S40-2 Search for anti-tuberculosis agent based on enviroment of infected region and identification of its target molecule

◯Masayoshi ARAI[1], Motomasa KOBAYASHI[1]

[1]Graduate School of Pharmaceutical Sciences, Osaka Univerisity

Tuberculosis, caused by *Mycobacterium tuberculosis* infection, is an infectious disease that is responsible for the deaths of around two million people a year. Aggravation of tuberculosis is evaded by host immune systems, even if infection is concluded completely. However, a small population of bacilli change their phenotype into non-replicating persistent (NRP) state in the granuloma formed by immune cells. Then, bacilli keep their ability to resume growth and aggravate disease as a result of deterioration of immune-system. This unique property also relates to resistance against conventional anti-tuberculosis drugs such as isoniazid. To explore new leads of anti-*mycobacterial* agents, which are effective to both active and NRP states, and novel target for drugs from based on the analysis of action-mechanism of anti-microbial compounds, we established a screening system in hypoxic condition inducing NRP state, and then executed screening from the extract library of marine organisms. As a result, a marine spongean cyclic alkalod, halicyclamine A, and nybomycin from a marine derived *Streptomyces* sp. were re-discovered as leads for anti-microbial agents, which are effective to both active and NRP states of tuberculosis. Analyses of target molecules for these compounds using genomic DNA library from *M. bovis* BCG origin are under way.