１．Title of Research and Development： Searching Lead Compounds of Anti-malarial and Anti-amebic Agents by Utilizing Diversity of Indonesian Bio-resources

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４．Results of Research and Development:

Achievement of the research and development

General objectives for this research initiative include the following.

1. By utilization of the microbial resources in Indonesia, we carry out screening of microbial culture extracts, and purification and structure determination of active compounds that selectively inhibit enzymes from malaria and entamoeba parasites. More than one lead compounds that show therapeutic effect against both protozoan diseases in the animal models are to be identified.

2. Similar screening for the lead compounds are to be done with inhibition of growth and proliferation as a hallmark. More than one lead compounds that show therapeutic effects in the animal models for both diseases are to be identified.

3. We also achieve the maintenance and application of the microbial resource libraries in Indonesia. Moreover, we aim for the establishment of intellectual and technical foundation which is indispensable for future drug discovery research in Indonesia, such as technology transfer of techniques for identification, purification, and structural elucidation of active compounds, evaluation of efficacy on animal models, and an establishment of a drug development consortium.

Specific activities in the year are as follows.

As the on-site screening has not been on schedule, technical trainings were done in Japan by inviting researchers from Biotech Center, BPPT (herein after BPPT) and Airlangga University (herein after called AU). In total, 12 researchers from BPPT and AU were invited to the University of Tsukuba (or National Institute of Infectious Diseases), Kitasato University and University of Tokyo for 1 to 2 months. Training was repeatedly provided to standardize production and purification of recombinant enzymes for screening, enzyme-based and cell-based screening protocols, and cultivation of cells. In addition, training for structural analysis based on NMR and mass spectrometric analysis was conducted. Repeated trainings for the same trainees are essential for securing the results with high credibility in the future and additional trainings for the same researchers are necessary in future.

As a dispatch of the specialists, a total of 11 experts were dispatched for 3 to 41 days for on-site trainings. From January 2016, an expert on malaria biochemistry was dispatched for 40 days, and implemented on-site enzyme-based screenings. Unfortunately installation of new equipment was delayed and it was not used for the training; however, technical transfer was adequately completed. To improve the quality of microbial libraries and increase the number of biological resources in the inventory for screening, new microbes need to be acquired. Experts on fungi and actinomycetes were dispatched for 2 to 3 weeks for training. During such training, 560 new microbes were collected and isolated. Moreover, 1700 microbial organisms that were frozen at BPPT were revived and cultivated and 1300 specimens were confirmed to have survived storage. Among them, 800 specimens were given to the actual screenings in Indonesia. Furthermore, at the trainings in Japan, 6500 previously collected extracts were evaluated by the malaria enzyme-based screening and 320 specimens were examined in the malaria cell-based screening. In addition, 5200 specimens were subjected to the Entameba enzyme-based screening and 320 specimens to the cell-based screeningto yield 13 and 4, respectively, extracts showing potent enzyme or growth inhibition. Finally, 3 compounds that showed inhibitory activity against the malarial enzyme (DHOD) were successfully purified, and 2 of the three compounds were structurally elucidated.

Some initial plans needed to be modified in this year due to a delay in the introduction of equipment to Indonesi. However, majority of plans were practically completed as scheduled by remedial measures and progresses exceeding the initial goal were achieved.