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EDITORIAL

Prospects of Microbial Natural Products and Their Biological Entities in Drug Discovery

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Natural products have been remarkable support for a diverse range of therapeutics, for treating a wide range of diseases with disparate chemical structures and extensive biological properties. These molecules serve as precursors for a wide array of semi-synthetic and synthetic compounds with important therapeutic functions. While a large number of biologics and natural products and their pharmacological properties are recognized, new insights and advances remain to be revealed. Chemical entities from natural microbial products remain relevant to the prospective drug discovery scheme, with a more urgent need for new drugs with anticancer, immunosuppressant and antibacterial effects, coupled with other pharmacological and biotechnological applications. An estimation of 77% of antimicrobial drugs approved by the FDA since 2000 is sourced from products of microbial natural origin.[1] There have been in-depth reviews of products approved by the FDA (natural, nature-inspired, and semi-synthetic products) which portray the sustained significance of natural products for health and medicine.[2] Biologics of microbial origin are projected to maintain their importance in the international market from 277 billion as of 2015 to 400 billion USD by 2025.[3] Many novel drug candidates with therapeutic potentials from natural compounds are isolated in low amounts and resource intensive, making the drug development and discovery process a burdensome one. There exist an assembly of drawbacks of microbial biologics and natural products which comprise challenges in structural identification or product isolation. An increase in microbial products from the microbial cell can result in overall stress culminating in cell growth reduction. In addition, biologically inactive proteins and misfolded formation can reduce recombinant protein yield. Frequently expressed in inclusion bodies include multi-domain, membrane, and high-molecular-weight proteins.[4] Likewise, there is considerable development as it relates to recombinant protein expression in microbial space. The combination of methods could result in improvements in natural microbial products (such as ribosome engineering and gene shuffling) to increase and improve the production of secondary metabolites. The addition of omics information such as metabolomics has significant potential in a novel drug discovery scheme, to accurately quantify metabolic pathways and biochemical changes. Advances in metagenomics have provided better resourcefulness for complex and diverse microbial producing-product sources such as lakes, rivers, and marine environs.[5] Extensive diversity of engineering schemes can be applied with genome editing, recombinant DNA techniques, overexpression of structural genes, precursor engineering, ribosome engineering and mutagenesis facilitating the resourceful production of pharmaceuticals and natural products in microbial systems. Hence, an evolving alternate resolution is to reveal biosynthetic determinants from primary producers of microbial origin, particularly fungi and bacteria (which function as the hosts).[6] Microbes that are engineered can form significant proportions of uncommon natural metabolites, thus expediting the target potent derivatives and novel compounds synthesis, coupled with the confirmation of their potentiality.[7] To expand our understanding of microbial natural products' efficacy and exploration of their applicability where microbiologically-derived bioactive metabolite and their analogues could strengthen the improvement of novel medicinal agents in industry and academia, research should be focused on current technologies such as Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR associated protein (CRISPR/Cas), which is a technique for editing genome to enable further improvement and enhance production.[8] The mining of the genome is an alternative technique to discovering secondary bioactive metabolites, which is carried out via information extraction from genomic sequences.[9] Bioinformatics methods can predict trends in microbial strains that produce molecules with new chemical structures that may have new mechanisms of action that inhibit bacterial growth.[10] Cryo-electron microscopy and X-ray crystallography are innovative procedures that aid the solving of structures with precision for structural characterization. Cryo-electron microscopy has found applications in assessing macromolecular structures at a resolution close to an atom.[11] These methods represent a subset of other techniques that should be well-thought-out for studying structures on novel bioactive product synthesis. Sequencing initiatives for natural product discovery should be focused on samples with the potential to produce novel bioactive products in combination with properly characterized strains (actinomycetes), as they are still yet to be fully exhausted. However, there is still an urgent need to discover more secondary metabolites for medicinal use. Investigation of microbial natural products from the natural source must remain as a result of unmet necessities. Opportunities accessible to us by natural products cannot be overlooked. Recent advanced technologies can be used to further improve natural microbial metabolites, which maintains a persistent means in the discovery of drugs from novel compounds.

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