AL07 Chemical Studies on Bioactive Natural Products Directed toward Development of Novel Anti-Infective and Anticancer Medicines

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Recent achievements of chemical studies on biologically active natural products discovered mainly by research groups at the Institute of Microbial Chemistry (BIKAKEN) will be discussed.

Caprazamycin B (**1**) was discovered as a natural anti-tuberculosis product, and semi-synthetically developed as CPZEN-45 (**2**), which is effective against extremely drug-resistant strains (XDR-TB).

Kawada and co-workers at BIKAKEN identified leucinostatin A (**4**) as a selective inhibitor of the proliferation of tumor cells co-cultured in the presence of the corresponding stromal cells (normal cells such as fibroblasts with close proximity to tumor cells in tumor tissues) but not in their absence; this class of compounds is expected to affect growth signals emitted from the stromal cells (tumor-stroma interactions).

Suenaga and co-workers at Keio University found that leptolyngbyolide C (**5**), a cytotoxic macrolide produced by cyanobacterium collected in Okinawa, depolymerizes actin. The synthetic routes to these natural products as well as caprazol (**2**), a core structure of caprazamycin B which itself is a natural product, were established by applying catalytic asymmetric processes developed by Shibasaki and co-workers to install the requisite stereochemistries. In the course of synthetic studies of these natural products, the reported stereochemistry of leucinostatin A was revised and the absolute configuration of leptolyngbyolide C was unequivocally determined.

Intervenolin (**6**) was also discovered as a modulator of tumor-stroma interactions by Kawada and co-workers, for which the synthetic scheme was elaborated to enable structure-activity relationship studies to generate lead compounds for clinical medicines.