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Commentary

Metagenomics in Italy and Europe: Three Actionable Challenges/Prospects in 2020

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Introduction

Metagenomics has gained worldwide prominence as one of the indispensable omics technologies for the past several years in particular. Metagenomics applications in clinical medicine, ecology, planetary health, and built environments are increasingly reported in the literature. Many countries are both striving and struggling to cultivate metagenomics scholarship as one of the drivers of life sciences innovation in early 21st century. Italy is no exception and has made important strides in metagenomics for the past decade.

As we shift our gaze toward the new year 2020, we highlight what we consider to be three actionable emerging challenges in the field of metagenomics, specifically in Italy, that can transform to prospects for clinical, translational, ecological, and/or discovery science innovation globally.

Actionable Challenge 1

Antimicrobial resistance and metagenomics

Antimicrobial resistance (AMR) is a global public health crisis that is impeding our ability to successfully treat infectious diseases. A recent report from the Italian Higher Health Institute highlights that Italy is one of the European Member states with the highest level of deaths caused by AMR, accounting for almost one-third of deaths in Europe due to resistance to antibiotics each year (Italian Government, Piano Nazionale di Contrasto AMR, 2017–2020).

The human microbiome is an important reservoir of AMR and a key player in the dissemination of AMR genes (Brinkac et al., 2017). A complete understanding of the structural and functional complexity of the microbial communities in humans, animals, and the environment is mandatory for halting and reversing the current AMR predicament in Italy and on a planetary scale. In this context, *single-cell metagenomics* offers a promising tool to improve our ability to taxonomically characterize human microbiota. Moreover, functional analyses of metagenomic data might enhance our comprehension of the rise of multidrug resistance. We believe that metagenomics will help in understanding the mechanisms underlying the development and spread of AMR and in successfully governing this threat to the worldwide public health.

Actionable Challenge 2

Novel molecules and strategies to fight against bacterial resistance

A report of the European Centre for Disease Prevention and Control concluded: ''The levels of carbapenem-resistant *Enterobacteriaceae* and *Acinetobacter baumannii* have now reached hyper-endemic levels and, together with meticillin-resistant *Staphylococcus aureus*, this situation causes Italy to be one of the Member States with the highest level of resistance in Europe'' (Cassini et al., 2017). To address the bacterial resistance crisis in Italy and Europe, there is an urgent need to develop more selective and safe biological therapies. Bacteriocins, which are antimicrobial peptides/proteins synthesized by certain bacteria, are interesting alternatives to conventional antibiotics (Cotter et al., 2013).

The increasing interest in bacteriocins is due to their diversified mechanisms of action that overcome bacterial resistance to antimicrobials while preserving commensal bacteria in microbiota. To date, these antimicrobial peptides have a long history of safe use in dairy industry as preservatives (Silva et al., 2018). This makes them quite appealing and promising as alternative therapeutics. We envision that functional metagenomics analyses of various Holobionts, delineated as a community of species that are closely associated and have complex interactions, will offer great promise for discovering novel human microbial bacteriocins gene clusters and for studying bacteriocins to manipulate and express them in host microbes.

Actionable Challenge 3

Probiotics

For the past decade, the growing interest in promoting health in ways attuned to the nature led to intensification of research in the field of probiotics on a global scale. During the last ''Probiotics, Prebiotics and New Foods'' symposium an overview about ''Probiotics: market, technical, scientific and quality topics in Italy and in Europe,'' report that the Italian probiotic market is one of the most notable in Europe; today it is worth >500 million euros, >50% of the European total (Probiotics, Prebiotics & New Foods, Nutraceuticals and Botanicals for Nutrition & Human and Microbiota Health 1st Science & Business Symposium, 2019).

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The potential applications of probiotics are continuously widening and offer a promising opportunity in the management of a wide range of human diseases in the near future. Therefore, monitoring effectiveness and safety of gut microbiota manipulation by prebiotics deserves further efforts. Taking advantage of microbial meta-pathways analyses based on metagenomics, characterization of community members, functions, and interactions, in specific ecosystems will be possible (Laudadio et al., 2019). This knowledge is crucial for optimal development of functional probiotics that requires not only a detailed insight into specific probiotic member strains, dosage, and long-term safety, but also the elucidation of the exact mechanisms by which probiotics produce health benefits.

Outlook

AMR poses a growing challenge to health care, in particular in Italy. Reducing such planetary health threats caused by uncontrolled antibiotic use through microbiome-based approaches is an ambitious but important research goal in each and every country, including in Italy. In this context, metagenomics is an invaluable tool to empower local public health systems around the world. Indeed, metagenomics is not only one of the newest omics technologies but also the one harboring the broadest set of applications and impacts. Metagenomics has rapidly expanded our understanding of the structure and function of environmental and clinical microbial communities, allowing to address previously unattainable biological questions as well as accelerating genome-based discovery of novel microbial genes associated with AMR.

We envision that this approach will revolutionize infectious disease treatments in the future by allowing the development of novel diagnostics and precision therapeutics. The challenges and possible solutions offered here highlight the growing importance of metagenomics in Italy, Europe, and worldwide.

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Abbreviation Used

AMR = antimicrobial resistance