生物活性に着目した天然化合物の探索

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天然化合物はその多様な構造や生物活性から今でも医薬品のソースとして重要である。しかし、複雑な混合物からの新しい生物活性物質の探索は非常に困難である。一方、近年機器分析、特に LC/MS を用いた構造プロファイリングによる新規化合物の探索方法などが多く利用されている。しかし、これらの方法は構造の新規性を中心に探索する方法であり、求められている化合物は生物活性を有するものである。本論文では、従来の構造情報に着目した方法をもとに生物活性情報を組み合わせることで、優位に新規活性化合物の探索を行う方法を検討している。我々の化合物探索にも参考になる点が多いと考え紹介することとした。

紹介論文

Bioactive Natural Products Prioritization Using Massive Multi-informational Molecular Networks
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要旨

Natural products represent an inexhaustible source of novel therapeutic agents. Their complex and constrained three-dimensional structures endow these molecules with exceptional biological properties, thereby giving them a major role in drug discovery programs. However, the search for new bioactive metabolites is hampered by the chemical complexity of the biological matrices in which they are found. The purification of single constituents from such matrices require such a significant amount of work that it should be ideally performed only on molecules of high potential value (i.e., chemical novelty and biological activity). Recent bioinformatics approaches based on mass spectrometry metabolite profiling methods are beginning to address the complex task of compound identification within complex mixtures. However, in parallel to these developments, methods providing information on the bioactivity potential of natural products prior to their isolation are still lacking and are of key interest to target the isolation of valuable natural products only. In the present investigation, we propose an integrated analysis strategy for bioactive natural products prioritization. Our approach uses massive molecular networks embedding various informational layers (bioactivity and taxonomical data) to highlight potentially bioactive scaffolds within the chemical diversity of crude extracts collections. Combined with efficient metabolite annotation tools, this bioactive natural products prioritization pipeline proves to be efficient. Implementation of this approach in drug discovery programs based on natural extract screening should speed up and rationalize the isolation of bioactive natural products.