Value and limitation of the reductionist principle for microbial biotechnology -illustrated with a phage therapy trial

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Résumé

One of the most fruitful concepts of biology was the reductionist principle. The detailed study of a handful of bacteriophages in a single bacterium, Escherichia coli, under simple laboratory growth conditions became the springboard for molecular biology. Thanks to a revolutionary progress in DNA sequencing, bioinformatics and statistical techniques, microbiologists now study highly complex systems like the microbiome of human populations under various physiological and disease states. However, when going from a descriptive to a seemingly simple interventional stage in microbiome research, namely phage therapy of E. coli diarrhea in children, data limitations in the literature become apparent. Phage-E. coli interaction in the gut, their natural ecological niche, are fragmentary, E. coli etiology in childhood diarrhea is unclear and the gut microbiome analysis in diarrhea is just starting. From a failed clinical phage therapy trial two conclusions are drawn: on one side we need an extension of the reductionist principle for E. coli phages into the gut of mice with controlled microbial colonization to understand their in vivo interaction as a basis for their medical application. On the other side, we need more exploratory clinical observations to confirm that infection concepts obtained from molecular pathogenesis work and animal models apply to the clinical reality.

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