Breaking Down Walls

Towards a Functional-Based Metagenomic Discovery Platform for Phage-Derived Lysins

Iris Pottie[1,2], Lisa Duyvejonck[1], Roberto Vázquez[1], Yves Briers[1]

AIM

Although broad-spectrum antibiotics have proven effective in treating acute bacterial infections, they impact the microbiome as well (figure 1). Moreover, the rise of antibiotic-resistant bacterial species urges to find alternative therapies (1, 2).

Therefore, there is an urgent need for **specific novel antibiotics** that kill bacteria causing disease, while maintaining and even restoring a balanced microbiome during treatment.

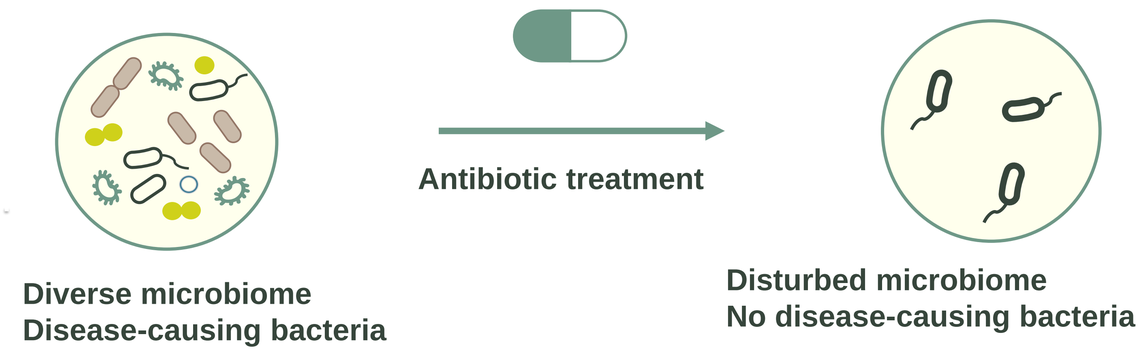

Figure 1: Broad-spectrum antibiotics impact microbiomes (1, 4, 5)

INSPIRATION

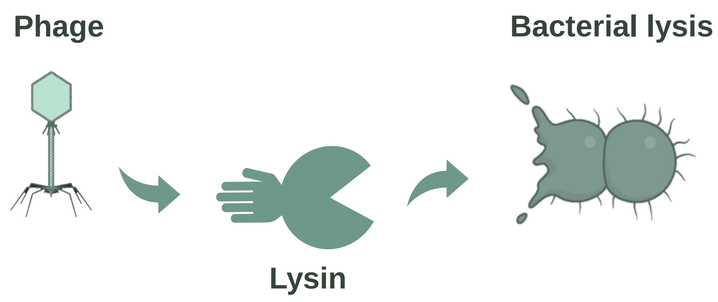

Figure 2: Lysins encoded by bacteriophages induce lysis of bacteria (2, 4, 5)

Lysins, peptidoglycan-degrading enzymes encoded by bacteriophages, are a potential new class of antibiotics. Because of their specificity at the genus-, species- or serovar level, they have a narrow spectrum. Therefore, they are considered microbiome-friendly (2, 3).

Thanks to the vast natural abundance of phages, lysins possess the potential to target virtually any bacterium. The **largely untapped metagenomes** from unculturable phages are a hidden source of an infinite number of potential lysins. To fully explore the potential of lysins, novel discovery platforms are required for the identification of new lysins.

METHOD

A metagenomic library is constructed by performing the following steps (figure 3):

1. Extraction environmental phages
2. Extraction phage DNA
3. DNA fragmentation and amplification
4. DNA cloning and expression

Subsequent screening directly assesses muralytic activity, allowing discovery of peptidoglycan-degrading enzymes with novel sequences.

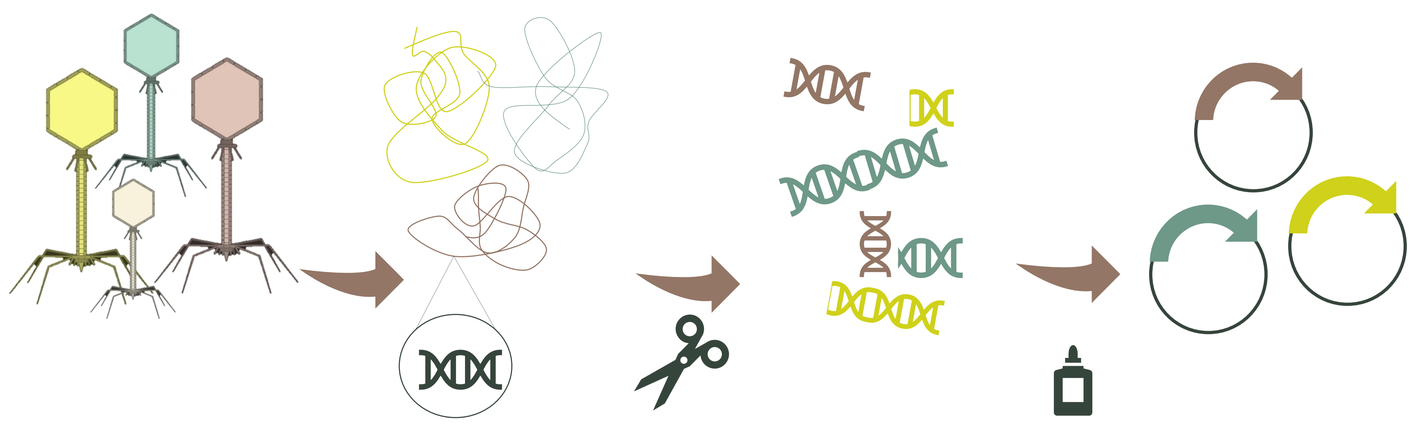

Figure 3: Steps for construction of a metagenomic library (5)

CONCLUSION

Classic broad-spectrum antibiotics can disturb the balance of **microbiomes**.

Lysins, bacteriophage-encoded enzymes degrading the bacterial cell wall with high specificity, are considered an alternative, narrow-spectrum antibiotic.

Using **functional metagenomics**, an approach to discover phage lytic proteins is developed. When the platform is established, phage lysins with novel sequences can be identified, which is not possible with traditional sequence-based metagenomics.

Affiliations

1. Laboratory of Applied Biotechnology, Department of Biotechnology, Faculty of Bioscience Engineering, Ghent University
2. CMET – Center for Microbial Ecology and Technology, Faculty of Bioscience Engineering, Ghent University

This work was supported by the Research Foundation Flanders (FWO) under the scope of the strategic funding of an SB scholarship (1SC9424N).

References

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Contact

iris.pottie@ugent.be

Iris Pottie