Efficient Synthetic Study of Bioactive Microbial Natural Products for New Drug Discovery

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Bioactive natural products produced by microbes have almost limitless potential in pharmaceutical applications. The identification and subsequent organic synthesis of such products, to generate lead compounds for research and development, will result in the creation of new, highly-practical and widely-used pharmaceutical products. With a focus on the drug discovery process, The Kitasato Institute (KI) is using cutting-edge, unique screening techniques to discover useful bioactive natural products from microbial metabolite origins. These novel products tend to have distinctive structures and attractive bioactivities.

The key challenge in synthetic organic chemistry remains how to more efficiently synthesize target compounds with unique molecular skeletons using short process pathways. The construction of novel molecular skeletons necessitates the development of new synthetic strategies and key reactions, which, in turn, will expedite progress in synthetic organic chemistry, as well as hastening the development of new drugs.

To date, we have succeeded total synthesis of 28 types of bioactive natural products. Our research program also involves the application of established methods to synthesize related compounds, elucidation of their structure-activity relationships and the possible creation of improved bioactive compounds. In this lecture, efficient total synthesis of naturally-occurring bioactive microbial metabolites, in order to create novel medicines for specific illnesses, is described. This covers diseases and conditions such as atherosclerosis, Alzheimer's, cancer, inflammation, and osteoporosis, etc. and focuses on several specific compounds: pyripyropenes (cholesterol lowering agents), arisugacins (acetylcholinesterase inhibitors), lactacystin (proteasome inhibitor), macrosphelides (cell-cell adhesion inhibitors), madindolines (IL-6 modulators), neoxaline (cell proliferation inhibitor), and argifin (chitinase inhibitor), so on.