Holzer, Gerhard G. Steinmann, Roland Mertelsmann

Submitted: 23. March 2026
Published: 25. March 2026
Volume: 13
Issue: 2
Affiliation: Journal of Science, Humanities and Arts (JOSHA), Freiburg im Breisgau, Germany
Languages: English
Keywords: Single-cell Transcriptomics; Therapeutic Colonization; Heme Piracy; Transcriptional Homeostasis; MCL-1 Metabolism; Platelet Biosensors.
Categories: News and Views
DOI: 10.17160/josha.13.2.1133

Abstract:

This collection brings together six research articles that illuminate the molecular and cellular mechanisms shaping microbial communities, host–pathogen interactions, and fundamental cell biology. It covers the application of single-cell transcriptomics to uncover functional diversity within microbiomes, the engineering of controllable gut bacteria for therapeutic colonization, and the design of AI-guided proteins that block iron acquisition by pathogenic E. coli. Additional studies explore a universal homeostatic mechanism governing transcription factor activity, the metabolic roles of the anti-apoptotic protein MCL-1 beyond cell death regulation, and the unexpected capacity of platelets to sequester circulating cell-free DNA with implications for cancer diagnostics and prenatal testing. Together, these findings advance understanding of gene regulation, microbial ecology, and translational biotechnology.

JOSHA Journal of Science, Humanities and Arts

March 2026 Volume 13, Issue 2

Spotlight on Microbial & Cellular Frontiers

Rohita Biswas, Cinthya Souza Simas, Sara Tóth Martínez, María Belén Moyano, Felicitas Holzer, Gerhard G. Steinmann, Roland Mertelsmann
editorial@josha-archive.org
Journal of Science, Humanities and Arts, Freiburg im Breisgau, Germany

Abstract

This collection brings together six research articles that illuminate the molecular and cellular mechanisms shaping microbial communities, host–pathogen interactions, and fundamental cell biology. It covers the application of single-cell transcriptomics to uncover functional diversity within microbiomes, the engineering of controllable gut bacteria for therapeutic colonization, and the design of AI-guided proteins that block iron acquisition by pathogenic *E. coli*. Additional studies explore a universal homeostatic mechanism governing transcription factor activity, the metabolic roles of the anti-apoptotic protein MCL-1 beyond cell death regulation, and the unexpected capacity of platelets to sequester circulating cell-free DNA with implications for cancer diagnostics and prenatal testing. Together, these findings advance understanding of gene regulation, microbial ecology, and translational biotechnology.

Keywords: Single-cell Transcriptomics; Therapeutic Colonization; Heme Piracy; Transcriptional Homeostasis; MCL-1 Metabolism; Platelet Biosensors.

1. Dissecting microbial communities with single-cell transcriptome analysis

By Andrew W. Pountain *et al*

This article reviews recent advances in applying single-cell transcriptome analysis to microbial communities, highlighting how these tools reveal functional diversity that bulk approaches cannot detect. Although microbiome research has traditionally focused on species-level composition, even genetically similar microbial cells can differ substantially in gene expression, physiology, and environmental responses, leading to functional diversification within a single species. It is described how new single-cell RNA sequencing methods, adapted from mammalian systems and including droplet-based and combinatorial barcoding approaches, now enable profiling of millions of bacterial and unicellular fungal cells despite technical challenges such as small cell size, cell walls, and rapid mRNA degradation. These technologies have uncovered transcriptional heterogeneity *in vitro,* variation in antibiotic responses, activity of mobile genetic elements, and functional diversification within complex ecosystems such as the *mammalian gut*. Despite remaining experimental and bioinformatic challenges, including low transcript capture and difficulties in sampling diverse communities, single-cell transcriptomics is positioned to transform understanding of microbiome dynamics, stress responses, and community-level interactions at true cellular resolution.

This article was previously published in *Science, Volume 389, Issue 6764,* on September 4, 2025.

Read the full article here

2. Controlled colonization of the human gut with a genetically engineered microbial therapeutic

By Weston R. Whitaker *et al*

Researchers developed a genetically engineered gut bacterium designed to controllably colonize the human intestine and treat hyperoxaluria, a cause of kidney stones. The strain of *Phocaeicola vulgatus* was engineered to use the seaweed nutrient porphyran, creating a tunable ecological niche. It also carried a five-gene pathway that degrades oxalate, which successfully lowered urinary oxalate in rat

models. To enable reversibility, the bacterium's survival was made dependent on porphyran. In human trials, colonization was dose-dependent and generally declined after porphyran withdrawal, with good safety and mostly mild side effects. However, some persistence occurred due to escape mutations, and patients with hyperoxaluria showed variable colonization and horizontal gene transfer that disrupted the therapy.

This article was previously published in *Science, Volume 389, Issue 6757,* on July 17, 2025.

Read the full article here

3. Inhibiting heme piracy by pathogenic Escherichia coli using de novo-designed proteins

By Daniel R. Fox *et al*

Pathogenic *E. coli* and closely related *Shigella* rely on heme acquisition to overcome host iron restriction, including "heme piracy" from hemoglobin via the outer-membrane transporter ChuA. Using a transporter-simplified *E. coli* background, growth assays across heme sources, binding measurements, structural modeling, and targeted mutagenesis, the work dissects how ChuA preferentially engages hemoglobin and coordinates heme transfer through key residues and extracellular loop interactions, consistent with a transient, dynamic extraction mechanism. Building on this mechanistic map, an AI-guided de novo protein design workflow generated compact ChuA-binding proteins that target the hemoglobin-interaction surface and competitively block hemoglobin-dependent growth at nanomolar potencies while sparing conditions where free heme is provided. X-ray and cryo-EM structures of representative binders alone and in complex with ChuA closely match the computational models, providing structural validation of the designed inhibitory mechanism and illustrating a generalizable strategy for targeting bacterial nutrient-uptake systems.

This article was previously published in *Nature Communications* on July 9, 2025.

Read the full article here

4. E. coli transcription factors regulate promoter activity by a universal, homeostatic mechanism

By Vinuselvi Parisutham *et al*

This article shows that in E. coli, diverse transcription factors (traditionally labeled as activators or repressors) all follow a common quantitative rule: the fold change they impose on gene expression decreases as the constitutive strength of the regulated promoter increases, yielding an inverse scaling between fold change and basal promoter activity. Using a thermodynamic model and systematically varying promoter strength via genetic and physiological perturbations while keeping the regulatory context fixed, the authors demonstrate that TF–RNA polymerase interactions behave effectively as stabilizing for all tested TFs, regardless of their classical classification. As a result, promoters that differ in unregulated activity by orders of magnitude converge to similar regulated expression levels for a given TF, implying that TFs inherently buffer genetic or physiological perturbations to maintain a relatively constant output. The authors interpret this universal scaling as a homeostatic mechanism: TFs act as built-in fail-safe regulators that reduce variability in expression across promoters and conditions, thereby supporting robustness of gene regulation in fluctuating environments.

This article was previously published in *Science, Volume 389, Issue 6765,* on September 11, 2025.

Read the full article here

5. Relative importance of the anti-apoptotic versus apoptosis-unrelated functions of MCL-1 in vivo

By Kerstin Brinkmann *et al*

This study investigates whether the essential protein MCL-1 is required mainly for preventing apoptosis or for other metabolic functions. Researchers generated mice in which the Mcl-1 gene was replaced with related anti-apoptotic proteins BCL-XL, BCL-2, or A1. This showed that its anti-apoptotic role is sufficient for early development. However, embryos with these substitutions later developed abnormalities and died mid-gestation. BCL-XL compensated better than BCL-2 but still could not fully replace MCL-1. Detailed analyses revealed severe defects in liver

function and fatty acid oxidation without increased apoptosis. Metabolomic and transcriptomic data indicated widespread metabolic dysregulation, including increased glycolysis and impaired lipid metabolism. Neither BCL-XL nor BCL-2 could substitute for MCL-1's role in fatty acid oxidation. These results demonstrate that MCL-1 has essential apoptosis-independent metabolic functions in later development and postnatal life. The findings help explain tissue toxicity seen with some MCL-1 inhibitors.

This article was previously published in *Science, Volume 389, Issue 6764,* on July 3, 2025.

Read the full article here

6. Platelets sequester extracellular DNA, capturing tumor-derived and free fetal DNA

By Lauren Murphy *et al*

Although platelets are anucleate blood cells traditionally assumed to be devoid of DNA, this study demonstrates that they actively sequester cell-free DNA (cfDNA) circulating in the bloodstream. Using high-resolution imaging, flow cytometry, live cell coculture experiments, fluorescence in situ hybridization, and droplet digital PCR, the researchers show that platelets internalize both DNA-loaded extracellular vesicles and membrane-free DNA fragments, protecting the sequestered material from external DNase degradation and releasing it upon activation in a dynamin-dependent manner. In mouse models of thrombocytopenia and in patients with low platelet counts, platelet depletion led to elevated plasma cfDNA levels, supporting a homeostatic role in clearing immunostimulatory DNA. In pregnant women carrying male fetuses, Y-chromosome fragments were confirmed in platelets, and tumor-derived DNA was detected in platelets of patients with advanced cancer, low-tumor burden disease, and premalignant colonic polyps. These findings reveal platelets as an overlooked reservoir of clinically relevant genetic material, with direct implications for improving liquid biopsy sensitivity in cancer screening and prenatal diagnostics.

This article was previously published in *Science* on August 14, 2025.

Read the full article here

Acknowledgements

GPT-5.2 version of Chat-GPT (OpenAI), Notebook LM (Google), and Perplexity AI (Perplexity AI Inc.) was used during the writing process as part of JOSHA's policy of experimentation with AI tools. However, JOSHA takes full responsibility for its content.